Turk J Anaesth Reanim 2016; 44: 21-5 DOI: 10.5152/TJAR.2016.80037

Original Article

Perioperative Effects of Different Narcotic Analgesics Used to Improve Effectiveness of Total Intravenous Anaesthesia

Ayten Saraçoğlu[1], Zeynep Eti[1], Deniz Konya[2], Kadir Kabahasanoğlu[1], Fevzi Yılmaz Göğüş[1]
[1]*Department of Anaesthesiology and Reanimation, Marmara University School of Medicine, İstanbul, Turkey*
[2]*Department of Neurosurgery, Marmara University School of Medicine, İstanbul, Turkey*

Abstract

Objective: We aimed to evaluate the depth of anaesthesia, perioperative haemodynamics, postoperative pain scores, analgesic consumption in patients receiving remifentanil- or alfentanil-based total intravenous anaesthesia for single-level lumbar discectomy.

Methods: Seventy patients undergoing discectomy were enrolled in the study. Patients were intravenously administered an initial bolus dose of 2 mg kg^{-1} propofol and 10 mcg kg^{-1} alfentanil or 1 mcg kg^{-1} remifentanil, followed by 6 mg kg^{-1} h^{-1} propofol and either 1 mcg kg^{-1} min^{-1} alfentanil or 0.25 mcg kg^{-1} min^{-1} remifentanil infusion. Bispectral index (BIS) values, mean arterial pressure, heart rate, end-tidal carbon dioxide and oxygen saturation were recorded. Postoperative pain scores at 0, 30 and 60 min were measured and recorded with additional opioid requirements.

Results: Postoperative pain scores at 0 and 30 min, total analgesic consumption and requirement for additional analgesics were significantly high in the remifentanil group. After the first hour, the pain scores were not significantly different. Mean arterial blood pressure was significantly low at 45 and 60 min preoperatively in the remifentanil group. In the remifentanil group, heart rate at 15, 30, 45, 60 min were significantly lower than those in the alfentanil group. BIS values of the two groups were not significantly different at any measurement time point. BIS values of remifentanil group at 30, 45, 60, 90 and 180 min significantly increased compared with those at 15 min.

Conclusion: Alfentanil provided more stable BIS and haemodynamic values preoperatively and less opioid consumption, along with lower pain scores, during the early postoperative period compared with remifentanil in patients undergoing single-level discectomy.

Keywords: Remifentanil, alfentanil, propofol, bispectral index, TIVA, anaesthesia

Introduction

Single-level lumbar discectomy is a surgical procedure that is commonly performed to treat disc herniation, which are unresponsive to medical therapy (1, 2). To rule out the development of neurological deficit resulting from reversible spinal cord injury, it is important to control the motor functions of patients during the early postoperative period. Therefore, the properties of anaesthetic agents, such as providing rapid recovery and efficient postoperative analgesia, are important for early mobilization. Despite the varying surgical stimuli, the depth of anaesthesia can be controlled by the combination of analgesic and hypnotic components of anaesthetic agents using total intravenous anaesthesia (TIVA). Stable haemodynamics, rapid recovery, fewer side effects and shorter hospital stay are the cornerstones in the selection of these anaesthetic agents. Faster recovery and lower postoperative side-effect profile of intravenous (IV) anaesthetics are advantages over inhalation anaesthetics in patients undergoing lumbar laminectomy or discectomy (3). Rapid and safe recovery of TIVA was revealed following lumbar discectomy (4, 5).

Remifentanil is an ultra-short acting potent opioid and is administered by constant rate infusion. Alfentanil has an elimination half-life of 8–32 min, which is three times longer than remifentanil. Both of them were previously compared in the TIVA procedure (6, 7). A dose of 0.1 mcg kg^{-1} min^{-1} remifentanil and 0.5 mcg kg^{-1} min^{-1} alfentanil were used, and both opioids were found to be associated with rapid recovery. However, remifentanil exhibited faster respiratory recovery and earlier postoperative pain (4). In a study, 0.25 mcg kg^{-1} min^{-1} remifentanil was compared with 1 mcg kg^{-1} min^{-1} alfentanil, and it was found that remifentanil had a faster recovery period but adequate postoperative analgesia (6). However, they did not evaluate their effects on the depth of anaesthesia. Bispectral index (BIS) monitoring was

Address for Correspondence: Dr. Ayten Saraçoğlu, İstanbul Bilim Üniversitesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, İstanbul, Türkiye
E-mail: anesthesiayten@gmail.com

Received: 22.04.2015
Accepted: 07.08.2015

not previously compared in patients undergoing lumbar discectomy.

We aimed to evaluate the depth of anaesthesia, perioperative haemodynamics, postoperative pain scores and analgesic consumption in patients administered remifentanil- or alfentanil-based total intravenous anaesthesia for single-level discectomy.

Methods

Following the ethics committee approval of the Marmara University and patients' written consent, 70 consecutive American Society of Anesthesiologists (ASA) I-II patients of both sexes between the ages of 18 and 60 years undergoing single-level discectomy because of lumbar disc herniation were enrolled in the study. The exclusion criteria were patient refusal, history of chronic opioid use, history of opioid allergy, hypo/hypertension, bradycardia or tachycardia and multilevel discectomy.

Patients were divided into two groups using sealed envelopes as alfentanil (Group A, n=35) or remifentanil (Group R, n=35) on the basis of TIVA. Forty-five minutes before the operation, 0.5 mg atropine sulphate and 0.07 mg kg^{-1} midazolam were intramuscularly administered as premedication. In the operating room, three-lead electrocardiogram, non-invasive blood pressure, end-tidal carbon dioxide, temperature, BIS and peripheral oxygen saturation of the patients were monitored. Anaesthesia was induced with propofol 2 mg kg^{-1} and rocuronium 0.6 mg kg^{-1} IV, and the patients were intubated. Muscle relaxation was monitored with peripheral nerve stimulation (TOF Watch SX, Organon Ltd Drynam Road Swords, Co. Dublin, Ireland). For the maintenance of anaesthesia, propofol was infused at 10 mg kg^{-1} h^{-1} during the first 10 min, 8 mg kg^{-1} h^{-1} during the second 10 min and 6 mg kg^{-1} h^{-1} during the rest of the operation. Patients in Group A were administered alfentanil 10 mcg kg^{-1} by slow IV bolus, and infusion was initiated with an initial dose of 1 mcg kg^{-1} min^{-1}. For the patients in Group R, 1 mcg kg^{-1} IV bolus was followed by infusion of 0.25 mcg kg^{-1} min^{-1}. Opioid solutions for both bolus doses and infusions were prepared by the same anaesthesiologist (A.S.). The names of the solutions were not written on the syringes. The anaesthesiologist who administered TIVA and followed up the patients in the postoperative period was blinded for the prepared opioid solutions.

Bispectral index values were monitored in both groups with the use of frontal and temporal electrodes, and pre- and perioperative values were recorded. Mean arterial pressure (MAP), heart rate (HR), end-tidal carbon dioxide tension ($EtCO_2$) and oxygen saturation (SpO_2) were recorded for all patients at 15-min intervals. When the modified Aldrete scores of the patients reached 10, they were allowed to leave the postoperative care unit. Perioperative opioid and propofol consumption were recorded at the end of the operation. Postoperative pain scores of the patients at 0, 30 and 60 min were measured using a 100-mm VAS scale and were recorded together with postoperative analgesic requirements. For postoperative analgesia, 1 mg kg^{-1} meperidine was intravenously administered to all patients. All operations were performed by the same neurosurgeon.

Statistical analysis

Demographic characteristics of the patients were statistically compared using independent samples t-test and chi-square test, while time-dependent variables were compared by independent samples t-test and non-parametric data were analysed using the Mann–Whitney U test. A p value of <0.05 was considered statistically significant, and the Tukey–Kramer test was used as the post hoc test. It was calculated that 32 patients in each group were required to detect a 30% difference in the postoperative pain scores with a significance level of 5% and a power of 80%. Independent Samples t test, Mann-Whitney U test and chi square test were used.

Results

Two patients of Group R were excluded from the study. One was excluded because a different surgeon performed the surgery. The other patient was excluded because the type of surgery was changed to instrumentation. Because of bleeding was more than expected, the duration of surgery was prolonged in one patient of Group A, and thus, was excluded. Following prone positioning, because of massive epistaxis, the surgery was postponed. A total of 66 patients were included in the statistical analysis.

There was no significant difference between groups A and R in terms of the patients' age, body weight, sex, perioperative propofol and opioid consumption, duration of anaesthesia and surgery ($p>0.05$) (Table 1).

Postoperative VAS scores at 0 and 30 min were significantly higher in the Group R than in Group A ($p<0.05$). After the first hour, the VAS scores of Group A were not significantly different from the values of Group R (Table 2). In Group A, VAS scores at 30 and 60 min significantly decreased compared with those at 0 min ($p<0.05$). However, in Group R, the VAS scores at 30 and 60 min did not reveal a significant difference compared with those at 0 min. Total analgesic requirement of patients in Group R was significantly higher than that in Group A ($p<0.05$). There was no significant difference between groups A and R in terms of the time of first analgesic requirement. None of the patients in Group A required additional analgesic during the first hour ($p<0.05$) (Table 3).

In Group R, HR was significantly lower than that in Group A at 15, 30, 45 and 60 min preoperatively ($p<0.05$) (Table 4). MAP was significantly low in Group R at 45 and 60 min ($p<0.05$) (Table 5).

There was no significant difference in MAP, SpO_2 and $ETCO_2$ values between the groups. BIS values of the groups were not significantly different at any measurement time points (Table 6). In Group R, BIS values at 30, 45, 60 and 90 min were significantly higher than those at 15 min.

Discussion

This study compared the effectiveness of alfentanil and remifentanil in patients undergoing single-level lumbar discectomy under TIVA. The patients who were administered remifentanil-based TIVA were found to have higher pain scores and more additional analgesic requirement than those who were administered alfentanil-based TIVA during the early postoperative period.

In this study, although both of the opioids caused a significant decrease in MAP and HR, the decrease in HR was significantly higher in Group R than in Group A during the first hour of anaesthesia. A similar clinical study on day case surgeries revealed that the decrease in HR with 0.5 mcg kg^{-1} min^{-1} remifentanil infusion was higher than the decrease with 2 mcg kg^{-1} min^{-1} alfentanil infusion (7). They also found no difference in blood pressure values. Hypoten-

Table 1. Patient demographics, duration of anaesthesia and surgery, preoperative propofol and opioid consumptions (mean±SD)

	Alfentanil (n=33)	Remifentanil (n=33)	p
Age (year)	40.3±10.5	41.2±8.5	0.702
Weight (kg)	74.0±12.6	74.5±12.0	0.881
Gender (M/F)	17/16	18/15	0.805
Duration of anaesthesia (min)	112.1±28.1	114.7±23.2	0.686
Duration of surgery (min)	91.7±28.4	94.2±23.6	0.690
Propofol dose (mg)	967.6±321.2	937.2±284.9	0.686
Alfentanil dose (μg)	6055.5±1989.6	-	
Remifentanil dose (μg)	-	1742.7±600.1	

Chi-square test/independent samples t-test. M: male; F: female; SD: standard deviation

Table 2. VAS scores of patients (mm) (mean±SD)

	Alfentanil (n=33)			Remifentanil (n=33)			
	Mean±SD	Median (min–max)		Mean±SD	Median (min–max)		p
0 min	1.2±4.2	0	0–20	27.3±29.7*	20	0–80	0.000
30 min	13.3±14.9	10	0–50	42.0±19.8*	40	0–80	0.000
60 min	10.6±12.0	10	0–40	17.6±24.8	10	0–90	0.645

Mann–Whitney U test. *p<0.05. VAS: visual analogue scale; SD: standard deviation; min: minimum; max: maximum

Table 3. Total meperidine consumption, meperidine requirement and first analgesic requirement time (mean±SD)

	Alfentanil (n=33)			Remifentanil (n=33)			
	Mean±SD	Median (min–max)		Mean±SD	Median (min–max)		p
Total analgesic consumption (mg)	20.5±25.5	0	0–60	82.4±19.2*	80	60–130	0.000
First analgesic administration time (min)	18.6±24.0	0	0–60	16.2±17.8	10	0–60	0.955
Additional analgesic requirement (%)	0.0			30.3*			0.000
Additional analgesic dose (mg)	0.0			25.5±8.9*	30	10–40	

Chi -square test/independent samples t-test/Mann–Whitney U test. *p<0.05. SD: standard deviation; min: minimum; max: maximum

Table 4. Heart rate (beat/min) (mean±SD)

	Alfentanil (n=33)			Remifentanil (n=33)			
	Mean±SD	Median	(min–max)	Mean±SD	Median	(min–max)	p
0 min	88.6±18.5	86	58–125	82.0±16.2	83	53–109	0.126
15 min	87.0±15.2	89	56–126	77.2±15.4	80	53–117	0.012
30 min	75.8±12.2	76	53–100	66.0±10.8	66	48–87	0.001
45 min	70.9±10.9	71	50–97	62.6±9.0	65	44–82	0.001
60 min	68.0±10.4	67	50–96	61.5±7.1	62	46–73	0.004
90 min	64.6±11.1	62	48–96	59.6±8.9	60	42–78	0.064
120 min	61.5±9.2	61	47–79	61.5±9.5	64	48–79	1.000

Independent samples t-test. *p<0.05. SD: standard deviation; min: minimum; max: maximum

Table 5. Mean arterial pressure (mmHg)

	Alfentanil (n=33)			Remifentanil (n=33)			
	Mean±SD	Median	(min–max)	Mean±SD	Median	(min–max)	p
0. min	101.2±14.4	102	72-128	95.0±14.0	95	71-123	0.083
15. min	95.6±15.3	91	68-134	88.8±18.3	84	56-125	0.108
30. min	84.9±13.2	87	52-114	81.0±14.8	79	60-121	0.262
45. min	84.3±13.1*	83	66-112	77.8±12.9	74	59-118	0.047
60. min	82.8±13.4*	81	63-114	76.1±11.2	75	55-101	0.033
90. min	84.4±12.7	83	65-109	78.8±10.2	79	59-98	0.072
120. min	88.0±12.6	85	70-113	80.8±13.0	80	63-98	0.136

*p<0.05. Independent Samples t test

sive anaesthesia decreases both the complication risk and the operation time (8). However, when it also causes bradycardia, it may result in adverse haemodynamic changes.

Early postoperative pain scores were found to be higher in patients administered remifentanil. The VAS scores at postoperative 0 and 30 min were significantly higher in Group R than in Group A. Moreover, additional analgesic requirement and total opioid consumption were higher in Group R than in Group A. This implicates the importance of providing effective analgesic effect in the early postoperative period. Ineffective analgesia will lead to complications, extended recovery and discharge periods with incremental cost (9, 10). Rapid degradation of remifentanil may be responsible for the failure in providing early postoperative analgesia (11).

Özköse et al. (3) has similarly demonstrated that 45% of patients administered remifentanil during intravenous anaesthesia for lumbar discectomy were found to have moderate to severe postoperative pain. However, there were no patients in Group A who had severe pain. Therefore, local infiltration of bupivacaine was performed to provide additional analgesia for patients administered remifentanil.

This study differs from other studies because we also monitored BIS values and analysed the effects of the agents on BIS indexes while comparing two different opioids for TIVA in patients undergoing lumbar discectomy. It was reported that the intermediate level of hypnosis was secured at 40–60 index range, and the mentioned level was appropriate for surgery (12). To provide that range for the patients included in this study, the propofol doses were re-adjusted. However, no significant change developed in total perioperative propofol consumption, duration of surgery and anaesthesia. A prospective, randomized, controlled, double-blind study conducted with 5228 patients concluded that perioperative awareness was significantly lower in patients administered TIVA and having BIS values between 40–60 than the control group where BIS monitorization was not used (13). Conversely, it was also reported that BIS monitorization reduced propofol consumption in lumbar discectomy during remifentanil-based TIVA but was insufficient to supress the response to painful stimulation and did not influence the risk of awareness during TIVA (14).

Table 6. BIS values of groups

	Alfentanil (n=33)			Remifentanil (n=33)			
	Mean±SD	Median	(min–max)	Mean±SD	Median	(min–max)	p
15 min	39.5±7.1	40	25–55	44.8±13.9	45	23–75	0.058
30 min	35.1±9.1	35	19–55	35.9±10.4	32	22–61	0.734
45 min	38.2±9.7	40	18–54	34.8±8.7	32	20–53	0.140
60 min	38.9±8.9	38	23–54	35.7±8.7	35	23–50	0.137
90 min	39.4±11.7	41	0–56	38.8±9.5	38	26–60	0.846
120 min	38.9±7.4	39	28–52	41.8±9.5	39	24–57	0.337

Independent samples t-test. BIS: bispectral index. SD: standard deviation; min: minimum; max: maximum

The main limitation of our study was that no test was performed to evaluate perioperative awareness in the postoperative period. Therefore, it could not be determined whether BIS values significantly changing at 30 min created a clinical difference or not.

Conclusion

Alfentanil provided a more stable haemodynamic and BIS values in patients receiving TIVA for single-level discectomy compared with remifentanil. Furthermore, because alfentanil reduced opioid consumption and pain scores in the early postoperative period, it may be preferred for TIVA during such surgeries.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Marmara University.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.S., Z.E., D.K., K.K., F.Y.G.; Design - A.S., Z.E., D.K., K.K., F.Y.G.; Supervision - F.Y.G., A.S., Z.E., D.K., K.K., Resources - A.S., D.K.; Materials - K.K.; Data Collection and/or Processing - A.S.; Analysis and/or Interpretation - A.S., Z.E.; Literature Search - A.S.; Writing Manuscript - A.S.; Critical Review - Z.E., F.Y.G., D.K. H.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

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

References

1. Parker SL, Xu R, McGirt MJ, Witham TF, Long DM, Bydon A. Long-term back pain after a single-level discectomy for radiculopathy: incidence and health care cost analysis. J Neurosurg Spine 2010; 12: 178-82. [CrossRef]
2. Lee P, Liu JC, Fessier RG. Perioperative results following open and minimally invasive single-level lumbar discectomy. J Clin Neurosci 2011; 18: 1667-70. [CrossRef]
3. Ozkose Z, Ercan B, Unal Y, Yardim S, Kaymaz M, Dogulu F, et al. Inhalation versus total intravenous anesthesia for lumbar disc herniation: comparison of hemodynamic effects, recovery characteristics, and cost. J Neurosurg Anesthesiol 2001; 13: 296-302. [CrossRef]
4. Ozkose Z, Yalcin Cok O, Tuncer B, Tufekcioglu S, Yardim S. Comparison of hemodynamics, recovery profile, and early postoperative pain control and costs of remifentanil versus alfentanil-based total intravenous anesthesia (TIVA). J Clin Anesth 2002; 14: 161-8. [CrossRef]
5. Ganidagli S, Cengiz M, Baysal Z. Remifentanil vs alfentanil in the total intravenous anaesthesia for paediatric abdominal surgery. Paediatr Anaesth 2003; 13: 695-700. [CrossRef]
6. Nilsson LB, Viby-Mogensen J, Møller J, Fonsmark L, Østergaard D. Remifentanil vs. alfentanil for direct laryngoscopy: a randomized study comparing two total intravenous anaesthesia techniques. TIVA for direct laryngoscopy. Acta Anaesthesiol Belg 2002; 53: 213-9.
7. Alper I, Erhan E, Ugur G, Ozyar B. Remifentanil versus alfentanil in total intravenous anaesthesia for day case surgery. Eur J Anaesthesiol 2003; 20: 61-4. [CrossRef]
8. Özcan AA, Özyurt Y, Saraçoğlu A, Erkal H, Süslü H, Arslan G, et al. Dexmedetomidine versus remifentanil for controlled hypotensive anesthesia in functional endoscopic sinus surgery. Turk J Anesth Reanim 2012; 40: 257-61. [CrossRef]
9. Fanelli G, Berti M, Baciarello M. Updating postoperative pain management: from multimodal to context-sensitive treatment. Minerva Anestesiol 2008; 74: 489-500.
10. Savoia G, Gravino E, Loreto M, Erman A. Analgesia in PACU: indications, monitoring, complications. Curr Drug Targets 2005; 6: 755-65. [CrossRef]
11. Ruggeri L, Landoni G, Guarracino F, Scolletta S, Bignami E, Zangrillo A. Remifentanil in critically ill cardiac patients. Ann Card Anaesth 2011; 14: 6-12.
12. Delfino AE, Cortinez LI, Fierro CV, Munoz HR. Propofol consumption and recovery times after bispectral index or cerebral state index guidance of anaesthesia. Br J Anaesth 2009; 103: 255-9. [CrossRef]
13. Zhang C, Xu L, Ma YQ, Sun YX, Li YH, Zhang L, et al. Bispectral index monitoring prevent awareness during total intravenous anesthesia: a prospective, randomized, double-blinded, multi-center controlled trial. Chin Med J (Engl) 2011; 124: 3664-9.
14. Akçali DT, Ozköse Z, Yardim S. Do we need bispectral index monitoring during total intravenous anesthesia for lumbar discectomies? Turk Neurosurg 2008; 18: 125-33.