e-ISSN: 3023-6738

Eurasian Journal of

Anesthesiology & Intensive Care

Volume: 1 Issue: 3 Year: 2024

EAJAIC

Eurasian Journal of
Anesthesiology & Intensive Care

Editorial Board

EDITOR-IN-CHIEF

ASSOCIATE EDITORS-IN-CHIEF

EDITORS

EDITORIAL BOARD

Eurasian Journal of
Anesthesiology & Intensive Care

Editorial Board

ENGLISH LANGUAGE EDITOR

STATISTICS EDITOR

Eurasian Journal of
Anesthesiology & Intensive Care

Contents

Volume: 1 Issue: 3 Year: 2024

ORIGINAL ARTICLES

CASE REPORT

MHA MEDIHEALTH ACADEMY

Eurasian Journal of
Anesthesiology & Intensive Care

Original Article

doi
10.51271/EAJAIC-0011

Comparison between patient-controlled tramadol infusion and additional thoracic paravertebral block in the management of post-thoracotomy pain; a retrospective study

Mustafa Cenk Çetin[1], Mehtap Tunç[1], Hilal Sazak[1], Onur Küçük[1], Musa Zengin[2], Ramazan Baldemir[1] Ali Alagöz[1]

[1]Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Turkiye
[2]Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Turkiye

Received: 15/05/2024 ◆ **Accepted**: 11/06/2024 ◆ **Published**: 06/08/2024

Cite this article: Çetin MC, Tunç M, Sazak H, et al. Comparison between patient-controlled tramadol infusion and additional thoracic paravertebral block in the management of post-thoracotomy pain; a retrospective study. *Eurasian J Anesthesiol Intens Care* . 2024;1(3):47-52.

Corresponding Author: Ali Alagöz, mdalagoz@gmail.com

ABSTRACT

Aims: Thoracic paravertebral block (TPVB) is provides effective analgesia in patients undergoing thoracotomy. In this study, we aimed to compare the level of analgesia, hemodynamic parameters, and analgesic consumption in post-thoracotomy patients who received iv patient-controlled analgesia (PCA) with the patients who received TPVB plus iv PCA.

Methods: We retrospectively evaluated the pain and anesthesia forms of 100 patients. Patients were divided into two groups according to analgesia methods. All patients were given 100 mg iv tramadol 30 minutes before the end of the operation. Intravenous tramadol infusion by using PCA was applied in both groups for postoperative 24 hours. In Group II, 5 levels of TPVB was performed just before the end of the operation. Additional analgesic (paracetamol 1 g infusion) was given when visual analog scale (VAS) was≥4. Demographic data of patients and analgesia methods of patients were recorded. Hemodynamic parameters, peripheral oxygen saturation, respiratory rate, sedation scores, resting and coughing VAS score, additional analgesic requirement, side effects and complications, amounts of consumed analgesics, and analgesia-related satisfaction scores were recorded preoperatively, before PCA, and 1, 6, 12, and 24. hours postoperatively to use patients' pain forms.

Results: Hemodynamic parameters were comparable between groups ($p > 0.05$). Resting and coughing VAS scores were significantly lower in the TPVB group ($p < 0.05$). The additional analgesic requirement was also lower in Group II ($p<0.05$). Cumulative tramadol conpsumption was significantly lower in Group II ($p <0.05$).

Conclusion: TPVB combined with iv tramadol PCA provided effective analgesia, and it decreased cumulative tramadol use in thoracotomy patients.

Keywords: Thoracotomy, thoracic paravertebral block, tramadol, visual analog scale.

INTRODUCTION

Post-thoracotomy pain is one of the most severe postoperative pains, is constantly stimulated by respiratory movements, and the first 4-6 hours postoperatively is the period with the highest analgesic requirement. Complications resulting from this pain include an inability to cough due to decreased respiratory movements, an inability to expel bronchial secretions, atelectasis, pneumonia, bronchitis, hypoxemia, respiratory failure, and prolonged mechanical ventilation.[1-3]

The administration of analgesics following a thoracotomy can effectively reduce the incidence of postoperative complications. The pharmacological and non-pharmacological methods employed to relieve pain following thoracotomy encompass a range of agents and techniques. These include systemic opioids, non-steroidal anti-inflammatory drugs (NSAIDs), systemic analgesia therapy, including ketamine, and regional techniques such as intercostal, paravertebral, intrapleural and epidural blocks.[1,4] To minimize the potential for complications and provide adequate analgesia, a combination of both drugs and techniques, rather than a single method, is more effective in patients undergoing thoracotomy.[4]

In recent years, post-thoracotomy pain has been successfully prevented with the use of a thoracic paravertebral block (TPVB). A review of the literature reveals that TPVB applications result in effective analgesia with a lower complication rate than that observed with thoracic epidural

applications.[4] The paravertebral nerves in the surgical area are the sole nerves blocked in a TPVB application, which results in a lower incidence of hypotension and bradycardia than in a thoracic epidural block.[4-7]

The hypothesis in this study is adding TPVB for postoperative analgesia in patients undergoing thoracotomy may positively affect postoperative analgesia and perioperative parameters. This retrospective study aimed to assess the analgesic efficacy, hemodynamic parameters, analgesic consumption, adverse effects and complications in patients who received a thoracic paravertebral injection in addition to intravenous patient-controlled analgesia (PCA) following a thoracotomy.

METHODS

The study was carried out with the permission of the Keçiören Training and Clinical Researches Ethics Committee (Date: 28.11.2012, Decision No: B.10.4.İSM.4.06.68.49). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Following the granting of, a retrospective analysis was conducted on the standard pain monitoring forms used in the postoperative analgesia practices of 100 patients who underwent thoracotomy between 2009 and 2012. Patients with incomplete or incorrectly recorded data were excluded from the study.

Interventions

Before undergoing surgery, patients were informed about TPVB, which is a method used to treat postoperative pain. They were also informed about the use of the PCA device and their consent was obtained. The Visual Analogue Scale (VAS) method was employed to assess pain intensity, with patients being provided with a detailed explanation of the method. Upon examination of the pain follow-up forms, the patients were divided into two groups, designated Group I and Group II, according to the postoperative analgesia methods applied. Patients were selected from those who underwent the same anesthesia method. The amounts of fentanyl used for induction and maintenance of anesthesia were recorded from the intraoperative anesthesia forms.

For postoperative analgesia, 100 mg of tramadol (Contramal ampul® 100 mg/2 ml, Abdi İbrahim, Turkiye) was administered via intravenous slow infusion 30 minutes prior to the patient's awakening after surgery. Once the patients had been discharged from the operating room and admitted to the surgical intensive care unit, intravenous PCA (Abbott Laboratories, North Chicago, IL, USA) was administered for 24 hours following the operation. A solution containing 5 mg of tramadol in 1 ml was prepared for intravenous PCA. The device was programmed as a 10 mg/hour infusion, a 20 mg bolus, a half-hour locked time, and a 4-hour limit of 120 mg. The same intravenous PCA analgesia protocol was applied to both groups. Patients in Group II underwent TPVB after the surgical procedure, immediately preceding the termination of anesthesia, with the patient positioned in the lateral decubitus position.

The TPVB application was initiated at the caudal and cephalad incision lines of the thoracotomy incision, with two levels each including the thoracic vertebral segment, resulting in a total of five levels. The spinous processes of the vertebrae were identified and a point 2.5 cm lateral to the spinous process on the thoracotomy side was marked as the injection point. A 22-gauge spinal needle (Exelint®, California, USA) was inserted at the designated point and the transverse process was palpated. The needle was then withdrawn and advanced just above the transverse process in a cephalic direction for a maximum of 2 cm. 4 ml of bupivacaine hydrochloride (Marcaine vial® 0.5% 20ml, Astra Zeneca, Turkey) was administered for each level.

During the follow-up of patients in the intensive care unit, 1 gram of paracetamol (Perfalgan 100ml vial® 10mg/ml Bristol-Myers Squibb Inc.) was administered via intravenous infusion as an additional analgesic when the VAS score was 4 or higher. Any adverse effects or complications that arose during this period were duly recorded.

The postoperative pain follow-up forms were examined, and the following variables were recorded: gender, age, diagnosis, body mass index (BMI), surgical method, ASA score, and postoperative analgesia methods. The follow-up data included systolic arterial pressure (SBP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO2), respiratory rate (RR), resting and cough VAS scores, the need for additional analgesics, side effects and complications related to analgesia, the number of analgesics consumed and ramsay sedation scores. The data above were recorded at a total of six time points: preoperatively, before the commencement of PCA, and at 1, 6, 12 and 24 hours postoperatively. Furthermore, analgesic method satisfaction scores were recorded after 24-hour (0=poor, 1=moderate, 2=good, 3=very good, 4=excellent).

Outcomes

The primary outcome of the study was the intensive care unit discharge VAS scores in patients who underwent thoracotomy with and without thoracic paravertebral injection in addition to intravenous PCA for postoperative pain control. The other outcomes of our study were hemodynamic parameter measurements, total tramadol consumption, need for additional analgesia and incidence of side effects in the first 24 hours postoperatively in patients with and without thoracic paravertebral injection.

Statistical Analysis

The data was analyzed using the Statistical Package for Social Science (SPSS) for Windows 11.5 package program. Descriptive statistics were expressed as mean±standard deviation or median (minimum-maximum) for continuous variables and as number of cases (n) and (%) for nominal variables. The significance of the difference between the groups in terms of means was investigated using a Student's t-test, while the significance of the difference in terms of median values was investigated through a mann-whitney U test. Nominal variables were analyzed using pearson's chi-Square, fisher's chi-square with fisher's exact test or likelihood ratio test. A repeated-measures analysis of variance was employed to assess the hemodynamic measurements. The percentage changes between follow-up times, which were considered clinically important, were calculated and comparisons were made between the groups.

The friedman test was employed to ascertain whether there was a statistically significant change in VAS and sedation scores according to time within the groups. If the result of the friedman test statistic was found to be significant, the Wilcoxon signed-rank test with Bonferroni correction was employed to ascertain the follow-up times that were responsible for the observed difference. The results were considered statistically significant if the p-value was less than 0.05.

RESULTS

There was no statistically significant difference between the groups in terms of age, gender, body weight, height, body mass index, and ASA assessment (p > 0.05), as shown in Table 1.

Table 1. Demographic and clinical characteristics of groups

Parameters		Group I (n:50) (mean ± SD)	Group II (n:50) (mean ± SD)	p
Age (year)		50.6 ± 14.8	50.9 ± 15.7	0.922
Gender	Male (%)	30 (60.0)	38 (76.0)	0.086
	Female (%)	20 (40.0)	12 (24.0)	
BMI (kg/m²)		24.9 ± 4.6	26.5 ± 5.1	0.092
ASA I/II/III		1 / 21 / 28	0 / 31 / 19	0.080

Demographic data are given as mean ± SD or %.
ASA: American Society of Anesthesiologists, BMI: Body mass index, SD: Standard devision

The change in SAB over time was statistically similar between the groups (F=0.379 and p=0.812). In Group I, the only statistically significant change in SAB was the decrease observed between pre-PCA and 24 hours (p=0.023). In group II, there was no statistically significant difference in mean SAB between the follow-up times (p=0.198). The change in DAB over time was statistically similar between the groups (F=0.623 and p=0.664). In group I, there was no statistically significant difference in DAB between the follow-up times (p=0.115). In group II, the only statistically significant change in DAB was the decrease observed between the preoperative and first-hour time points (p=0.004).

There was no statistically significant difference in MAP between the groups (F=0.254 and p=0.900). There was no statistically significant difference in MAP between the follow-up times in both Group I and Group II (p=0.433 and p= 0.713), as shown in Table 2.

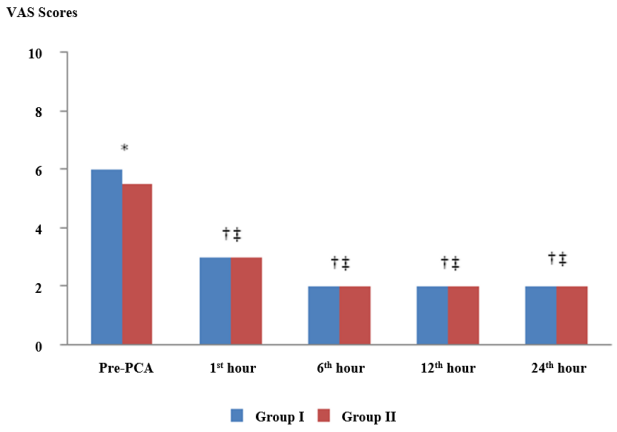
Table 2. Mean arterial pressure (map) levels according to monitoring times

Times	Group I (n:50) (mean ± SD)	Group II (n:50) (mean ± SD)	p[a]
Preoperative	91.5 ± 9.7	91.6 ± 8.2	0.938
Pre-PCA	92.5 ± 16.6	90.4 ± 15.1	0.506
1st hour	89.7 ± 11.2	88.8 ± 11.2	0.669
6th hour	91.2 ± 11.5	90.0 ± 13.2	0.623
12th hour	91.0 ± 11.0	89.4 ± 13.5	0.527
24th hour	89.3 ± 8.5	89.7 ± 10.8	0.814

a: Results were considered statistically significant for p < 0.0083 according to Bonferroni Correction. PCA: patient-controlled analgesia

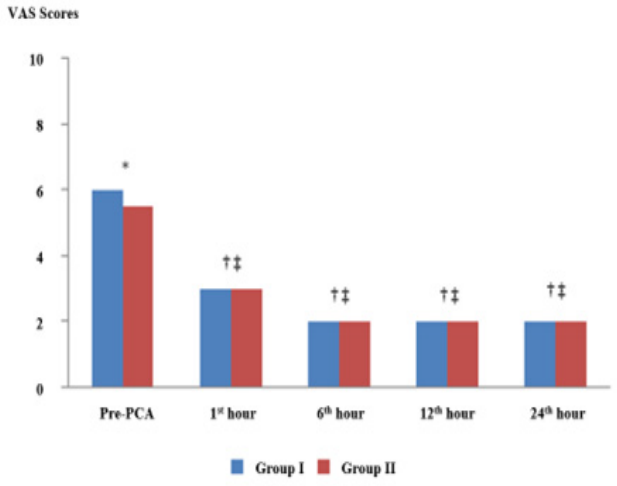
In Group I, there was a statistically significant increase in HR at 12 hours compared to all follow-up times (p<0.025). In Group II, the HR values at pre-operative and before PCA were statistically lower (p<0.001). In the context of intergroup comparison, it was observed that the HR in the pre-operative period was significantly higher in Group I (p=0.008).

There was no statistically significant difference in SpO_2 between the groups (p>0.05). The SpO_2 values were found to be statistically lower than the preoperative values at all times (p<0.01). A statistically significant decrease was observed in the resting VAS values in Group I and Group II when the data from the pre-PCA and all follow-up times were compared (p<0.001). In the intergroup comparison, resting VAS values in Group II were found to be statistically significantly lower before PCA (p =0.001) (Figure 1).



*: The difference between groups is statistically significant (p = 0.001).
†: In Group I, the difference between pre-PCA and other follow-up times was statistically significant (p < 0.001).
‡: In Group II, the difference between pre-PCA and other follow-up times was statistically significant (p < 0.001).
Figure 1. Resting visual analog scale (VAS) levels according to monitoring times.

A statistically significant decrease in cough VAS values was observed in both Group I and Group II at all other follow-up times in comparison to the pre-PCA values (p<0.001). In the intergroup comparison, cough VAS values before PCA were found to be statistically significantly lower in Group II (p< 0.002), as illustrated in Figure 2.



*: The difference between groups is statistically significant (p = 0.002).
†: In Group I, the difference between pre-PCA and other follow-up times was statistically significant (p < 0.001).
‡: In Group II, the difference between pre-PCA and other follow-up times was statistically significant (p < 0.001).
Figure 2. Coughing visual analog scale (VAS) levels according to monitoring times.

A comparison of sedation levels within Group I revealed a statistically significant reduction at all subsequent follow-up times in comparison to the baseline measurement prior to PCA (p<0.001). There was no statistically significant difference between the other follow-up times in terms of sedation levels (p > 0.025). In Group II, the lower sedation levels observed at other follow-up times in comparison to the pre-PCA period were found to be statistically significant (p<0.001). There was no statistically significant difference between the other follow-up times in terms of sedation levels (p>0.025).A comparison of the groups in terms of the need for additional analgesics revealed a statistically significant reduction in this need in Group II (p<0.05) (Table 3).

Table 3. Rates of additional analgesic requirement

Times	Group I (n:50) n (%)	Group II (n:50) n (%)	p
Pre-PCA	50 (%100.0)	37 (%74.0)	<0.001
1st hour	1 (%2.0)	4 (%8.0)	0.362
6th hour	1 (%2.0)	-	1.000
12th hour	-	-	-
24th hour	-	-	-

p<0.05 statistically significant. PCA: patient-controlled analgesia

In terms of analgesic method satisfaction, three patients in Group I indicated moderate satisfaction, 37 patients indicated high satisfaction, and 10 patients indicated very high satisfaction. In Group II, three patients were moderately satisfied, 30 were well satisfied, and 17 were very well satisfied with the analgesia method. Although the overall satisfaction rate was higher in Group II, there was no statistically significant difference between the groups (p=0.277).

Although there was no statistically significant difference between the groups in terms of total tramadol consumption at I and 6 hours, total tramadol consumption at 12 and 24 hours was found to be statistically significantly lower in Group II compared to Group I (p=0.040 and p=0.006) (Table 4).

Table 4. Total amounts of tramadol (mg) consumed

Times	Group I (n:50) (mean ± SD)	Group II (n:50) (mean ± SD)	p
1st hour	51.7 ± 10.3	48.7 ± 10.9	0.162
6th hour	183.5 ± 70.9	158.9 ± 59.3	0.063
12th hour	308.6 ± 80.1	271.2 ± 98.7	0.040
24th hour	502.9 ± 70.4	443.8 ± 128.1	0.006

p < 0.05 statistically significant, SD:Standard Deviation, n: Number

DISCUSSION

In this retrospective study, hemodynamic parameters were found to be similar in both groups. VAS scores at admission to intensive care were found to be statistically significantly lower in the TPVB group. Additionally, the need for additional analgesics was found to be less in this group. It was observed that the TPVB application also reduced 24-hour cumulative tramadol use.

TPVB is a regional blockade method that is becoming increasingly popular due to its ease of application and similar results to thoracic epidural analgesia. The sympathetic blockade is less observed in TPVB application compared to thoracic epidural analgesia. TPVB can also be applied with multiple injection or catheter techniques.[8-11] Although there are studies on paravertebral catheter application in thoracotomies, studies combining multiple paravertebral injections with iv PCA are limited.[4,12]

LA and opioid administration via thoracic epidural catheter negatively affects hemodynamic parameters due to the blocking of sympathetic cardiac fibers. This situation may also occur during iv PCA administration due to the systemic effects of iv opioids. Studies indicate that sympathetic blockade is less after TPVB and that complications that may develop due to this can be limited.[4] In a study comparing TPVB with thoracic epidural analgesia, Richardson et al.[5] found lower pain scores and less morphine consumption in the thoracic paravertebral group. They also reported that pulmonary functions were better preserved in the TPVB group and nausea-vomiting and hypotension were more common in the epidural group. In our study, no difference was detected in hemodynamic parameters in the iv PCA group (Group I) and the TPVB+iv PCA group (Group II), and no hemodynamic complications occurred due to analgesic treatment. We think that the lower 24-hour iv analgesic consumption in the TPVB group will also reduce the complications that may develop due to iv opioid use.

After thoracic surgery, respiratory functions may deteriorate due to inadequate pain treatment. Additionally, the risk of respiratory depression with excessive opioid use makes pain treatment difficult. Therefore, a situation that requires multimodal analgesia arises.[13] In multimodal analgesia, different analgesia combinations can be used in combination with central and peripheral blocks.[14] Tramadol is an agent with weak opioid effects and limited respiratory depressant effects. It is widely used in postoperative analgesia.[15-17] Considering the negative effects that may occur on respiratory functions after thoracotomy, iv PCA application with tramadol is also used as a component of multimodal analgesia in our clinic. Although SpO_2 values in the postoperative period were found to be statistically lower than in the preoperative period, no situation requiring treatment was encountered.

Although thoracic epidural analgesia is considered the gold standard in the treatment of post-thoracotomy pain, in recent years it has been advocated that TPVB application may be an alternative to thoracic epidural block.[18,19] It has been shown that opioid+LA or LA-only administration with a paravertebral catheter in the treatment of pain after thoracotomy provides effective and safe analgesia, reducing the need for iv opioids and the incidence of side effects.[9] In a study conducted by Hill et al.[20] in which they performed multiple paravertebral injections for the treatment of pain after video-assisted thoracoscopic surgery, they observed a significant decrease in VAS scores and a significant decrease in morphine consumption in the first 6 hours. Kaya et al.[21] found a significant decrease in VAS scores and cumulative morphine consumption in patients who underwent video-assisted thoracoscopic surgery, in their 24-hour postoperative follow-up after multiple TPVB. In the present study, it was observed that in the TPVB+iv PCA group, both resting and cough VAS scores were lower and there was a significant

decrease in 24-hour tramadol consumption in the pre-PCA period. The need for additional analgesics in the group in which TPVB was not performed in the pre-PCA period (Group I) was found to be statistically higher than in the group in which TPVB was performed (Group II). In our study, we observed that since severe pain occurred after thoracotomy, a decrease in VAS scores could not be achieved in the early period, and accordingly, the need for additional analgesics was higher in this period. In the group that received only iv PCA, VAS levels were high before PCA despite 100 mg tramadol administered at the end of surgery. More additional analgesics were required to achieve acceptable VAS scores in this group. While VAS levels were 5 and above in all patients in this group before PCA, VAS resting scores were between 0 and 4 in 12 patients in the TPVB+iv PCA group (Group II).

Kotze et al.,[22] in a study they conducted on TPVB, stated that studies on complications developing after TPVB application are limited. They concluded that most studies focused on complications specifically on LA toxicity. In most of these studies, bupivacaine was used as LA. In our study, no LA toxicity or method-related complications were encountered in any of the patients after TPVB.

Limitations

There are some limitations in this study. First of all, the study is single-center and retrospective. Secondly, we could only access 24-hour follow-up in patient records. There was a lack of data for the 48th and 72nd hours after surgery in terms of long-term analgesic effectiveness. Finally, the chronic pain conditions of the patients could not be accessed from the records.

CONCLUSION

As a result, we think that multiple TPVB applications in the acute postoperative period in thoracotomy, when combined with iv PCA applied with tramadol, provide effective analgesia without causing any complications in hemodynamic and respiratory parameters.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Keçiören Training and Research Hospital Clinical Researches Ethics Committee (Date: 28.11.2012, Decision No: B.10.4.İSM.4.06.68.49).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Senturk M. Acute and chronic pain after thoracotomies. *Curr Opin Anaesthesiol*. 2005;18(1):1-4.
2. Zengin M, Ülger G, Baldemir R, Sazak H, Alagoz A. Is there a relationship between body mass index and postoperative pain scores in thoracotomy patients with thoracic epidural analgesia? *Medicine*. 2021;100(50):28010.
3. Zengin M, Alagoz A. Comparison of thoracic epidural analgesia and thoracic paravertebral block applications in the treatment of acute pain after thoracotomy in geriatric patients. *Cureus*. 2021;13(10):18982. doi: 10.7759/cureus.18982
4. Dhole S, Mehta Y, Saxena H, Juneja R, Trehan N. Comparison of continuous thoracic epidural and paravertebral blocks for postoperative analgesia after minimally invasive direct coronary artery bypass surgery. *J Cardiothorac Vasc Anesth*. 2001;15(3):288-292.
5. Richardson J, Sabanathan S, Jones J, et al. A prospective, randomized comparison of preoperative and continuous balanced epidural or paravertebral bupivacaine on post-thoracotomy pain, pulmonary function and stress responses. *Br J Anaesth*. 1999;83(3):387-392. doi: 10.1093/bja/83.3.387
6. Zengin EN, Alagöz A, Yiğit H, et al. The effect of body mass index on thoracic paravertebral block analgesia after video-assisted thoracoscopic surgery; a prospective interventional study. *BMC Anesthesiol*. 2023;23(1):297. doi: 10.1186/s12871-023-02264-0
7. Zengin M, Alagöz A, Sazak H, et al. Comparison of efficacy of erector spinae plane block, thoracic paravertebral block, and erector spinae plane block and thoracic paravertebral block combination for acute pain after video-assisted thoracoscopic surgery: a randomized controlled study. *Minerva Anestesiol*. 2023;89(3):138-148. doi: 10.23736/S0375-9393.22.16639-3
8. Lönnqvist PA, MacKenzie J, Soni AK, Conacher ID. Paravertebral blockade. Failure rate and complications. *Anaesthesia*. 1995;50(9):813-815. doi: 10.1111/j.1365-2044.1995.tb06148.x
9. Karmakar MK. Thoracic paravertebral block. *Anesthesiology*. 2001;95(3):771-780. doi: 10.1097/00000542-200109000-00033
10. Richardson J, Sabanathan S. Thoracic paravertebral analgesia. *Acta Anaesthesiol Scand*. 1995;39(8):1005-1015. doi: 10.1111/j.1399-6576.1995.tb04219.x
11. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy--a systematic review and meta-analysis of randomized trials. *Br J Anaesth*. 2006;96(4):418-426. doi: 10.1093/bja/ael020. *Br J Anaesth*. 2007;99(5):768.
12. Das S, Bhattacharya P, Mandal MC, et al. Multiple-injection thoracic paravertebral block as an alternative to general anaesthesia for elective breast surgeries: a randomised controlled trial. *Indian J Anaesth*. 2012;56(1):27-33. doi: 10.4103/0019-5049.93340
13. Cuschieri RJ, Morran CG, Howie JC, McArdle CS. Postoperative pain and pulmonary complications: comparison of three analgesic regimens. *Br J Surg*. 1985;72(6):495-498. doi: 10.1002/bjs.1800720631
14. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. *Anesth Analg*. 1993;77(5):1048-1056. doi: 10.1213/00000539-199311000-00030
15. James MF, Heijke SA, Gordon PC. Intravenous tramadol versus epidural morphine for postthoracotomy pain relief: a placebo-controlled double-blind trial. *Anesth Analg*. 1996;83(1):87-91. doi: 10.1097/00000539-199607000-00015
16. Bloch MB, Dyer RA, Heijke SA, James MF. Tramadol infusion for postthoracotomy pain relief: a placebo controlled comparison with epidural morphine. *Anesth Analg*. 2002;94(3):523-528.
17. Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. *Ann Thorac Surg*. 200;75(4):1349-1357. doi: 10.1016/s0003-4975(02)04647-7
18. Savage C, McQuitty C, Wang D, Zwischenberger JB. Postthoracotomy pain management. *Chest Surg Clin N Am*. 2002;12(2):251-263. doi: 10.1016/s1052-3359(02)00011-x
19. Elsayed H, McKevith J, McShane J, Scawn N. Thoracic epidural or paravertebral catheter for analgesia after lung resection: is the outcome different? *J Cardiothorac Vasc Anesth*. 2012;26(1):78-82.
20. Hill SE, Keller RA, Smith SM, et al. Efficacy of single-dose, multilevel paravertebral nerve blockade for analgesia after thoracoscopic procedures. *Anesthesiology*. 2006;104(5):1047-1053.

21. Kaya FN, Turker G, Mogol EB, Bayraktar S. Thoracic paravertebral block for video-assisted thoracoscopic surgery: single injection versus multiple injections. *J Cardiothorac Vasc Anesth*. 2012;26(1):90-94.

22. Kotzé A, Scally A, Howell S. Efficacy and safety of different techniques of paravertebral block for analgesia after thoracotomy: a systematic review and metaregression. *Br J Anaesth*. 2009;103(5):626-636. doi: 10.1093/bja/aep272. PMID: 19837806

MHA MEDIHEALTH ACADEMY

Eurasian Journal of
Anesthesiology & Intensive Care

Original Article

doi
10.51271/EAJAIC-0012

Comparison of the use of remifentanil in infusion and patient-controlled methods for sedation purposes

Oya Kale[1], Jülide Ergil[1], İbrahim Haluk Gümüş[2]

[1]Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Turkiye
[2]Department of Anesthesiology and Reanimation, Dışkapı Yıldırım Beyazıt Traininng and Research Hospital, University of Health Sciences, Ankara, Turkiye

Received: 15/05/2024 ◆ **Accepted**: 11/06/2024 ◆ **Published**: 06/08/2024

Cite this article: Kale O, Ergil J, Gümüş İH. Comparison of the use of remifentanil in infusion and patient-controlled methods for sedation purposes. *Eur J Anesthesiol Intensive Care.* 2024;1(3):53-58.

Corresponding Author: Oya Kale, oyakale@yahoo.com

ABSTRACT

Aims: In this study, remifentanil infusion and patient-controlled bolus use with a patient-controlled analgesia (PCA) device were compared in terms of sedation in patients who underwent spermatic vein ligation under local anesthesia.

Methods: Thirty patient between the ages of 15-45 who were in the ASA I-II group were included in the study. They were randomly divided into 3 groups using the closed envelope method; continuous infusion (Group I), patient-controlled sedation (Group P) and control group (Group C). All patients were premedicated with intravenous (IV) 0.07 mg/kg midazolam. Group I was given 0.1 µg/kg/min remifentanil, Group P was given a patient-controlled 0.5 µg/kg bolus remifentanil via PCA, Group I and Group C were given physiological saline via PCA device. We hypothesized that patient-controlled bolus use would result in less drug consumption than infusion. Primary outcome; was determined as the amount of drug consumption. Secondary outcome; Intraoperative and postoperative side effects and sedation levels. In addition, hemodynamic parameters, anxiety scores, number of PCA applications and patient satisfaction were also recorded. During the operation, 2-3 L/min oxygen was administered via mask to patients whose SpO2 fell below 93%.

Results: Respiratory depression was more common in Group I, but the respiratory rate did not fall below 8 in any group. Intraoperative oxygen was required in 7 patients in Group I and 4 patients in Group P. The total amount of drug consumed was 64.4 µg in Group P and 147.5 µg in Group I. Although there was no difference in the number of PCA requests, 4 patients in Group I, 2 patients in Group P, and 1 patient in Group C never pressed the device. In terms of patient satisfaction, 30% of patients in Group I said it was excellent, while patients in Group C said it was not excellent. The number of patients who evaluated the method as excellent and very good was higher in Group P than in Group I.

Conclusion: Patient-controlled bolus administration of remifentanil provided superior primary outcome with significantly less drug consumption. Secondary outcome were similar. Patient-controlled bolus administration with respiratory monitoring can be used safely.

Keywords: Local anesthesia, patient-controlled sedation, remifentanil, spermatic vein ligation

* This study was presented as an oral presentation at the 7th Balkan Anesthesia Days (30 April - 02 May, 2021).

INTRODUCTION

Spermatic vein ligation can be performed under general, spinal or local anesthesia (LA). The choice of anesthesia technique depends on various factors such as suitability of the procedure for the patient, surgeon's choice, patient acceptance, safety, perioperative pain control, time to return to normal activity, need for monitoring and cost effectiveness. Compared to general anesthesia, local anesthesia has less pain, postoperative analgesic requirement, postoperative nausea and vomiting, and is associated with shorter anesthesia and hospital stay.[1] However, preoperative and intraoperative anxiety is common in all patients undergoing LA. For this reason, sedation is needed in local and regional anesthesia.[2] An ideal sedative agent should have a rapid onset of action, allow control of the duration and level of sedation, and provide rapid recovery and uncomplicated discharge.[3,4] The drugs used may cause significant respiratory depression or delayed recovery in increasing doses. It has been shown that continuous IV infusions of anesthetic and analgesic drugs provide fewer intraoperative side effects, less cardiorespiratory depression and shorter recovery time.[5,6]

Intermittent bolus doses of drugs may cause temporary respiratory and circulatory depression, the patient does not lose cooperation in conscious sedation without suppressing protective reflexes, Complies with commands. As the sedation level increases, loss of cooperation, confusion and hypoxemia may occur.[7]

The primary aim of Monitored Anesthesia Care (MAC) recommended by ASA is the patient's comfort and safety during surgery. It involves the administration of IV drugs to provide sedation, anxiolysis, amnesia and analgesia in minor diagnostic, therapeutic and local-regional anesthetic procedures. Monitoring is the same as that required for general anesthesia (ECG, non-invasive blood pressure measurement, peripheral oxygen saturation and end-tidal CO2 monitoring).[5]

In order to obtain suitable conditions for the anesthetist and surgeon as well as the patient during the operation, IV sedative-hypnotic and analgesic drugs are frequently used as intermittent bolus or infusion. Infusion is administered in two ways: doctor- controlled or patient-controlled.[8]

Patient-controlled sedation (PCS) method using the PCA device, where the patient participates in the treatment, has now also entered practice. It has been shown that the general condition and expectations of patients who participate in treatment with this method are positively affected.[9]

In this study, we compared the short-acting μ-receptor agonist remifentanil with placebo using continuous IV infusion and PCS methods for sedation after midazolam premedication in patients who will undergo spermatic vein ligation under local anesthesia. We aimed to evaluate the amount of medication used, side effects, sedation levels, anxiety scores and patients' satisfaction with the method. In this study, superior primary outcome were obtained and less drug consumption was observed with patient-controlled bolus administration of remifentanil in patients who underwent spermatic vein ligation under local anesthesia. As a secondary outcome, it was observed that intraoperative and postoperative side effects were less and sedation levels were similar with patient-controlled bolus use of remifentanil. With respiratory monitoring, 0.5 μg/kg bolus remifentanil could be administered safely via PCA device.

METHODS

The study was conducted in 2001 as an anesthesiology and reanimation specialty thesis. This study was initiated after institutional approval was obtained. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. In this study, 30 patient from the American Society of Anesthesiologist (ASA) physical status I-II group, aged between 15 and 45, who would undergo spermatic vein ligation under local.

Urology Clinic, were included in the study with their informed consent. Patients with any neurological disorder, renal or hepatic failure, a history of benzodiazepine and opioid use, anesthetic drug intolerance and cooperation difficulties were not included in the study. In patients whose oral intake had been restricted for at least 6 hours in advance, an IV line was opened with a 22G on the back of the hand and physiological saline infusion was started. The PCA device was introduced to the patients and they were told to press the button of the device when needed during the operation.

All cases were given 0.07 mg/kg IV midazolam for premedication. They were random divided into 3 groups according to sedation techniques: continuous infusion (Group I), patient-controlled sedation (Group P) and control group (Group C). All patients were administered local anesthesia with 2% prilocaine hydrochloride by the surgeon. Group I was given 0.1 μg/kg/min remifentanil infusion with a simple syringe-infusion pump system (Pilot A2- Fresenius vial) and saline solution with a locked period of 5 minutes with a PCA (Acute pain manager apm abbott) device. Group P was given remifentanil (ULTIVA TM glaxo wellcome) via PCA at a bolus dose of 0.5 μg/kg. Group C received only PCA and physiological saline. In order to ensure accurate evaluation of the number of requests, physiological saline was administered to the subjects in the control and infusion groups via the PCA device. The patients' heart rate (HR), mean arterial pressure (MAP), SpO2 and respiratory rates were recorded before sedation and every 5 minutes throughout the procedure. Intraoperative and postoperative side effects of remifentanil (MAP <60 mmHg, pulse <60, bradypnea <8, desaturation <93%, nausea, vomiting, itching, tremor, arrhythmia) were examined. At the end of the procedure, the operation time and the total remifentanil doses used were recorded. Anxiety was evaluated with VAS (0 mm-none, 100 mm-very present). Mini mental test was applied to evaluate orientation and adaptation. In this test, which consists of a total of 30 points, a score of 24 or below was considered an indicator of serious cognitive dysfunction.[10]

Cooperation was evaluated with a 5-score test.[11] Sedation level was evaluated with Ramsey sedation score. Two-three points were considered sufficient for conscious sedation.[12] A picture card test was performed intraoperatively to evaluate amnesia.[13] At the end of the operation and 2 hours later, their failure to remember the previously shown picture cards was considered as anterograde amnesia. Patient satisfaction was evaluated with a 5-point verbal scale 2 hours postoperatively (1 excellent, 2 very nice, 3 nice, 4 not bad, 5 bad).[14]

The total button pressing frequency of the subjects during sedation was recorded from the memory information of the device. At the end of the 2nd and 24th postoperative hour, the patients were questioned about their complaints of nausea, vomiting and pain.

Statistical Analysis

'SPSS for Windows version 9.01' program was used for statistical evaluation. Kruskal wallis ANOVA and median test were used where necessary. mann-whitney U test was used to find different groups. chi-square test was used to compare side effects grouped as present or absent. The significance level was accepted as $p<0.05$.

RESULTS

There was no difference between the groups in terms of age, body weight and operation times ($p>0.05$) (Table 1). There was no difference in MAP values between the three

groups. Hypotension and bradycardia were not observed in any case (p>0.05). There was no statistical difference in HR values within and between groups.Desaturation was considered when peripheral O_2 saturation fell below 93%. O_2 was administered continuously to 7 patients in the infusion group, and to 4 patients in the PCS group intermittently via a mask at a rate of 2-3 L/min. Respiratory depression was observed in fewer cases in the PCS group.

Table 1. Demographic data and operation times (Med ± SD)

	Grup I	Grup P	Grup C
Age (year)	25.1±5.46	30.6±8.74	26.5±6.51
Weight (kg)	76.8±9.56	81.2±12.7	69.0 ±15.93
Operation time (min)	27.3±6.11	28.0±6.74	23.3 ± 7.07

Min: Minumum, SD: Standard Devision

As seen in Figure 1 (p<0.01), respiratory rate showed a significant difference in Group I (p<0.05). However, it never fell below the hypoventilation limit of.[8]

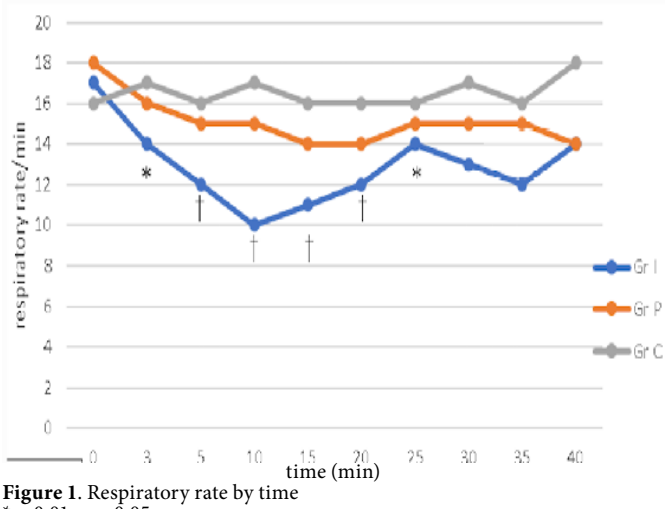


Figure 1. Respiratory rate by time
*p<0.01, +p<0.05

While preoperative and postoperative anxiety levels did not differ between the groups, the postoperative anxiety levels of the patients in all three groups were significantly lower than before surgery (P<0.001) (Table 2).

Table 2. Preoperative and postoperative anxiety levels

	Grup I	Grup P	Grup C
Preoperative anxiety	43.7± 5.19.7	48.5± 28.2	46.8± 31.3
Postoperative anxiety	0.0 ± 0.0*	0.5 ± 0.5*	5.0 ± 12.6*

* p < 0.001

According to the mini-mental test results, which evaluate mental status and orientation, postoperative values were lower than before surgery, but this was not statistically significant (p>0.05). There was no difference between the groups in amnesia evaluation (p>0.05).

Patients who were awake and cooperative throughout the operation did not remember how many times they pressed the PCA button.The total amount of drug consumption was statistically significantly different between the two groups receiving remifentanil. In Group P, it was 147.5±48.37 and 64.4±40.95 (p<0.001) (Figure 2). All patients evaluated with the 5-point cooperation test were cooperative throughout the operation.[4-5] There was no statistical difference between the groups.Sedation scores are shown in Figure 3. Level 2-3 was considered sufficient for conscious sedation. In group I, the deepest sedation was seen in the 20th-30th minutes with a value of 3.5, while in group P the deepest sedation was seen in the 10th-20th minutes with a value of 3. In the Group C the sedation score was always 2. The scores at the 5th, 10t^{h}, 20th and 30th minutes in Group I and the scores at the 10th and 20th minutes in Group P were significantly different compared to Group C (p<0.05). Patients who were cooperative and alert even at the deepest levels of sedation responded fully to verbal stimulation.

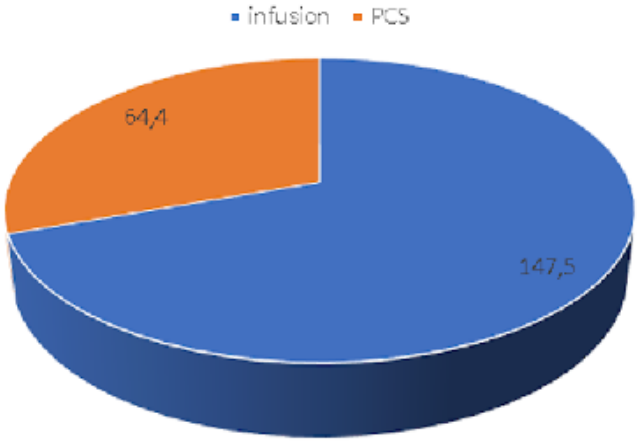


Figure 2. Remifentanil consumption amount(ug)

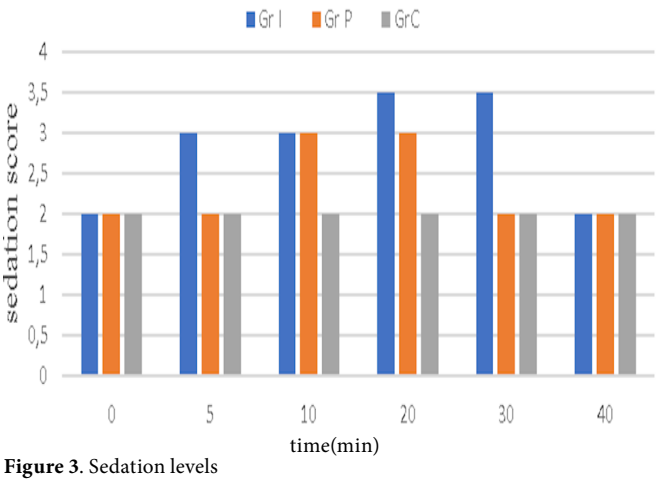


Figure 3. Sedation levels

Patient satisfaction; It can be seen in Table 3. No statistical difference was found between the groups (p>0.05). While 30% of the patients in Group I evaluated the method as excellent, it was not evaluated as excellent in the control group that did not receive remifentanil. The number of patients who evaluated the method as excellent and very good was higher in Group P than Group I. No negative comments were made regarding the method used in any group. In the perioperative period, pain was observed in 2 patients in the infusion and PCS group and in 4 patients in the control group (p>0.05). During this period, the rate of PCA use increased. In this situation, additional local anesthetic was administered.

Table 3. Patients' satisfaction

	Grup I	Grup P	Grup C
Excellent	3	1	-
Very good	2	5	4
Good	5	4	5
Not bad	-	-	1
Bad	-	-	-

The amount of local anesthetic used was similar in all groups. The numbers of medication request are shown in Table 4. It was similar in Group P and Group C, but less in Group I. It was not significant (p>0.05). Four patient in Group I, 2 patients in Group P and 1 patient in Group C had never pressed the PCA device.

Table 4. PCA Request count

	Grup I	Grup P	Grup C
Successful demands	9	14	14
Failed demands	5	8	9
Total demands	14	22	23
No demand(n)	4	2	1

Among the side effects of remifentanil, itching, bradycardia, hypotension, rigidity, tremor and arrhythmia were not observed in any patient. Nausea was observed in 2 patients in Group I, one in the postoperative 10th minute and the other in the postoperative 30th minute and 2nd hour. There was no vomiting. No nausea or vomiting was observed in Group P. In the control group that did not receive remifentanil, orthostatic hypotension and vomiting were observed in one patient in the 2nd postoperative hour (p>0.05).There were no complaints of pain, nausea or vomiting in the patients contacted by phone at the 24th postoperative hour.

DISCUSSION

In general, stress is a very important factor in all surgical interventions. Even if patients do not feel any pain under local or regional anesthesia, the discomfort caused by stress affects both the patient and the surgical team. To control perioperative anxiety, sedative agents are usually given as IV boluses under the supervision of the anesthesiologist. In PCS, the patient self-administers the medication in small doses as needed. It is a great pleasure for the patient to be able to control his anxiety. Sedative agents that have a rapid onset of action, a short half-life, no active metabolites, and a rapid and trouble-free recovery are ideal for PCS use. While the selected agent, locking conditions and bolus amounts primarily affect PCS settings, the patient's psychological state, intellectual level and informing about the procedure are other effective factors.

Research has shown that patients are better aware of their discomfort, pain, and the sedation they need during interventions than an anesthesiologist or nurse. The idea that patients can best respond to their own needs creates positive emotions in the patient. It has been noted that these feelings caused by PCS in patients are due to the following three factors. The first is that the worry of someone giving too much medication is eliminated, the second is that the patient is free from dependence on someone, and the third is that it is possible to receive immediate treatment.[9] Benzodiazepines are generally used in this method. While patient-controlled IV therapy was previously used only for analgesia, the foundations of PCS were first laid in 1989 when Galleti et al used diazepam for anxiolysis in a group of 50 people.[15] PCS has also been successfully applied to elderly and pediatric patients.[16,17] The success of PCS depends on the sedative agent chosen, the level of sedation provided, and the patient.[18] In addition to postoperative pain control, PCA devices are also used in sickle cell anemia crisis, gynecology, intensive care units and intraoperatively.[19,20]

Although patient satisfaction in PCS applications is better than other sedation methods, the expensiveness of PCA devices causes additional costs such as the need for a special set for each patient, which creates limitations and disadvantages in practice.[21] Benzodiazepines are drugs commonly used for anxiolysis, amnesia and sedation. Midazolam has a rapid onset of action, a short elimination half-life (1-4 hours) and good recovery properties. In addition to its hypnotic and anticonvulsant effects, it causes anterograde amnesia.[22]

Although there are studies showing that the use of remifentanil alone is sufficient to provide sedation, it has been reported that it should be given with 2 mg IV midazolam at a dose of 0.05-0.1 μg/kg/min to provide amnesia and analgesia.[6] In another study, clinically significant respiratory depression was detected after a bolus dose of remifentanil in patients premedicated with midazolam.[23] Additionally, it was observed that respiratory depression occurred in direct proportion to the increase in the midazolam dose in the combination of remifentanil and midazolam. Gold et al.[25] also used remifentanil alone and in combination with midazolam during outpatient surgery for MAC. They reported that low-dose (0.05 μg/kg/min) remifentanil combined with midazolam (2 mg) caused slightly more sedation, less anxiety and side effects.[24] A 0.07 mg/kg sedation dose of midazolam has been recommended, but it has been reported that it may reduce protective reflexes if opioids are used before treatment.

In ESWL, it has been stated that in addition to the lower infusion dose of remifentanil with the PCS method, the 10mcg bolus dose is more effective and causes fewer side effects.[26] In some studies, dose adjustments were made to reach the desired level of sedation in continuous infusion.[11] In our study, the rate was kept constant in the infusion group. Based on previous studies, we preferred the 0.1 μg/kg/min infusion dose and 0.5 μg/kg bolus dose as we found them reliable throughout the surgery. We provided adequate sedation and did not encounter excessive sedation in any patient.

PCS is also recommended to avoid unnecessary deep sedation during ERCP.[21] Remifentanil, used at a dose of 0.1-0.5μg/kg/min in awake fiberoptic intubation, increased tolerance by providing significant analgesia and suppressing the cough reflex. Although recovery from remifentanil is very rapid, it can be reversed with naloxone if necessary.[27] It has been reported that 0.05-0.15 μg/kg/min remifentanil infusion may be an alternative to 25-75 μg/kg/min propofol infusion in ambulatory operations performed under LA. In the same study, it was clearly shown that drug infusion rates generally need to be changed after 15-20 minutes and that active site

concentrations of drugs continue to increase during the early infusion period.[23]

Remifentanil was used together with the PCA device for analgesia and sedation in 3 pregnant women who could not have an epidural due to thrombocytopenia, and it was found to be well tolerated. Oxygen was not required at a bolus dose of 0.5 μg/kg. There was a slowdown in fetal heartbeat, but it recovered 10 minutes after the device was turned off. Remifentanil consumption (426-1050 μg/h) was observed to be strikingly variable. In this publication, in which the use of remifentanil along with PCA at birth was reported for the first time, the use of artificial respiration and naloxone was not required. PCA effectiveness is related to the size of the bolus. When the dose is low, distrust of the method may occur, and when it is high, unwanted side effects may occur.[28]

A bolus dose of 0.5 μg/kg, which was tolerated without oxygen, was also found to be appropriate in our study (20- 47.5 μg bolus dose). The doses of remifentanil required for sedation are close to the doses that cause respiratory depression. Remifentanil side effects are similar to other μ-opioid receptor agonists. Studies have shown that remifentanil reduces tidal volume and respiratory rate. However, unlike other opioids, it does not have an accumulating effect and has a short half-life, so the condition can improve within a few minutes.[6] In our study, we encountered desaturation (SpO2<93%) in two groups receiving remifentanil, more in the infusion group, but there was no significant difference between the groups.The decrease in respiratory rate seen in Group I was never below 8, but the difference between the groups was statistically significant.

Sa'Rego et al.[29] compared intermittent bolus doses of remifentanil (25 μg) and continuously variable dose infusion (0.025-0.15μg/kg/min) in addition to the use of midazolam (2 mg) and propofol (50 μg/kg/min) under MAC in ESWL. Although patient comfort is better when using remifentanil by infusion, the incidence of desaturation is higher. Although more medication was used in the infusion group, a lower pain score was found in the low dose infusion+bolus (0.05 μg/kg/min+12.5 μg) and bolus only group. Compared to infusion, it has been observed that the risk of hypoventilation does not increase and rapid recovery is achieved with bolus doses, which are found to be simple, reliable and effective, and it has been reported that dose titration should be done very carefully because it reduces tidal volume and respiratory rate.[6] In our study, respiratory depression was also seen in the infusion group, and bolus administration did not occur.

In contrast to the use of infusion in general anesthesia, it has been observed that the response to temporary noxious stimuli is better prevented by intermittent bolus application in MAC.[24] Studies have reported that it causes nausea and vomiting during remifentanil administration or in the early postoperative period.[6] In our study, we observed nausea in the infusion group, although it was not statistically significant. In the control group, one patient experienced orthostatic hypotension and vomiting at the 2nd postoperative hour.

In the studies conducted, when 0.1 μg/kg/min remifentanil infusion combined with 2, 4 or 8 mg midazolam was compared, the respiratory rate decreased more in the group combined with high dose midazolam, but intraoperative itching and postoperative nausea were observed in the deep sedation (4-5) group. Side effects such as vomiting were less common in the light sedation group.[6] PCS has been recommended for patients undergoing ERCP to avoid unnecessary deep sedation.[21] In our study, there was no difference in amnesia between the 3 groups. It has been shown in the literature that patients taking remifentanil alone fully remember intraoperative events, the degree of amnesia depends on the dose of midazolam administered, and recovery from remifentanil is rapid.[6] In our study, all cases transferred themselves from the operating table to the stretcher at the end of the operation. In Group I, stopping the infusion (while skin stitching begins) before the end of the procedure may also have an effect. Early postoperative pain is expected after remifentanil, but the 1.5-2 hour effect of local anesthetic infiltration ensures the continuation of the analgesic effect after of surgery. Our patients did not need analgesics before 2 hours. There are positive publications regarding the use of PCS in otorhinolaryngology and breast surgery performed under local anesthesia and in labor analgesia.[20,30,31]

In women using the PCA device, the duration of active labor was shorter compared to epidural, the rate of spontaneous birth was higher, and side effects were less.[32] The deeper level of sedation in the infusion group may have resulted in fewer PCA requests. The number of requests in Group C was similar to Group P, but patient satisfaction and sedation level were better in Group P. The study has limitations. Since it was a single-center study and the number of patients was small, it may not be appropriate to generalize these results to the general population.

CONCLUSION

In this study, adequate sedation was achieved with a lower dose of remifentanil using the PCS method compared to infusion. Intraoperative pain was less in the group receiving remifentanil than in the control group, and side effects were less in the PCS group than in the infusion group. We concluded that PCS can be used safely with a bolus remifentanil dose of 0.5 μg/kg under respiratory monitoring in cases undergoing surgery under local anesthesia.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted in 2001 as an anesthesiology and reanimation specialty thesis. This study was initiated after institutional approval was obtained.

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Wang X, Pan C, Li J, et al. Prospective comparison of local anesthesia with general or spinal anesthesia in patients treated with microscopic varicocelectomy. *J Clin Med*. 2022;11(21):6397
2. Doğruer K, Köprülü AŞ, Karpat H. Summary book. A new perspective on sedation; anxiolysis, patient-controlled sedation. I*ntensive Care Med*. 1996;42(2):89-90.
3. Mackenzie N, Grant IS. Propofol for intravenous sedation. *Anaesthesia*. 1987;42(1):3-6. doi: 10.1111/j.1365-2044.1987.tb02936
4. Sutcliffe N. Sedation during loco-regional anaesthesia. *Acta Anaesthesiol Belg*. 2000;51(2):153-156.
5. Rêgo MM, Watcha MF, White PF. The changing role of monitored anesthesia care in the ambulatory setting. *Anesth Analg*. 1997;85(5): 1020-1036.
6. Avramov MN, Smith I, White PF. Interactions between midazolam and remifentanil during monitored anesthesia care. *Anesthesiology*. 1996;85 (6):1283-1289. doi: 10.1097/00000542-199612000-00009
7. Nagengast FM. Sedation and monitoring in gastrointestinal endoscopy. *Scand J Gastroenterol Suppl*. 1993;200(1):28-32. doi: 10.3109/00365529309101572
8. Grattidge P. Patient-controlled sedation using propofol in day surgery. *Anaesthesia*. 1992;47(8):683-685.
9. Chumbley GM, Hall GM, Salmon P. Why do patients feel positive about patient-controlled analgesia? *Anaesthesia*. 1999;54(4):386-389. doi: 10.1046/j.1365-2044.1999.00836.x
10. Folstein MF, Folstein SE, McHugh PR. Mini mental state. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189-198. doi: 10.1016/0022-3956(75)90026-6
11. Osborne GA, Rudkin GE, Jarvis DA, et al. Intra-operative patient-controlled sedation and patient attitude to control. A crossover comparison of patient preference for patient-controlled propofol and propofol by continuous infusion. *Anaesthesia*. 1994;49(4):287-292.
12. Fisher NC, Bailey S, Gibson JA. A prospective, randomized controlled trial of sedation vs. no sedation in outpatient diagnostic upper gastrointestinal endoscopy. *Endoscopy*. 1998;30(1):21-24. doi: 10.1055/s-2007-993723
13. Bethune DW. Test of delayed memory recall suitable for assessing postoperative amnesia. *Anaesthesia*. 1981;36(10):942-948. doi: 10.1111/j.1365-2044.1981.tb08652.x
14. Di Palo MT. Rating satisfaction research: is it poor, fair, good, very good, or excellent? *Arthritis Care Res*. 1997;10(6):422-430. doi: 10.1002/art.1790100610.
15. Galletly DC, Short TG, Forrest P. Patient administered anxiolysis-a pilot study. *Anaesth Intensive Care*. 1989 May;17(2):144-50. doi: 10.1177/0310057X8901700204
16. Kerschbaum G, Altmeppen J, Funk W, Taeger K. Patient-controlled analgesia. PCA in a three year old child after traumatic amputation. *Anaesthesist*. 1998;47(3):238-242.
17. Herrick IA, Gelb AW, Nichols B, Kirkby J. Patient-controlled propofol sedation for elderly patients: safety and patient attitude toward control. *Can J Anaesth*. 1996;43(10):1014-1018
18. Mazanikov M, Pöyhia R. Patient controlled sedation. *Duodecim*. 2011; 127(9):883-889.
19. Rudkin GE, Osborne GA, Curtis NJ. Intra-operative patient-controlled sedation. *Anaesthesia*. 1991;46(2):90-92.
20. Güneş S, Türktan M, Güleç ÜK, Hatipoğlu Z, Ünlügenç H, Işık G. The comparison of patient-controlled remifentanil administered by two different protocols (bolus and bolus+infusion) and intramuscular meperidine for labor analgesia. *Turk J Anaesthesiol Reanim*. 2014;42 (5):264-269.
21. Mazanikov M, Udd M, Kylanpaa L, et al. Patient-controlled sedation with propofol and remifentanil for ERCP: a randomized, controlled study. *Gastrointest Endosc*. 2011;73(2):260-266.
22. Veselis RA, Reinsel RA, Feshchenko VA, Wroński M. The comparative amnestic effects of midazolam, propofol, thiopental, and fentanyl at equisedative concentrations. *Anesthesiology*. 1997;87(4):749-764. doi: 10.1097/00000542-199710000-00007
23. Smith I, Avramov MN, White PF. A comparison of propofol and remifentanil during monitored anesthesia care. *J Clin Anesth*. 1997;9(2):148-154. doi: 10.1016/S0952-8180(96)00240-1
24. Gold MI, Watkins WD, Sung YF, et al. Remifentanil versus remifentanil/midazolam for ambulatory surgery during monitored anesthesia care. *Anesthesiology*. 1997;87(1):51-57.
25. White PF. Clinical uses of intravenous anesthetic and analgesic infusions. *Anesth Analg*. 1989;68(2):161-171.
26. Medina HJ, Galvin EM, Dirckx M, et al. Remifentanil as a single drug for extracorporeal shock wave lithotripsy: a comparison of infusion doses in terms of analgesic potency and side effects. *Anesth Analg*. 2005;101(2):365-370. doi: 10.1213/01.ANE.0000159379.54705.84
27. Puchner W, Egger P, Pühringer F, et al. Evaluation of remifentanil as single drug for awake fiberoptic intubation. *Acta Anaesthesiol Scand*. 2002;46(4):350-354. doi: 10.1034/j.1399-6576.2002.460403.x
28. Jones R, Pegrum A, Stacey RG. Patient-controlled analgesia using remifentanil in the parturient with thrombocytopaenia. *Anaesthesia*. 1999;54(5):461-465.
29. Sa Rego MM, Inagaki Y, White PF. Remifentanil administration during monitored anesthesia care: are intermittent boluses an effective alternative to a continuous infusion? *Anesth Analg*. 1999;88(3):518-522.
30. Choi J, Choi H, Kang HS, Kang H. Comparison of alfentanil and remifentanil for the use of patient controlled sedation under local anesthesia during ear, nose and throat surgery. *Korean J Anesthesiol*. 2009;56(5):507-512.
31. Joo JD, In JH, Kim DW, et al. The comparison of sedation quality, side effect and recovery profiles on different dosage of remifentanil patient-controlled sedation during breast biopsy surgery. *Korean J Anesthesiol*. 2012;63(5):431-435.
32. Thorbiörnson A, Charvalho P, Gupta A, Stjernholm YV. Duration of labor, delivery mode and maternal and neonatal morbidity after remifentanil patient-controlled analgesia compared with epidural analgesia. *Eur J Obstet Gynecol Reprod Biol X*. 2020;7(6):100106.

Eurasian Journal of
Anesthesiology & Intensive Care
Original Article
doi
10.51271/EAJAIC-0013

Comparing the effects of propofol dosing based on total body weight and lean body weight on hemodynamics and intraoperative awareness during sleeve gastrectomies

Şerife Yıldırım[1], Seyyid Furkan Kına[2], Esra Özayar[1]

[1]Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Turkiye
[2]Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Turkiye

Received: 20/05/2024 ◆ **Accepted**: 11/06/2024 ◆ **Published**: 06/08/2024

Cite this article: Yıldırım Ş, Kına SF, Özayar E. Comparison of the effects of dosing propofol according to total body weight and lean body weight on hemodynamics and intraoperative awareness in sleeve gastrectomies. *Eurasian J Anesthesiol Intens Care* . 2024;1(3):59-63.

Corresponding Author: Seyyid Furkan Kına, kinafurkan@gmail.com

ABSTRACT

Aims: According to the World Health Organization, obesity is an abnormal or excessive fat accumulation in adipose tissue that impairs health. In recent years, due to the increase in the number of patients referred for surgery with diagnoses of obesity surgery or other clinical conditions, the perioperative evaluation and anesthesia management of these patients have become crucial. Obesity is associated with increased anesthesia risk due to its effects on metabolic, cardiovascular, and pulmonary functions. This study compares the effects of propofol dosing based on lean body weight (LBW) and total body weight (TBW) on hemodynamics and intraoperative awareness in patients undergoing laparoscopic sleeve gastrectomy.

Methods: This study is a prospective observational and randomized clinical trial. It included 54 patients aged 18-60 who underwent elective laparoscopic sleeve gastrectomy under general anesthesia at Ankara Keçiören Training and Researches Hospital. The patients were ASA I-III, with surgeries lasting less than 2 hours, and propofol was used for induction. Patients were randomized into Group LBW and Group TBW based on the calculation of the propofol dose according to their lean body weight and total body weight, respectively. Clinical, demographic, perioperative, and hemodynamic data were recorded for all patients. Additionally, all patients were assessed using the Appendix 1 questionnaire.

Results: The dose of propofol administered was higher in Group TBW than in Group LBW ($p<0.001$). When propofol was administered based on TBW, systolic blood pressure was significantly lower at the 1st and 2nd minutes of induction ($p<0.05$). There was no significant difference in systolic blood pressure recorded during the intraoperative period and post-extubation between the two groups. Diastolic blood pressure, mean arterial pressure, and heart rate were significantly lower in Group TBW post-extubation ($p=0.003$). Intraoperative BIS values were significantly lower in Group TBW at the 1st, 2nd, and 3rd minutes post-induction and post-extubation. No intraoperative awareness (IOA) was detected in either group according to the Appendix 1 questionnaire.

Conclusion: In obese patients undergoing sleeve gastrectomy, propofol doses calculated based on LBW during induction were associated with less hemodynamic instability compared to doses calculated based on TBW.

Keywords: Laparoscopy, obesity, total body weight, lean body weight, intraoperative awareness, sleeve gastrectomy

INTRODUCTION

Obesity is defined by the body mass index (BMI), which is the ratio of body weight (kilograms) to the square of height (meters). According to the World Health organization's classification, individuals with a BMI over 30 are considered obese.[1,2] The prevalence of obesity has increased in recent decades, particularly in the United States and Asian countries.[3,4] The rise in the number of obese patients has also led to an increase in obesity-related surgical procedures.[4-6] Due to the increase in the number of obese patients referred for surgery with diagnoses of obesity surgery or other clinical conditions, the preoperative evaluation and anesthesia management of these patients have become increasingly important.

The pharmacokinetic parameters of anesthetic drugs are affected by obesity due to their solubility in fat and distribution in tissues. Dose adjustments for these drugs should consider the volume of distribution for the loading dose and clearance

for the maintenance dose.[7] Obese individuals can metabolize lipophilic drugs to a greater extent compared to lean individuals.

Propofol is an intravenous (IV) anesthetic agent commonly used for induction of anesthesia. Although propofol has high fat solubility, its induction dose should be calculated based on lean body weight (LBW), whereas the maintenance dose should be adjusted according to total body weight (TBW) due to its high clearance.[1,4] Recent studies on anesthesia in obesity surgery have primarily focused on total IV anesthesia or specific infusion models like target-controlled infusion.[4,8] In rapid induction models, individuals receiving propofol based on TBW have faster induction times. When compared to normal-weight individuals, obese patients receiving propofol based on LBW during induction have similar times to loss of consciousness.[8,9] This can be explained by the unchanged initial volume of distribution in patients receiving propofol based on LBW. [8,9]

The primary aim of this study is to compare the hemodynamic parameters of groups by applying two different doses of propofol (TBW or LBW) during induction in obese patients. The secondary aim is to compare their intraoperative awareness (IOA).

METHODS

The study was carried out with the permission of Ethics Committe of the Keçiören Training and Researches Hospital (Date: 13.12.2017, Decision No: 1563). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study is a prospective observational randomized clinical comparison conducted in a tertiary education and research hospital and from the Turkish Medicines and Medical Devices Agency (decision number 93189304-514.05.01-E7287, dated 11.01.2018). Written informed consent was obtained from all patients participating in the study, and no interference was made in their perioperative management.

The study included patients aged 18-60 who were planned for elective laparoscopic sleeve gastrectomy at the General Surgery Clinic under general anesthesia, classified as American Society of Anesthesiologists (ASA) physical status I-III, with surgeries lasting less than 2 hours, and who consented to participate postoperatively. Exclusion criteria were patients who refused to participate, had a history of allergy to anesthetic drugs, had preoperative hemoglobin levels below 10 mg/dl, received premedication, were assessed as difficult intubation, developed intraoperative complications, had surgery lasting more than 2 hours, consumed alcohol daily, were diagnosed with severe anxiety, used benzodiazepines, opioids, sedatives, or anxiolytic drugs preoperatively, had stage 2-3 hypertension or any chronic disease, and had dementia.

Patients were randomized in the operating room using the sealed envelope draw method. They were divided into two groups: the group given propofol according to TBW (Group TBW) and the group given propofol according to LBW (Group LBW). The dose of propofol used for anesthesia induction in patients was calculated according to TBW and LBW, while other drugs used for anesthesia induction and maintenance were dosed according to LBW.

In patients included in the study, demographic information, BMI, ASA score, comorbidities, mechanical ventilator settings, administered drug doses, perioperative hemodynamic monitoring (Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), Mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2), End-tidal carbon dioxide (EtCO2)], Bispectral index (BIS) values, anesthesia and surgery duration, loss of consciousness time (time elapsed until loss of eyelash reflex after propofol administration), TOF unresponsiveness time (Time elapsed until TOF 0 after muscle relaxant administration), intubation time, insufflation and desufflation time, intraoperative inhalation anesthetic consumption measured by fresh gas flow method, and whether additional medication was used intraoperatively were evaluated. Additionally, the dose of medication used during extubation, time to reach TOF 90%, extubation time, and the time in the postoperative recovery unit (PACU) (when Aldrete score >9) were recorded. Patients were evaluated with the PO Appendix 1 questionnaire a total of 3 times: within the first 24 hours postoperatively, between 24-72 hours, and 30 days after the surgery. Patients were asked to answer these questions with 'Yes' or 'No'.

Statistical Analysis

The required sample size for each group was determined to be 27, with a total of 54 patients, based on BIS results from the study by Lam et al.,[4] using the Minilab program with α 0.05 and β 0.10 for power analysis. Data were evaluated using SPSS (Statistical Package for Social Science) 22.0. Categorical data were presented as numbers (n) and percentages (%), and continuous numerical data were presented as mean± standard deviation (SD). The Kolmogorov-Smirnov test was used to assess the normality of continuous data distribution. Student's t-test was used for group comparisons of normally distributed parameters, and paired t-test for within-group comparisons. The Mann-Whitney U test was used for group comparisons of non-normally distributed parameters, and the Wilcoxon test for within-group comparisons. Categorical data comparisons were made using the Chi-Square or Fisher's exact test. Results were considered significant at $p<0.05$ within a 95% confidence interval.

RESULTS

Twenty-seven patients were assigned to each group, and the data of all 54 patients were analyzed. Demographic and preoperative assessment data of the groups were similar (Table 1). Induction doses of rocuronium and fentanyl, calculated according to LBW, were administered similarly in both groups. However, the propofol dose administered was significantly higher in Group TBW ($p<0.001$) (Table 2). No significant difference was found between the groups regarding the need for additional medication. Total nitrogen and sevoflurane consumption during maintenance of anesthesia, guided by BIS monitoring to maintain BIS values between 40-60, were similar between the groups.

There was no significant difference in the time of consciousness loss between the groups. Consequently, the time from anesthesia drug administration to intubation was also similar (Table 3).

Table 1. Distribution of some descriptive and clinical features among study groups

	Total body weight (n=27) group 1	Lean body weight (n=27) group 2	p
Age*	40.51±11.50	38.62±12.26	0.562
Gender, n(%)			
Woman	23 (85.2)	22 (81.5)	
Male	4 (14.8)	5 (18.5)	0.715
Height length (cm)*	162.33±9.11	166.03±6.65	0.094
Body weight (kg)*	127.27±16.69	136.55±21.15	0.079
Body mass index (BMI)*	48.36±5.72	49.53±7.44	0.523
Lean body weight (kg)*	64.01±10.11	69.18±7.44	0.097
Comorbidity status, n(%)			
None	19(70.4)	15 (55.6)	
There is	8(29.6)	12 (44.4)	0.260
Comorbidities, n (%)			
DM	6 (22.2)	14 (14.8)	0.484
H.T.	7 (25.9)	6 (22.2)	0.750
Obst . Akc . Hast	1 (3.7)	4 (14.8)	0.159
ASA Classification, n (%)			
I	19 (70.4)	15 (55.6)	
II	8 (29.6)	12 (44.4)	0.260
Anesthesia duration (min)*	70.07±14.14	66.66±7.55	0.267
Surgery time (min)*	55.22±13.98	48.74±9.25	0.051
*: mean±sd			

ASA : American Society of Anesthesiologist , min : Minute, cm: Centimeter, kg: Kilogram, DM: Diabetes mellitus , HT: Hypertension, mean : Median, SD : Standard deviation, KOAH: Kronik obstrüktif akciğer hastalığı

Table 2. Intravenous Drug Doses Used During Induction

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Arrhythmal (mg)	40.55±4.00	40.37±1.97	0.829
Propofol (mg)	310.00±50.15	183.88±37.42	<0.001
Rocuronium (mg)	42.03±8.57	43.70±7.54	0.452
Fentanyl (mg)	132.18±25.71	141.11±23.91	0.192
*: mean±SD			

mg : Milligram, mean : Median, SD : Standard deviation

Table 3. Induction times

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Duration of loss of consciousness (sec)	34.96±13.27	35.70±15.79	0.853
TOF non-response time (sec)	225.59±100.02	257.00±122.75	0.307
Intubation time (sec)	326.85±95.98	364.44±125.71	0.222

n : Number, sec : Seconds, mean : Median, SD : Standard deviation, *: mean±sd

SAP was found to be significantly lower in Group TBW at the 1st and 2nd minutes of induction ($p<0.05$). No significant difference was found in SAP between the groups post-intubation intraoperatively and post-extubation. DAP and MAP values were found to be significantly lower in Group TBW post-intubation ($p=0.003$ and $p=0.001$, respectively). However, at 30-40-50 minutes post-intubation, DAP and MAP values were significantly higher in Group TBW ($p<0.05$).

Comparing HR at 1 minute post-induction, no significant difference was found, but HR was significantly lower in Group TBW at the 2nd and 3rd minutes post-induction, 20-30 minutes post-intubation, and post-extubation ($p<0.05$). No difference was found between the groups for SpO_2 and $EtCO_2$ values. BIS measurements at 1-2-3 minutes post-induction and during the intraoperative and post-extubation periods were significantly lower in Group TBW ($p<0.05$) (Table 4). The TOF values were similar preoperatively and postoperatively in both groups, with similar sugammadex doses, time to TOF 90%, and extubation times post-surgery. The average Modified Aldrete score in Group TBW post-extubation in the operating room was 7.22±1.01, compared to 6.62±1.07 in Group LBW ($p=0.046$). However, no difference was found between the groups in the PACU Modified Aldrete score (Table 5).

Appendix 1 questionnaire responses, collected at three different times with 16 questions, showed no statistical difference between the groups. Only the question "Do you remember the moment you fell asleep?" in the questionnaire administered within the first 24 hours showed that Group TBW significantly more often answered "yes" ($p=0.033$) (Table 6).

Table 4. Comparison of BIS values

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Preinduction	95.1481±8.45669	96.7778±5.24282	0.922
Induction 1 min	36.9630±16.27996	47.0370±14.42349	0.005
Induction 2 min	33.4074±9.43504	50.4815±16.23475	<0.001
Induction 3 min	35.4800±11.99347	53.2692±11.44572	<0.001
Postintubation	42.0741±10.94717	62.5926±10.06998	<0.001
Intubation 10 min	44.7037±5.68273	50.8889±9.10762	0.006
Intubation 20 min	43.6296±7.14223	47.3704±6.98982	0.073
Intubation 30 min	42.8519±6.79198	45.7778±5.92474	0.049
Intubation 40 min	42.2308±5.27111	46.1538±6.03783	0.023
Intubation 50 min	42.7143±5.01142	48.8421±9.64517	0.025
Intubation 60 min	46.2667±5.84889	49.6667±6.15359	0.225
Intubation 70 min	40.7500±6.23832		
Intubation 80 min	46.0000±5.65685		
Intubation 90 min	42,0000		
Intubation 100 min	45,0000		
Postextubation	88.6296±15.79715	81.4444±6.29611	0.013

min : Minute

Table 5. Postoperative recovery data

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Extubation aldrete	7.22±1.01	6.62±1.07	0.046
Aldrete 9 time (min)	8.07±2.60	9.59±3.38	0.137

mean : Median, sd : Standard Deviation , min : Minutes, *: mean±SD

Table 6. Appendix 1 survey 'Yes' answers comparison table

	0-24. Hour			24-72.Hour			Postop Day 30		
	TVA n (%)	YVA n (%)	p	TVA n (%)	YVA n (%)	p	TVA n (%)	YVA n (%)	p
1	25 (92.6)	27 (100)	0.150	25 (92.6)	26 (96.3)	0.552	25 (92.6)	26 (96.3)	0.552
2	4 (14.8)	5 (18.5)	0.710	4 (14.8)	6 (22.2)	0.484	7 (25.9)	7 (25.9)	1.000
3	6 (22.2)	7 (25.9)	0.750	5 (18.5)	5 (18.5)	1.000	4 (14.8)	7 (25.9)	0.311
4	16 (59.3)	23 (85.2)	0 .033	17 (63)	20 (74.1)	0.379	18 (66.7)	18 (66.7)	1.000
5	0(0)	0(0)	1.000	0 (0)	0 (0)	1.000	0 (0)	1 (3.7)	0.313
6	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	1(3.7)	-
8	0(0)	0 (0)	1.000	0 (0)	0(0)	1.000	0(0)	0(0)	1.000
9	1 (3.7)	0 (0)	0.313	1 (3.7)	0(0)	0.313	1(3.7)	2(7.4)	0.552
10	0(0)	0 (0)	1.000	0(0)	0(0)	1.000	0(0)	1(3.7)	0.313
11	0(0)	0 (0)	1.000	0(0)	0(0)	1.000	1(3.7)	0(0)	0.313
12	-	-	-	-	-	-	-	-	-
13	0(0)	0 (0)	1.000	1 (3.7)	0(0)	0.313	0(0)	0(0)	1.000
14	0(0)	0 (0)	1.000	0(0)	0(0)	1.000	0(0)	0(0)	1.000
15	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-

TVA: Total body weight, YVA: Lean body weight

Appendix 1. Intraoperative awareness appendix 1 survey	
1	Do you remember being transferred to the operating room and being prepared for anesthesia?
2	Do you remember the end of the operation?
3	Do you remember sleeping during the operation?
4	Do you remember the moment of falling asleep?
5	Do you remember the dreams you had while you were under anesthesia?
6	If yes; Were they pleasant dreams?
7	If yes; Were they disturbing unpleasant dreams?
8	Did you feel pain during anesthesia?
9	Do you remember not being able to breathe during anesthesia?
10	Do you remember anything from the operation?
11	Did you hear anything during the surgery?
12	If yes; Can you specify if it is a personal conversation?
13	Did you hear any noise during surgery?
14	Did you feel anything during the surgery?
15	If yes; Did you feel any touch?
16	If yes; Did you feel anything in your throat or mouth?

DISCUSSION

The increase in the prevalence of obesity has led to a rise in obesity-related surgical procedures.(4-6) Compared to the normal population, anesthesia complications are higher in obese patients, causing confusion regarding the dose-effect strategy of anesthetic drugs due to their pharmacokinetic and pharmacodynamic interactions. Propofol is a frequently used drug with high fat solubility. Besides providing rapid loss of consciousness, it has cardiac effects such as hypotension and myocardial depression due to its redistribution.[10,11] In this prospective observational clinical study compared the hemodynamic effects and IOA in patients administered propofol doses based on TBW and LBW. According to this study, it was shown that dosing propofol according to LBW during induction had significantly better results on hemodynamic parameters.

In a similar study by Ingrande et al.[12] with 60 morbidly obese patients (BMI>40), propofol doses calculated according to TBW and LBW were administered by infusion. The time to loss of consciousness was defined as the moment the patient dropped a small object from their hand, and the propofol infusion was stopped. A significant difference was found between the amounts of propofol administered in the groups (TVA: 244.7 mg LBW: 183.3 mg, p=0.0002).[12] The time to loss of consciousness was shorter in Group TBW (65.86 s vs 94 s, p=0.0001). Another study by Lam et al.,[4] similar to our study, administered propofol as a rapid single bolus and found a significant difference in propofol amounts between the groups during induction (TVA - LBW; 217.3 ± 39.1 mg- 189.5±36.3 mg, p=0.03). No difference was found in the time to loss of consciousness and the need for additional drugs, similar to our study.

There are studies in the literature investigating BIS monitoring. Ibraheim et al.[13] examined the effect of BIS monitoring on PO recovery and IO sevoflurane consumption in morbidly obese patients undergoing laparoscopic gastric banding and found higher sevoflurane consumption in the group without BIS monitoring (19.60 ml vs 15.66 ml, p<0.05). Gan et al.[14] compared the amounts of propofol, alfentanil, and nitrous oxide used in normal-weight individuals and found significantly lower anesthetic consumption in the BIS-monitored group. In our study, BIS monitoring was applied to all patients. Inhaled anesthesia was administered to maintain BIS values between 40-60. Despite the different propofol doses administered, BIS monitoring allowed balanced and safe anesthesia maintenance without significant differences in inhaled anesthetic doses between the groups.

Lam et al.4 Ingrande et al.[12], Kazama et al.[15], and found a dose relationship between the rate and amount of propofol administration and hypotension. Particularly, in the absence of surgical or anesthetic complications, a decrease in MAP of more than 40% within 5 minutes post-induction was defined as post-induction hypotension. In the control group, hypotension was observed in 3 patients, 5 in the LBW group, and 9 in the TBW group, with no significant statistical difference.[5] In Lam et al.'s study, propofol administered based on TBW allowed for rapid loss of consciousness accompanied by hypotension, with at least 83% of patients experiencing hypotension and at least 44% experiencing significant hypotension. Another study by Kazama et al.[15] found that propofol administration leading to SAP <75 mm Hg or a decrease of more than 40% was associated with the relationship between propofol plasma concentration and infusion rate and lean body mass.

In our study, the decrease in SAP and greater impact on Group TBW attributed to propofol's effects on the cardiovascular system. Administering propofol based on LBW was shown to cause less cardiac instability, similar to other studies. The significant differences in SAP, DAP, and MAP at the 30th minute measurements between the groups were not associated with propofol's pharmacodynamics and pharmacokinetics. Propofol undergoes biotransformation in the liver and is excreted by the kidneys. Its effect begins within seconds and ends rapidly due to its short distribution half-life (2-8 minutes). Patients included in our study were selected to be free of liver and kidney dysfunction, eliminating factors that could affect propofol's duration and elimination. Therefore, the changes in SAP, DAP, and MAP during the IO period were not related to the propofol induction dose but rather to surgical conditions or inhalation anesthetic dose adjustments.

Lam et al.[4] Ingrande et al.,[12] Kazama et al.[15] found no significant statistical difference in HR changes due to propofol in their studies. The lack of similar changes in HR despite observed SAP changes was attributed to propofol's inhibition of baroreflex response, which normally occurs due to decreased systemic vascular resistance, cardiac contractility, and preload. However, in our study, we observed a greater decrease in MAP (Mean arterial pressure) after induction in Group TVA and considered that it might be due to cardiac depression associated with the high dose of propofol used in obese patients.

BIS can be used for IOA diagnosis. Differences have been found between groups with and without BIS monitoring in the literature. In our study, preoperative BIS averages were the same in both groups, but a greater decrease was observed post-induction in Group TBW. Particularly, BIS averages below 40 were found in Group TBW at 1-2-3 minutes post-induction, indicating deep hypnosis and brain activity close to an isoelectric EEG, which is considered unsafe.[18] In Group LBW, BIS values between 40-60 during the first 1-2-3 minutes post-induction indicated sufficient hypnosis for safe anesthesia and

rapid recovery. A significant difference was found between the groups in BIS values at 1-2-3 minutes post-induction and post-intubation.

In our study, comparison of postoperative effectiveness between the groups was limited to 30 days and did not assess long-term effects and complications. New studies with larger sample sizes are needed to evaluate long-term effects and complications.

CONCLUSION

There is no consensus on the dose-effect strategy for propofol in obese patients in the literature. Our study demonstrated that using propofol doses calculated based on LBW during induction in obese patients undergoing sleeve gastrectomy resulted in less hemodynamic instability. Based on our findings, sufficient and safe anesthesia depth can be achieved with BIS monitoring, with no IOF detected. Administering propofol doses based on TBW in obese patients may negatively affect hemodynamic responses, predispose to cardiovascular complications, and lead to unnecessary costs. Further studies with larger sample sizes, different surgical types, and various weight scales are needed to determine the optimal dose.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethics Committe of the Keçiören Training and Researches Hospital (Date: 13.12.2017, Decision No: 1563).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERANCE

1. Üstün YB, Köksal E. Obezite ve anestezi. *Clin Exp Reprod Med*. 2013;1(30)141-145.
2. Organization WH. Obesity: preventing and managing the global epidemic. 2000: World Health Organization.
3. Chu NF. Prevalence of obesity in taiwan. *Obes Rev.* 2005;6(4):271-274.
4. Lam F. Different dosing regimens for propofol induction in obese patients. *Acta Anaesthesiol Taiwan*. 2013;51(2):53-57.
5. Kopelman PG. Obesity as a medical problem. *Nature*. 2000;404(6778): 635-643.
6. Casati A, Putzu M. Anesthesia in the obese patient: pharmacokinetic considerations. *J Clin Anesth*. 2005;17(2):134-145.
7. Arora L, Sharma S, Carillo JF. Obesity and anesthesia. *Curr Opin Anaesthesiol*. 2024;37(3):403-412.
8. Albertin, A. Predictive performance of servins formuladuring BIS®-guided propofol-remifentanil target-controlled infusion in morbidly obese patients. *Br J Anaesth*. 2006;98(1):66-75.
9. Bouillon, T, Shafer SL. Does size matter? *Anesthesiology*. 1998;89(3):557-560.
10. Price HL. A dynamic concept of the distribution of thiopental in the human body. *Anesthesiology*. 1960; 21(1):40-45.
11. Saidman LJ, Eger EI. The effect of thiopental metabolism on duration of anesthesia. *Anesthesiology*. 1966;27(2):118-126.
12. Ingrande J, Brodsky JB, Lemmens HJ. Lean body weight scalar for the anesthetic induction dose of propofol in morbidly obese subjects. *Anesth Analg*. 2011;113(1):57-62.
13. Ibraheim O. Effect of bispectral index (BIS) monitoring on postoperative recovery and sevoflurane consumption among morbidly obese patients undergoing laparoscopic gastric banding. *Middle East J Anaesthesiol*. 2008;19(4):819.
14. Gan TJ. Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. *Anesthesiology*. 1997;87(4):808-815.
15. Kazama T. Investigation of effective anesthesia induction doses using a wide range of infusion rates with undiluted and diluted propofol. *Anesthesiology*. 2000;92(4):1017-1028.
16. Morgan G, Michail M. Clinical anesthesiology 1'nci Baskı. Los Angeles: Appleton & Lange. 1992;(1):116-134.
17. Myles P. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. *Lancet*. 2004;363 (9423):1757-1763.
18. Jeejeebhoy Farida M. Cardiac arrest in pregnancy: a scientific statement from the American Heart Association. *Circulation*. 2015;132(18):1747-1773.

MHA MEDIHEALTH ACADEMY

Eurasian Journal of
Anesthesiology & Intensive Care

Original Article

doi
10.51271/EAJAIC-0014

Effect of pericapsular nerve group block on perioperative analgesia characteristics for hip fracture operations

Veysel Yasin Yömen, Semih Başkan, İsmail Aytaç, Nurettin Mantı, Eyüp Horasanlı

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Turkiye

Received: 10/05/2024 • **Accepted**: 05/06/2024 • **Published**: 06/08/2024

Cite this article: Yömen VY, Başkan S, Aytaç İ, Mantı N, Horasanlı E. Effect of pericapsular nerve group block on perioperative analgesia characteristics for hip fracture operations. *Eurasian J Anesthesiol Intens Care* . 2024;1(3):64-71.

Corresponding Author: Semih Başkan, drsemkan@gmail.com

ABSTRACT

Aims: Pericapsular nerve group (PENG) block is a new regional analgesia technique that has recently been used for perioperative analgesia for hip fracture operations. This study, it was aimed to investigate the perioperative analgesia characteristics of PENG block in patients scheduled for hip fracture operation under spinal anesthesia.

Methods: The study was conducted as a prospective randomized controlled study between February 2021 and May 2021 after ethics committee approval. Patients with consent were included in the study. The patients were randomly divided into two groups (Group-I and Group-II). Patients in Group I underwent a PENG block with a 0.25% concentration of 20 cc bupivacaine in the preoperative waiting room 30 minutes before the operation. Afterward, spinal anesthesia was applied in the operating room. Only spinal anesthesia was applied to the patients in Group II. Preoperative visual analog scale (VAS) scores were recorded for both groups in the preoperative period. ECG, arterial blood pressure, pulse, and oxygen saturation measurements were performed in all patients preoperatively, intraoperatively, and postoperatively. Pulse, arterial blood pressure, oxygen saturation measurements, and VAS scores were recorded in the lateral decubitus position before and at the 5th minute after spinal anesthesia. In addition, the comfort of the anesthetist who will administer the spinal anesthesia during the application was questioned (0: poor, 1: moderate, 2: good, 3: very good). All patients 5 min after spinal anesthesia. It was kept in the lateral position throughout. In the postoperative period, VAS scores at 0th, 2nd, 8th, 16th, and 24th hours and the time of first analgesic administration were recorded. The total amount of paracetamol and tramadol consumed in the first 24 hours postoperatively were recorded.

Results: Patients; gender, age, body weight, height, BMI, and ASA values were statistically similar ($p > 0.05$). In comparisons between the groups; During position, postoperative 2nd, 8th, 16th, 24th hours, and their sum, VAS values were found to be statistically lower in Group-I ($p < 0.05$). While it was found that the first analgesic administration time was statistically longer in Group-I patients ($p<0.001$), the amounts of paracetamol and tramadol consumed in the first 24 hours were found to be statistically lower ($p<0.001$). In addition, the comfort of the anesthetist during spinal anesthesia was found to be better in Group-I (p:0.014).

Conclusion: PENG block can be used effectively as a part of perioperative multimodal analgesia in hip fracture surgery. PENG can reduce the pain levels of patients with hip fractures as well as reduce the need for additional analgesia. It also increases the comfort of the anesthetist who will administer regional anesthesia.

Keywords: Hip fracture, pericapsular nerve group, PENG block, position pain, spinal anesthesia

INTRODUCTION

Hip fractures are a common public health problem.[1] In the perioperative period, 75% of the patients suffer from moderate to severe pain associated with movement.[2] Pain causes endocrine and metabolic changes in the body. These physiological responses may contribute to chronic persistent pain after surgery in patients.[3] It can also cause pain, delirium, sleep disorders, and depression in patients.[4]

There is no standardized approach to hip fracture anesthesia because neither regional nor general anesthesia has been

shown to be superior in specific outcomes such as 30-day mortality, myocardial infarction, pneumonia, delirium, or renal failure.[5] The choice of anesthesia is therefore based on surgical concerns, including the expected operative time and complexity of the operation, as well as the patient's comorbidities and preferences. The patient should be aware of the risks and benefits of both general and neuraxial anesthesia, and a joint decision should be made on the most appropriate anesthesia technique.[6]

Positioning patients with hip fractures for regional anesthesia is very difficult due to pain. Opioids and nonsteroidal anti-inflammatory drugs are widely used for analgesia, but these drugs can cause serious side effects due to decreased hepatic and renal functions in the geriatric age group.[7] Regional anesthesia techniques (nerve blocks or field blocks) applied by experienced personnel provide perioperative analgesia, lead to a decrease in the amount of opioids administered to patients, and are recommended because they cause a decrease in opioid-related side effects such as nausea, vomiting, and respiratory depression.[8]

The anterior hip capsule is innervated by the obturator nerve, the accessory obturator nerve, and the femoral nerve. These three nerves should be targeted to provide analgesia for hip fractures. A recent anatomical study confirmed the innervation of the anterior hip capsule by these three main nerves.[9]

The application of regional anesthesia techniques such as femoral nerve block, fascia iliaca block, psoas compartment block, or lateral femoral cutaneous nerve block, which are applied with ultrasound and/or nerve stimulator, which is an effective perioperative analgesia method in pain control in patients with hip fractures and reduces opioid consumption, is becoming increasingly common. In addition, new peripheral nerve block methods are being investigated in this field. Pericapsular nerve group (PENG) block, defined in 2018, is a new regional anesthesia technique first developed for postoperative analgesia in total hip arthroplasties (THA) where the motor functions of the quadriceps muscle are preserved.[10] It is thought that it provides comprehensive analgesia by administering a local anesthetic to the myofascial area between the psoas muscle and the superior pubic ramus.[11]

The hypothesis in this study is that PENG block application in patients scheduled for hip fracture operation under spinal anesthesia may reduce the VAS scores of the patients as well as reduce the need for additional postoperative analgesia. VAS scores were determined as the primary outcome at the time of spinal anesthesia application and during the postoperative 24-hour period. First analgesia need, total analgesic consumption, and anesthetist comfort during spinal anesthesia were determined as secondary outcomes.

METHODS

This study was conducted as a prospective, randomized controlled study after the approval of the Ankara Bilkent City Hospital Clinical Researches Ethics Committee (Date: 24.02.2021 and Decision No: E2-21-200). After the patients were informed about the study and their consent was obtained, they were included in the study. Patients over the age of 50, with ASA I-III, who will be operated on due to hip fracture in the Department of Anesthesiology and Reanimation of the Ankara Bilkent City Hospital between February 2021 and May 2021 were included in the study. ASA IV and above, coagulopathy and using anticoagulant drugs, accompanying severe cardiac, respiratory, hepatic, and renal disease, known diabetic neuropathy, motor or sensory deficit after a previous cerebrovascular accident, known neuropsychiatric disorder, local anesthetic allergy, patients with infection or wound scar at the application site, were excluded from the study.

The patients were randomly divided into two groups using the closed envelope method (Group-I and Group-II). Visual analogue scale (VAS) was recorded for both groups in the preoperative period before the applications (0:No pain, 10: Unbearable pain). ECG, arterial blood pressure, pulse, and oxygen saturation measurements were routinely performed in all patients during the preoperative, intraoperative, and postoperative periods.

Patients in Group-I underwent PENG block with 20 ml, 50 mg of 0.25% bupivacaine using linear probe (HFL 38x/13-6 MHz Transducer) USG (Sonosite S-Nerve; SonoSite Inc, Bothell, WA, USA) in the preoperative waiting room 30 minutes before the operation. In the PENG block, the USG probe was placed parallel to the imaginary line passing between the anterior inferior iliac spine and iliopubic eminence. The iliopubic eminence, iliopsoas muscle and tendon, femoral artery, and pectineus muscle were visualized. A peripheral block needle (22G 80 mm iğne, Pajunk, GmbH, Medizintechnologie, Karl-Hall-Strasse 1, 78187 Geisingen / Germany) was advanced between the psoas tendon and the iliopubic ramus with the in-plane technique. 20 ml of 0.25% bupivacaine was injected after negative aspiration showed that there was no hemorrhagic injury (Figure 1).

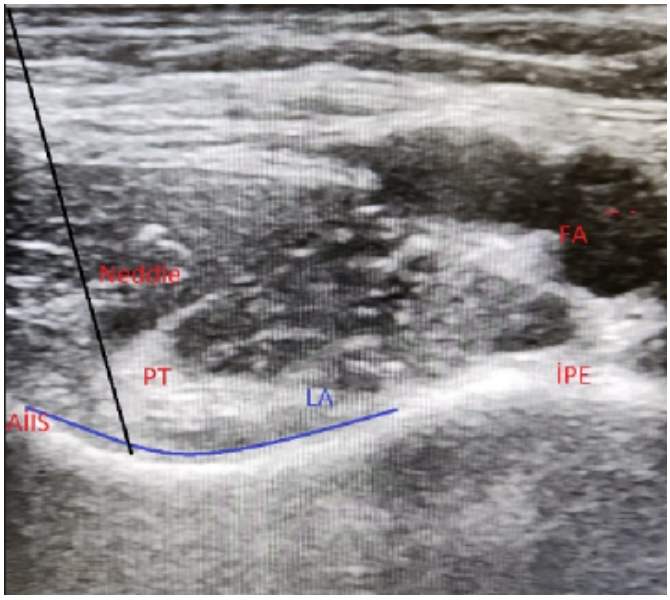


Figure 1. Sonographic view of PENG block. (FA: Femoral artery, PT: Psoas tendon, IPE: Ileopubic eminence, AIIS: Anterior inferior iliac spine, LA: Local anesthetic)

Sensory block time after the block was recorded every 5 minutes for 30 minutes. While evaluating sensory block, pinprick sensory examination was used (sensation: 0,

hypoesthesia:1, no sensation:2). Patients with hypoesthesia were considered suitable for positioning.

Intravenous fentanyl 1 mcg/kg was administered to the patients in Group II, 1 minute before positioning for spinal anesthesia.

All patients were placed in the lateral decubitus position with the fractured side down. Meanwhile, arterial blood pressure, pulse, oxygen saturation values, and VAS scores were recorded. 1 mcg/kg of intravenous fentanyl was administered to patients with a VAS score higher than 4 during the position. Heavy bupivacaine 10 mg at 0.5% concentration was administered to the patients through the L4-L5 or L3-L4 spinal space. All patients were kept in the side position for 5 minutes after spinal anesthesia. Arterial blood pressure, pulse, oxygen saturation measurements, and VAS scores at the 5th minute after spinal anesthesia were recorded. The patients were then placed in the supine position. In addition, the comfort of the anesthetist who will administer the spinal anesthesia during the application was questioned. (0: bad, 1: fair, 2: good, 3: very good).

The patients' age, gender, height, weight, body mass index, ASA score, comorbidities, type of fracture, type of operation (endoprosthesis, proximal femoral nail, etc.), and duration of operation were recorded.

In the postoperative period, VAS scores at 0th, 2nd, 8th, 16th, and 24th hours and the time of first analgesic administration were recorded. Paracetamol was given to patients with a VAS score above 4 in the postoperative period. A minimum of 6 hours waited between two paracetamol doses. During the follow-up of the patients, tramadol was given to patients with a pain score above 4 despite paracetamol. The total amount of paracetamol and tramadol consumed in the first 24 hours postoperatively were recorded.

Statistical Analysis

Data analysis was performed using the IBM SPSS 25.0 (Armonk, NY: IBM Corp.) statistical package program. While evaluating the study data, chi-square[2] test was used to compare qualitative data as well as descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min-max). The suitability of the data to the normal distribution was evaluated using the kolmogorov-smirnow test, skewness-kurtosis, and graphical methods (histogram, Q-Q Plot, stem and leaf, boxplot). In the study, in the comparison of normally distributed quantitative data between groups; the Independent samples t-test (t-test in independent groups) and repeated measures anova (repeated measure analysis of variance) were used for within-group comparison. The statistical significance level was accepted as <0.05. Power analysis was made with G*Power 3.1.9.4 statistical package program; n1=34, n2=34, α=0.05, Effect Size (d) = 0.80; power = 90% was found.

RESULTS

The data of 68 patients who were operated on under spinal anesthesia for hip fractures between February 2021 and May 2021 were analyzed (Figure 2).

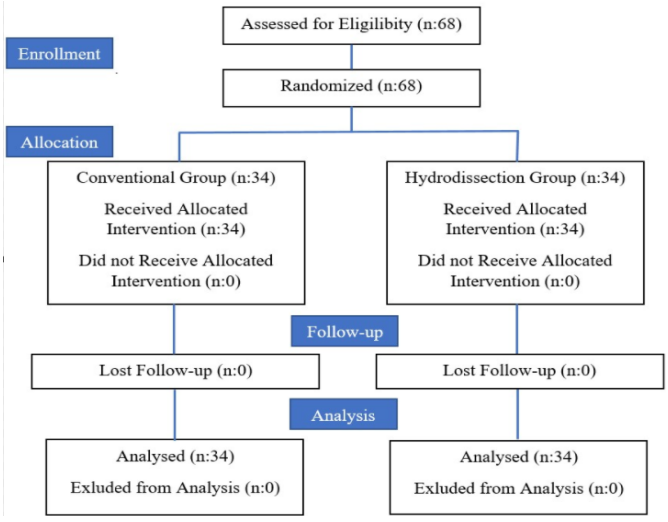


Figure 2. Flow chart.

The demographic and operational characteristics of the patients were statistically similar. The comfort scale of the anesthetist during spinal anesthesia was found to be better in Group I (Table 1).

Table 1. Comparison of patient characteristics between groups

		Group I (n=34)	Group II (n=34)	p
Gender	Male	14 (41.2 %)	8 (23.5 %)	0.195 [a]
	Female	20 (58.8 %)	26 (76.5 %)	
Age (Year)		78.7 ± 9.0	81.6 ± 6.7	0.147 [b]
Body weight (kg)		73.9 ± 12.5	74.8 ± 10.2	0.751 [b]
Height (cm)		163.4 ± 10.3	161.1 ± 9.2	0.324 [b]
Body mass index (kg/m²)		27.7 ± 4.2	28.7 ± 3.8	0.291 [a]
ASA	I	1 (2.9 %)	0 (0.0 %)	0.956 [a]
	II	14 (41.2 %)	11 (32.4 %)	
	III	19 (55.9 %)	23 (67.6 %)	
Fracture type	Intertrochanteric femur fracture	19 (55.9 %)	21 (61.8 %)	0.741 [a]
	Subtrochanteric femur fracture	5 (14.7 %)	3 (8.8 %)	
	Femur neck fracture	10 (29.4 %)	10 (29.4 %)	
Fracture side	Right	18 (52.9 %)	17 (50.0 %)	1.000 [a]
	Left	16 47.1 %)	17 (50.0 %)	
Type of surgery	Endoprosthesis	15 (44.1 %)	21 (61.8 %)	0.224 [a]
	PFN	18 (52.9 %)	13 (38.2 %)	
Anesthetist's comfort scale during spinal anesthesia	Bad	2 (5.9 %)	3 (8.8 %)	0.014 [a]
	Middle	8 (23.5 %)	19 (55.9 %)	
	Good	14 (41.2 %)	10 (29.4 %)	
	Very good	10 (29.4 %)	2 (5.9 %)	
Operation time (min)		119.5 ± 28.4	107.7 ± 29.3	0.097 [b]

ASA: American Society Of Anesthesiologists, ARIF: Arthroscopic reduction and internal fixation, PFN: Proximal femoral nail, a: Chi-square test (n / %), b: Independent samples T test (Mean ± SD), Min:Minumum

While SAB was found to be lower in Group-I at the preoperative time (p:0.007), there was no significant difference between the groups during the position and at the 5th minute after spinal anesthesia (p >0.05). The groups were similar in terms of DAB and heart rate (p >0.05). When the groups were compared in terms of SpO_2, they were found to be similar at the time of preoperative (p >0.05), while the SpO_2 values of the patients in Group-I were found to be higher during the position (p:0.002) and at the 5th minute after spinal anesthesia (p <0.001) (Table 2).

In comparisons between groups in terms of VAS scores; there was no statistically significant difference between the groups in terms of preoperative, 5th minute after spinal anesthesia, and postoperative 0th-hour VAS values (p >0.05). There was a statistically significant difference between the groups in terms

of VAS values during position (p:0.009), at postoperative 2nd, 8th, 16th, 24th hour, and their sum (p <0.001). The values in group II were higher in all cases where there was a difference (Figure 3). In group comparisons; It was found that there was a statistically significant difference between the VAS values at the preoperative, during the position, and 5th minute after spinal anesthesia in both groups (p < 0.05), and the values at the three measurement times in both groups were different from each other.

Table 2. Comparison of SAP, DAP, Pulse, and SpO_2

	Group I (n=34)	Group II (n=34)	p*
SAP (mmHg)			
Preoperative[1]	143.9±21.2	157.9±20.2	0.007
During position[2]	147.2±20.9	157.1±22.4	0.065
5 min after spinal anesthesia[3]	119.3±18.7	117.4±22.6	0.714
DAP (mmHg)			
Preoperative[1]	78.1±11.2	77.9±10.4	0.956
During position[2]	71.2±14.0	75.6±13.4	0.190
5 min After spinal anesthesia[3]	63.6±13.2	58.4±12.6	0.107
Pulse (min)			
Preoperative[1]	91.2±17.4	87.3±15.7	0.326
During position[2]	90.8±16.3	87.0±13.8	0.301
5 min after spinal anesthesia[3]	89.9±18.5	84.6±18.0	0.238
SpO_2 (%)			
Preoperative[1]	93.5±3.2	92.9±3.9	0.541
During position[2]	92.7±3.4	89.6±4.4	0.002
5 min after spinal anesthesia[3]	92.8±3.1	89.4±4.2	<0.001

Group I: PENG, Group II: Kontrol, *: Independent samples t Test (Mean ± SD), SAP: Systolic arterial pressure, DAP: Diastolic arterial pressure, SpO2: Peripheral oxygen saturation

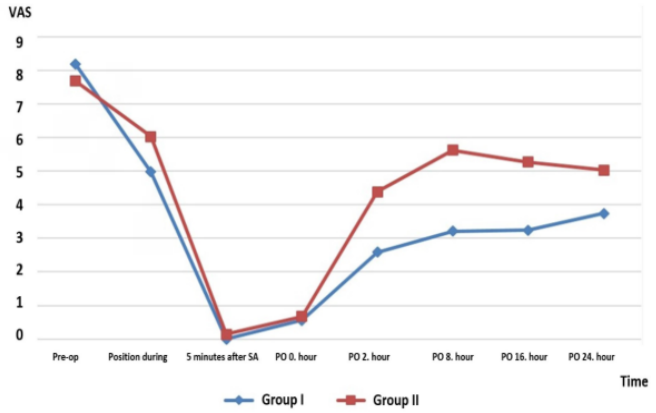


Figure 3. Comparison of VAS between groups. VAS: Visual analog scale, Pre-op: Preoperative, PO: Postoperative.

In intra-group comparisons of the postoperative period; It was found that there was a statistically significant difference (p < 0.05) in terms of VAS values between the measurement times in both groups. Post-hoc tests were applied to find out which time(s) the difference was. In both groups, postoperative 0th-hour values were found to be lower than the values at other times. In addition, it was found that there was a difference between the postoperative 2nd and 24th-hour VAS values in Group I, and between the postoperative 2nd and 8th-hour VAS values in Group II (Table 3).

In comparisons between groups; It was found that there was a statistically significant difference between the groups in terms of the first analgesic administration time in the postoperative period, and the amounts of paracetamol and tramadol consumed in the first 24 hours postoperatively (p <0.001). It was found that the first analgesic administration time was longer and the amounts of paracetamol and tramadol consumed in the first 24 hours were lower in patients in Group I (Table 4).

Table 3. Comparison of VAS between and within groups

VAS	Group I (n=34)	Group II (n=34)	p*
Preoperative	8.2±1.1	7.7±1.4	0.109
During position	5.0±1.6	6.0±1.6	0.009
5 min After spinal anesthesia	0.0±0.0	0.1±0.9	0.325
p**	<0.001	<0.001	
Difference	All	All	
Postoperative 0th hour [1]	0.6±1.0	0.7±1.0	0.634
Postoperative 2nd hour [2]	2.6±1.7	4.4±2.0	<0.001
Postoperative 8th hour [3]	3.2±1.3	5.6±1.6	<0.001
Postoperative 16th hour [4]	3.2±1.6	5.3±1.3	<0.001
Postoperative 24th hour [5]	3.7±1.2	5.0±1.1	<0.001
p**	<0.001	<0.001	
Difference	1 with others 2 with 5	1 with others 2 with 3	
Sum of VAS scores at five separate times	13.4±4.6	21.1 ± 3.9	<0.001

Group I: Peng, Group II: Kontrol, VAS: Visual analog scale, *: Independent Samples T test (Mean ± SD), **: Repeated measures anova (Mean ± SD)

Tablo 4. Comparison of the first analgesic administration time in the first 24 hours postoperatively, the average amounts of paracetamol-tramadol consumed, and the doses of paracetamol-tramadol administered between the groups

Postoperative First 24 Hours		Group I (n=34)	Group II (n=34)	p
Time to first analgesic		9.0 ± 6.7	3.7 ± 2.1	<0.001 a
Paracetamol amount	1 gr	12 (%35.3)	0 (%0.0)	<0.001 b
	2 gr	22 (%64.7)	28 (%82.4)	
	3 gr	0 (%0.0)	6 (%17.6)	
Total paracetamol amount (gr)		1,6 ± 0.5	2.2 ± 0.4	<0.001 a
Tramadol amount	0 gr	21 (%61.8)	3 (%8.8)	<0.001 b
	100 mg	9 (%26.5)	7 (%20.6)	
	200 mg	4 (%11.8)	24 (%70.6)	
Total tramadol amount (mg)		50 ± 70.7	161.8 ± 65.2	<0.001 a

Grup I: PENG, Grup II: Kontrol, A: Independent samples t test (Mean ± SD), b: Chi-square test (n / %)

DISCUSSION

In this study performed on patients who will be operated under spinal anesthesia due to hip fracture, it has been observed that PENG block reduces the pain that may occur due to the fracture during the position and in the postoperative period. In addition, it has been observed that patients need less additional analgesia in the postoperative period with this application. In addition, thanks to the PENG block, the comfort of the anesthetist who applies the spinal anesthesia increases due to giving the patients a more comfortable position.

Hip fracture is a traumatic condition that is usually treated with neuraxial anesthesia techniques and is mostly seen in elderly patients. It causes severe pain both in the lateral position of the patients during neuraxial anesthesia and in the postoperative period. Pain control may affect the success of the neuraxial anesthesia method in the lateral position. In addition, successful pain management in the postoperative period shortens the discharge time and contributes positively to postoperative patient outcomes.[12] Regional techniques are generally preferred for pain management in hip fractures, as the patient population is at risk for the adverse effects of opioids and nonsteroidal anti-inflammatory drugs (NSAIDs), including cognitive impairment, respiratory depression, gastrointestinal complications, and renal dysfunction.[8,13,14] One of the main goals of anesthesia in hip fracture surgery is to limit the use of opioid-based drugs in perioperative pain management while providing position-dependent and postoperative pain control during spinal anesthesia application.[15]

Regional analgesia techniques are widely used because they limit the use of opioids in perioperative hip fracture

analgesia and provide relatively effective, effective, and safe analgesia. Perioperative regional analgesia methods have been recommended in perioperative pain management since the 1990s, and fascia iliaca block, femoral nerve block, and 3-in-1 femoral nerve block are used for this purpose. A recent Cochrane study of nerve blocks for hip fractures, which included fascia iliaca block, femoral nerve block, and 3-in-1 femoral nerve block, showed high-quality evidence supporting a reduction in dynamic pain within 30 minutes post-block. However, no analgesic superiority of any of these techniques over the other has been demonstrated.[16]

Although each of these blocks alone provides a certain level of perioperative analgesia for hip fractures and positively affects patient outcomes, it has been discussed in the literature that these blocks do not cover all the nerves associated with hip fracture and cause varying degrees of quadriceps weakness due to the involvement of the femoral nerve. To summarize these discussions; Although femoral nerve block has been shown to provide effective postoperative analgesia, it has also been associated with postoperative quadriceps muscle weakness. This may cause a delay in mobilization and recovery times.[17–19] The fascia iliaca block has been defined as a suitable alternative with less apparent quadriceps weakness due to injection at a point farther from the femoral nerve.[20] However, it has been reported in the literature that it causes moderate quadriceps weakness and does not provide effective analgesia after hip arthroscopy.[21] 3-in-1 femoral block, which was not as effective as the fascia iliaca block before the use of USG, has been shown to be as effective as the fascia iliaca block with the initiation of the use of USG.[22,23]

Femoral nerve block and fascia iliaca block have shown good results for post-surgical analgesia. However, the obturator nerve and accessory obturator nerve should also be targeted to achieve more effective perioperative pain control.[24,25] The anterior hip capsule is innervated by the obturator nerve, the accessory obturator nerve, and the femoral nerve. These three nerves should be targeted to provide analgesia in hip fractures.[11] Short et al.[26] confirmed the innervation of the anterior hip by these three nerves in a recent anatomical study. It also found that the accessory obturator nerve and the femoral nerve play a larger role in anterior hip innervation than previously reported.[9]

The branches from the femoral nerve and accessory obturator nerve are located between the anterior inferior iliac spine (AIIS) and the iliopubic eminence (IPE), while the obturator nerve is located close to the inferomedial acetabulum. Using this information, Girón et al.[11] described a new regional anesthetic technique, which they named pericapsular nerve group (PENG) block, for pain control on hip fractures. In this study conducted on five patients, a significant decrease in pain scores was found in patients without quadriceps muscle weakness. Orozco et al.[15] demonstrated successful perioperative pain control using the PENG block technique in five patients who underwent hip arthroscopic surgery.

Although peripheral nerve blocks are widely used for perioperative analgesia for hip fracture surgery, the effectiveness of each is a matter of debate, so new blocks continue to be investigated. PENG block is a block that has just started to be applied and is becoming more common in clinical use. Although PENG block has been shown to be effective in postoperative analgesia for hip fracture surgery, we did not find any randomized controlled studies investigating the perioperative pain characteristics, including the postoperative period, as well as the preoperative application of the PENG block for neuroaxial anesthesia and positioning during spinal anesthesia. We found only studies in which case series were collected on this subject.[11,27] This study, it was aimed to investigate the effectiveness of PENG block in pain management starting from positioning for spinal anesthesia and up to the first 24 hours postoperatively for hip fracture surgery under unilateral spinal anesthesia.

The results of our study showed that PENG block provides more effective analgesia than the sedoanalgesia method applied with fentanyl at doses specified in the literature during spinal anesthesia positioning.[28] In accordance with the literature, it was determined that it is necessary to provide analgesia during the position while applying spinal anesthesia, PENG block application provides analgesia, albeit partial, and this application is more effective than the frequently used fentanyl analgesia. Acharya et al.,[27] in their study on 10 patients, found the average pain score of 7.5 before the block to 1.2 when the spinal anesthesia position was given. In our study, we found that the mean pain score, which was 8.2 before the PENG block, decreased to 5 during the pre-spinal anesthesia position. As shown in the literature, we preferred unilateral spinal anesthesia to traditional spinal anesthesia because it has fewer hemodynamic side effects.[29] In our study, we found that the VAS score decreased significantly during position with the effect of the PENG block. Unlike the literature, the pain scores we detected were higher. The reason for this difference may be that, unlike Acharya et al.,[27] we placed the lateral position (for unilateral spinal anesthesia using low dose local anesthetic to provide hemodynamic stability) with the fractured side down instead of the traditional spinal anesthesia position in our study. In this regard, new studies are needed to evaluate the analgesic efficacy of PENG block in different spinal anesthesia positions.

In our study, we observed that the need for total sedoanalgesia before spinal anesthesia was less in the PENG block group, and we found that early peripheral oxygen saturations during spinal anesthesia were significantly higher in this group compared to the control group. In addition, we found that the comfort level reported by the anesthetists during spinal anesthesia was more positive in the PENG group. Anesthetists in the PENG block group reported that they performed a more comfortable spinal anesthesia application. The reason for this difference may be that the patients in the control group could not be effectively positioned due to sedation and impaired cooperation due to higher position-related pain levels. The reason for the decrease in saturation values, albeit minimally, in the control group may be opioid-related respiratory depression, which is also mentioned in the literature in the elderly patient group.[13,14]

Hwang et al.[31] show that approximately 36% of hip fractures do not receive any analgesia, and opioids are used in 57%.30 Foss et al. showed that regional analgesia techniques were

more effective in reducing dynamic pain compared to systemic opioids and that similar results were obtained with regional analgesia techniques and opioids in pain at rest.

The prevalence of delirium after hip fracture surgery was found to be 40% with the effect of opioid narcotics.[32] Lee et al.[33] found that the 1-year mortality rate was almost 2 times higher in patients with dementia or delirium after hip fracture. Despite the known adverse effects of opioid analgesia in the vulnerable elderly population, schepis and McCabe published findings from the National survey on Drug Use and Health that showed a sustained increase in opioid use in the older adult population.[34]

The morbidity and mortality associated with delirium are being struggled with. Alternatives to opioids are being explored, including various nerve blocks and systemic treatments such as methylprednisolone, to control pain in elderly hip fracture patients.[35,36]

A Cochrane study concluded that the use of peripheral nerve blocks made no difference in pain relief, length of hospital stay, or patient satisfaction compared to a neuraxial block.[37]

In Freeman and Clarke's extensive literature review, it was emphasized that analgesia in the elderly population should be focused on minimizing risk factors for delirium, including pain and constipation side effects. They found that fascia iliaca block is safe and easy to apply in the elderly population, reduces the need for opioids, and is effective in reducing pain and preventing delirium.[38] Bang et al.[39] conducted a prospective, randomized study in postoperative hemiarthroplasty patients who received patient-controlled analgesia versus fascia iliaca block and found that VAS scores were similar in both groups, but opioid use was significantly lower in the block group.

There is limited literature comparing PENG block with other regional anesthesia techniques for postoperative analgesia of hip fractures. Lin et al.[40] compared PENG and femoral block for postoperative analgesia in hip fractures. In this single-center randomized controlled double-blind study, it was found that patients who underwent PENG block had lower pain scores than patients who underwent femoral block.

Bhattacarya et al.[41] compared the onset of analgesia and total analgesia time of PENG block and fascia iliaca block in their study on 50 patients with femoral neck fractures. They found that PENG block had a faster onset of pain control compared to fascia iliaca block in patients with femoral neck fractures, however, it was almost equally effective (mean 10 hours) in terms of block duration in both groups. In our study, we found that VAS scores at the 2nd, 8th, 16th, and 24th hours in the postoperative period were significantly lower in patients who underwent PENG block compared to the control group and that the total amount of paracetamol and tramadol consumed in the postoperative period was significantly lower. We found that the PENG block group was significantly later than the control group at the time of first dose analgesic administration in the postoperative period. This result shows us that PENG block provides effective analgesia in the postoperative period in hip fractures and can be used to reduce opioid consumption. More randomized controlled trials are needed on the efficacy of PENG block. We think that the PENG block is an easily applicable field block because spina iliaca anterior superior, iliopubic eminence and psoas tendon are easily identifiable sonographic points. In our study, no serious adverse events such as permanent nerve damage, major vascular damage, or local anesthetic systemic toxicity were observed after PENG block, which is quite satisfactory.

PENG block may have potential advantages over traditional regional analgesia techniques such as femoral nerve or fascia iliaca blocks for hip fracture operations. One of these potential advantages may be more extensive blocking of the sensory nerves that innervate the hip. Due to this feature, it can provide more effective analgesia in perioperative analgesia. This situation increases patient satisfaction and postoperative i.v. may lead to decreased consumption of analgesics and/or opioids. It can be used as part of perioperative multimodal analgesia, which ultimately results in effective but less adverse events. In addition, if studies with large patient numbers confirm the absence of quadriceps weakness after PENG block, this may contribute to early postoperative recovery by enabling early mobilization of patients.

This study has some limitations. First of all, our study is single-centered. Therefore, we cannot generalize to the whole population. Therefore, multicenter studies may give better results in this regard. Second, pain monitoring was limited to 24 hours. Prospective randomized studies at 48 and 72 hours postoperatively may be appropriate to evaluate the longer-term analgesic efficacy.

CONCLUSION

In this study, we found that patients who underwent PENG block had reduced pain during spinal anesthesia positioning and lower VAS scores while providing less opioid consumption in the postoperative period. This study shows that PENG block is promising as a viable and perioperative analgesia technique. In the light of all this information, randomized controlled studies are needed to compare PENG block with blocks such as femoral nerve block and fascia iliaca block. We believe that this study will lead to the proliferation of studies using PENG blocks and contribute to its use in clinical practice.

ETHICAL DECLARATIONS

Ethical approval

The study was carried out with the permission of Ethics Committe of the Ankara Bilkent City Hospital (Date: 24.02.2021, Decision No: E2-21-200).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Maggi S, Kelsey JL, Litvak J, Heyse SP. Incidence of hip fractures in the elderly: a cross-national analysis. *Osteoporos Int*. 1991;1(4):232-241.
2. Maxwell L, White S. Anaesthetic management of patients with hip fractures: An update. *Anaesthesia and Intensive Care Med*. 2013;13(5): 179-183.
3. Layzell MJ. Use of femoral nerve blocks in adults with hip fractures. *Nurs Stand*. 2013;27(52):49-56. doi: 10.7748/ns2013.08.27.52.49.e7390
4. Abou Setta AM, Beaupre LA, Rashiq S, et al. Comparative effectiveness of pain management interventions for hip fracture: a systematic review. *Ann Intern Med*. 2011;155(4):234-245. doi: 10.7326/0003-4819-155-4-201108160-00346
5. O'Donnell CM, McLoughlin L, Patterson CC, et al. Perioperative outcomes in the context of mode of anaesthesia for patients undergoing hip fracture surgery: systematic review and meta-analysis. *Br J Anaesth*. 2018;120(1):37-50. doi: 10.1016/j.bja.2017.09.002
6. Liu K, Chan TC, Irwin MG. Anaesthesia for fractured neck of femur. *Anaesthesia and Intensive Care Med*. 2022;22(1):24-27.
7. Parker MJ, Griffiths R, Appadu BN. Nerve blocks (subcostal, lateral cutaneous, femoral, triple, psoas) for hip fractures. *Cochrane Database Syst Rev*. 2000;2(1):001159. doi: 10.1002/14651858.CD001159
8. Parker MJ, Handoll HH, Griffiths R. Anaesthesia for hip fracture surgery in adults. *Cochrane Database Syst Rev*. 2004;18(4):000521.
9. Bhatia A, Hoydonckx Y, Peng P, Cohen SP. Radiofrequency procedures to relieve chronic hip pain: an evidence-based narrative review. *Reg Anesth Pain Med*. 2018;43(1):72-83. doi:10.1097/AAP 0000000000000694
10. Berlioz BE, Bojaxhi E. PENG regional block. 2021 Mar 25. In: statpearls (Internet). Treasure Island (FL): StatPearls. 2022;15(5):33351429.
11. Arango GL, Peng PWH, Chin KJ, Brull R, Perlas A. Pericapsular nerve group (PENG) block for hip fracture. *Reg Anesth Pain Med*. 2018;43(8): 859-863. doi: 10.1097/AAP.0000000000000847
12. Morrison SR, Magaziner J, McLaughlin MA, et al. The impact of post-operative pain on outcomes following hip fracture. *Pain*. 2003;103(3): 303-311. doi: 10.1016/S0304-3959(02)00458-X
13. Pergolizzi J, Böger RH, Budd K, et al. Opioids and the management of chronic severe pain in the elderly: consensus statement of an international expert panel with focus on the six clinically most often used World health organization step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain Pract*. 2008;8(4):287-313. doi: 10.1111/j.1533-2500.2008.00204.x
14. Jahr JS, Breitmeyer JB, Pan C, Royal MA, Ang RY. Safety and efficacy of intravenous acetaminophen in the elderly after major orthopedic surgery: subset data analysis from 3, randomized, placebo-controlled trials. *Am J Ther*. 2012;19(2):66-75. doi: 10.1097/MJT.0b013e3182456810
15. Orozco S, Muñoz D, Jaramillo S, Herrera AM. Pericapsular nerve group (PENG) block for perioperative pain control in hip arthroscopy. *J Clin Anesth*. 2020;59(1):3-4. doi: 10.1016/j.jclinane.2019.04.037
16. Guay J, Parker MJ, Griffiths R, Kopp S. Peripheral nerve blocks for hip fractures. *Cochrane Database Syst Rev*. 2017;11(5):001159.
17. Luo TD, Ashraf A, Dahm DL, Stuart MJ, McIntosh AL. Femoral nerve block is associated with persistent strength deficits at 6 months after anterior cruciate ligament reconstruction in pediatric and adolescent patients. *Am J Sports Med*. 2015;43(2):331-336.
18. Krych A, Arutyunyan G, Kuzma S, et al. Adverse effect of femoral nerve blockade on quadriceps strength and function after ACL reconstruction. *J Knee Surg*. 2015;28(1):83-88. doi: 10.1055/s-0034-1371769
19. El Ahl MS. Femoral nerve block versus adductor canal block for postoperative pain control after anterior cruciate ligament reconstruction: a randomized controlled double blind study. *Saudi J Anaesth*. 2015;9(3):279-282. doi: 10.4103/1658-354X.154708
20. Mudumbai SC, Kim TE, Howard SK, et al. An ultrasound-guided fascia iliaca catheter technique does not impair ambulatory ability within a clinical pathway for total hip arthroplasty. *Korean J Anesth*. 2016;69(4): 368-375. doi: 10.4097/kjae.2016.69.4.368
21. Behrends M, Yap EN, Zhang AL, et al. Preoperative fascia iliaca block does not improve analgesia after arthroscopic hip surgery, but causes quadriceps muscles weakness: a randomized, double blind trial. *Anesthesiology*. 2018;129(3):536-543.
22. Reavley P, Montgomery AA, Smith JE, et al. Randomised trial of the fascia iliaca block versus the '3-in-1' block for femoral neck fractures in the emergency department. *Emerg Med J*. 2015;32(9):685-689. doi: 10.1136/emermed-2013-203407
23. Capdevila X, Biboulet P, Bouregba M, et al. Comparison of the three-in-one and fascia iliaca compartment blocks in adults: clinical and radiographic analysis. *Anesth Analg*. 1998;86(5):1039-1044. doi: 10.1097/00000539-199805000 00025
24. Shin JJ, McCrum CL, Mauro CS, Vyas D. Pain management after hip arthroscopy: systematic review of randomized controlled trials and cohort studies. *Am J Sports Med*. 2018;46(13):3288-3298. doi: 10.1177/0363546517734518
25. Steinhaus ME, Rosneck J, Ahmad CS, Lynch TS. Outcomes after peripheral nerve block in hip arthroscopy. *Am J Orthop*. 2018;47(6):1. doi: 10.12788/ajo.2018.0049
26. Short AJ, Barnett JJG, Gofeld M, et al. Anatomic study of innervation of the anterior hip capsule: implication for image-guided intervention. *Reg Anesth Pain Med*. 2018;43(2):186-192.
27. Acharya U, Lamsal R. Pericapsular nerve group block: an excellent option for analgesia for positional pain in hip fractures. *Case Rep Anesthesiol*. 2020;12(1):1830136. doi: 10.1155/2020/1830136
28. Bantie M, Mola S, Girma T, Aweke Z, Neme D, Zemedkun A. Comparing analgesic effect of intravenous fentanyl, femoral nerve block and fascia iliaca block during spinal anesthesia positioning in elective adult patients undergoing femoral fracture surgery: a randomized controlled trial. *J Pain Res*. 2020;26(13):3139-3146. doi: 10.2147/JPR.S282462
29. Salem BF, Grati L, Gahbiche M. Rachianesthésie unilatérale et bénéfice hémodynamique des faibles doses de bupivacaïne hyperbare (Unilateral spinal anaesthesia and haemodynamic benefit of low dose hyperbaric bupivacaine). *Ann Fr Anesth Reanim*. 2003;22(2):145-146. doi: 10.1016/s0750-7658(02)00865-1
30. Hwang U, Richardson LD, Sonuyi TO, Morrison RS. The effect of emergency department crowding on the management of pain in older adults with hip fracture. *J Am Geriatr Soc*. 2006;54(2):270-275. doi: 10.1111/j.1532-5415.2005.00587.x
31. Foss NB, Kristensen BB, Bundgaard M, et al. Fascia iliaca compartment blockade for acute pain control in hip fracture patients: a randomized, placebo-controlled trial. *Anesthesiology*. 2007;106(4):773-778. doi: 10.1097/01.anes.0000264764.56544.d2
32. Sieber FE, Mears S, Lee H, Gottschalk A. Postoperative opioid consumption and its relationship to cognitive function in older adults with hip fracture. *J Am Geriatr Soc*. 2011;59(12):2256-2262.
33. Lee HB, Oldham MA, Sieber FE, Oh ES. Impact of delirium after hip fracture surgery on one-year mortality in patients with or without dementia: a case of effect modification. *Am J Geriatr Psychiatry*. 2017;25(3):308-315. doi: 10.1016/j.jagp.2016.10.008
34. Schepis TS, McCabe SE. Trends in older adult nonmedical prescription drug use prevalence: results from the 2002-2003 and 2012-2013 National survey on drug use and health. *Addict Behav*. 2016;60(9):219-222. doi: 10.1016/j.addbeh.2016.04.020
35. Amiri HR, Safari S, Makarem J, Rahimi M, Jahanshahi B. Comparison of combined femoral nerve block and spinal anesthesia with lumbar plexus block for postoperative analgesia in intertrochanteric fracture surgery. *Anesth Pain Med*. 2012;2(1):32-35. doi: 10.5812/aapm.4526
36. Rahimzadeh P, Imani F, Faiz SH, Nikoubakht N, Sayarifard A. Effect of intravenous methylprednisolone on pain after intertrochanteric femoral fracture surgery. *J Clin Diagn Res*. 2014;8(4):1-4. doi: 10.7860/JCDR/2014/8232.4305
37. Guay J, Johnson RL, Kopp S. Nerve blocks or no nerve blocks for pain control after elective hip replacement (arthroplasty) surgery in adults. *Cochrane Database Syst Rev*. 2017;(31)10:011608.
38. Freeman N, Clarke J. Perioperative pain management for hip fracture patients. *Orthopaedics and Trauma*. 2016;30(2):145-152.
39. Bang S, Chung J, Jeong J, Bak H, Kim D. Efficacy of ultrasound-guided fascia iliaca compartment block after hip hemiarthroplasty: a prospective, randomized trial. *Medicine*. 2016;95(39):5018.

40. Lin DY, Morrison C, Brown B, et al. Pericapsular nerve group (PENG) block provides improved short-term analgesia compared with the femoral nerve block in hip fracture surgery: a single-center double-blinded randomized comparative trial. *Reg Anesth Pain Med*. 2021;46(5):398-403. doi: 10.1136/rapm-2020-102315

41. Bhattacharya A, Bhatti T, Haldar M. Pericapsular nerve group block–is it better than the rest for pain relief in fracture neck of femur? *Reg Anesth Pain Med*. 2019;44(1):116. doi: 10.1136/rapm-2019-ESRAABS2019.139

MHA MEDIHEALTH ACADEMY

Eurasian Journal of
Anesthesiology & Intensive Care
Case Report

doi
10.51271/EAJAIC-0015

Malign hyperthermia in beating heart coronary artery bypass surgery

Harun Zengin, Emine Nilgün Zengin, Nevriye Salman, Sumru Şekerci

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Turkiye

Received: 10/07/2024 ◆ **Accepted**: 26/07/2024 ◆ **Published**: 06/08/2024

Cite this article: Zengin H, Zengin EN, Salman N, Şekerci S. Malign hyperthermia in beating heart coronary artery bypass surgery. *Eur J Anesthesiol Intensive Care*. 2024;1(3):72-74.

Corresponding Author: Emine Nilgun Zengin, nilbavullu@gmail.com

ABSTRACT

Malignant hyperthermia (MH) is a rare but one of the most serious complications of general anesthesia due to the hypermetabolic state of skeletal muscle. This case report aims to share the diagnosis and treatment of the patient who was diagnosed with MH intraoperatively during cardiac surgery. Consent was obtained from a 59-year-old patient who was scheduled for CABGx2 surgery on his beating heart. The patient had no comorbidities other than hypertension, was a non-smoker, and had no history of previous surgery. Hypermetabolic findings began in the 90th minute of the operation. The body temperature: 39°C; pCO2: 72 mmHg; pH: 7.15; potassium was 5.13 mEq/L and pulse was over 120 min-1. MH was considered when the color change in soda lime was observed. Following these findings, anesthesia was maintained with 100% oxygen and total intravenous anesthesia (TIVA). The patient, whose hemodynamic stabilization was achieved, was taken to the intensive care unit (ICU) in an intubated state at the end of the surgery. A single dose of 2.5 mg/kg iv dantrolene was administered in the ICU. After dantrolene, body temperature, hemodynamic and metabolic values returned to normal. The patient was extubated on the first postoperative day. The patient was followed up in the ICU for 2 days and in the ward for 5 days before being discharged without complications. Dantrolene is the specific antidote for MH. With early application, the risk of complications and mortality can be reduced. Therefore, attention should be paid to the clinical symptoms of MH, and as soon as MH is suspected, triggering agents should be removed immediately and dantrolene supply and treatment should be provided.

Keywords: Beating heart, coronary artery bypass surgery, malign hyperthermia

INTRODUCTION

Malignant hyperthermia (MH) is an autosomal dominant condition, rarely encountered but considered one of the most serious complications of general anesthesia.[1] Triggering drugs such as volatile anesthetics and depolarizing muscle relaxants increase calcium release from the sarcoplasmic reticulum, leading to a continuous rise in intracellular calcium concentration and causing uncontrolled skeletal muscle hypermetabolism.[1] As a result, MH manifests as a hypermetabolic state with symptoms such as respiratory and metabolic acidosis, hyperthermia, rhabdomyolysis, tachycardia, fatal arrhythmias, and hypoxemia.[2]

Variability in the expression of malignant hyperthermia (MH) may also stem from anesthesia-related factors, including the triggering potency of the inhalation anesthetic employed, drug dosage, and the duration of anesthesia.[3] Factors such as age and gender can additionally influence MH expression. Studies have indicated that MH predominantly occurs in younger patients, and MH reactions are reported to be twice as frequent in males compared to females.[3,4]

Due to genetic diversity, the incidence and prevalence of MH exhibit significant variations among different populations. The remarkable decrease in MH mortality since the 1970s is attributed to increased awareness of MH, the growing use of non-triggering anesthetics, enhanced monitoring standards allowing for early diagnosis, and the availability of dantrolene sodium.[4] In this case, the intention is to share the diagnosis and treatment of a patient diagnosed with intraoperative malignant hyperthermia during cardiac surgery.

CASE

The patient was 59-year-old and male. His body mass index was 30.4 kg/m^2. The patient presented with no comorbidities other than controlled hypertension. With a smoking history

of 20 pack-years, the patient was classified as ASA II. Informed consent was duly obtained from the patient. The surgical plan involved the on-pump beating heart protocol.

The patient was positioned on the operating table, and following monitoring, anesthesia induction was initiated with 200 mg propofol, 90 mg ketamine, 80 mg rocuronium, 100 mcg fentanyl, and 100 mg lidocaine. The maintenance involved the use of 1 minimum alveolar concentration (MAC) of Sevoflurane and a continuous infusion of 0.5 mcg kg min-1 remifentanil. Extracorporeal circulatory support was commenced at the 80th minute of the operation. A blood gas analysis at the 85th minute revealed mild acidosis (pH: 7.23) and an elevation in pCO_2 (54 mm Hg).

Upon repeating the blood gas analysis at the 90th minute, the pH remained constant, with pCO_2 at 72 mmHg, K at 5.13 mEq/L, a pulse rate of >120 min-1, and a body temperature of 39 °C. The observation of a change in soda-lime color prompted the consideration of malignant hyperthermia (MH). In response to this, 100% oxygen and total intravenous anesthesia (TIVA) were administered. Dantrolene was urgently requested from the pharmacy.

To address the potential MH crisis, the anesthesia circuit and soda lime were replaced, the respiratory circuit was flushed with maximum fresh gas flow, the patient underwent external cooling, and metabolic disorders were addressed. Once hemodynamic stabilization was achieved, the patient was intubated and transferred to the intensive care unit (ICU).

In the ICU, a single dose of 2.5 mg kg^1 intravenous dantrolene was administered. Following the administration of dantrolene, the patient's body temperature, hemodynamic parameters, and metabolic values normalized. Extubating was performed on the first postoperative day. The patient received intensive care for 2 days and continued to be monitored in the ward for an additional 5 days before being discharged without complications.

DISCUSSION

Malignant hyperthermia continues to pose a serious and life-threatening condition, underscoring the importance of early detection to minimize mortality and MH-related complications. Early administration of dantrolene is crucial in mitigating the risk of complications and mortality associated with MH.

Dantrolene serves as a specific antidote for MH events. Early application is associated with a decreased risk of complications and mortality.[5] According to the European malignant hyperthermia group, dantrolene should be prepared for administration within 5 minutes of recognizing the first sign of MH.6 It is reported that the risk of complications increases by 1.6 times for every 30-minute delay between the first sign of MH and the administration of dantrolene.[4]

Upon the clinical diagnosis of MH, we promptly requested dantrolene from the pharmacy and incorporated it into the patient's postoperative treatment. Following the administration of dantrolene, the patient's clinical manifestations were completely resolved. Many patients have seemingly undergone uneventful general anesthesia with triggering agents before manifesting MH reactions.[7] The exact reasons for this phenomenon are not fully elucidated, but it could be related to factors such as the duration of surgery, the choice of volatile anesthetic agent, and the concentration of the agent administered during the surgery.[2] All potent inhalation anesthetics commonly used in general anesthesia (such as desflurane, sevoflurane, isoflurane, halothane, and methoxyflurane) and the depolarizing neuromuscular blocking agent succinylcholine have the potential to induce MH.[6,8]

CONCLUSION

Dantrolene is a specific antidote for malignant hyperthermia (MH).[1] Early administration can reduce the risk of complications and mortality. It has been reported that for every 30-minute delay between the onset of the first MH symptom and the administration of dantrolene, the risk of complications increases by 1.6 times.[4] Therefore, careful attention should be given to clinical signs of MH, and as soon as MH is suspected, triggering agents should be promptly removed, dantrolene should be obtained, and treatment initiated.

ETHICAL DECLARATIONS

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Toyota Y, Kondo T, Shorin D, et al. Rapid dantrolene administration with body temperature monitoring is associated with decreased mortality in japanese malignant hyperthermia events. *Biomed Res Int*. 2023;22(23):8340209. doi: 10.1155/2023/8340209
2. Gupta P, Hopkins PM. Diagnosis and management of malignant hyperthermia. *BJA Education*. 2017;17(7):249-254. doi: 10.1093/bjaed/mkw079
3. Riazi S, Kraeva N, Hopkins PM. Updated guide for the management of malignant hyperthermia. *Can J Anaesth*. 2018;65(6):709-721. doi: 10.1007/s12630-018-1108-0
4. Riazi S, Larach MG, Hu C, Wijeysundera D, Massey C, Kraeva N. Malignant hyperthermia in Canada: characteristics of index anesthetics in 129 malignant hyperthermia susceptible probands. *Anesth Analg*. 2014;118(2):381-387. doi: 10.1213/ANE.0b013e3182937d8b
5. Larach MG, Gronert GA, Allen GC, Brandom BW, Lehman EB. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110(2):498-507. doi: 10.1213/ANE.0b013e3181c6b9b2
6. Glahn KPE, Bendixen D, Girard T, et al. Availability of dantrolene for the management of malignant hyperthermia crises: european malignant hyperthermia group guidelines. *Br J Anaesth*. 2020;125(2):133-140.

7. Hopkins PM. Malignant hyperthermia: advances in clinical management and diagnosis. *Br J Anaesth*. 2000;85(1):118-128.

8. Rüffert H, Bastian B, Bendixen D, et al. Consensus guidelines on perioperative management of malignant hyperthermia suspected or susceptible patients from the European Malignant hyperthermia group. *Br J Anaesth*. 2021;126(1):120-130. doi: 10.1016/j.bja.2020.09.029