Tropical Journal of Pharmaceutical Research April 2024; 23 (4): 753-759
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v23i4.11

Original Research Article

Effect of remifentanil in clinical anesthesia and postoperative analgesia

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Sent for review: 3 October 2023 *Revised accepted: 26 March 2024*

Abstract

Purpose: *To investigate the effect of remifentanil in clinical anesthesia and postoperative intravenous analgesia.*
Methods: *A retrospective analysis was conducted on the medical records of 100 patients who received remifentanil for anesthesia and postoperative intravenous analgesia at Zibo Center Hospital, Zibo, China from February 2020 to February 2023. The patients were divided into study and control groups comprising 50 patients in each group. The study group received remifentanil intravenously (8 g/kg) while the control group received fentanyl (3 - 4 μg/kg). Heart rate (HR), mean arterial pressure (MAP), and Bispectral Index (BIS) were monitored 5 min before anesthesia (T1), 10 min after (T2), 40 min after (T3), and 5 min before the end of surgery (T4). The levels of blood glucose (Glu), angiotensin II (Ang II), and cortisol (Cor) were measured at T1, T2, T3, and T4. Analgesic and sedative effects were evaluated 3, 12 and 24 h after surgery using the visual analog scale (VAS) and Ramsay sedation score.*
Results: *At T1, T2, T3, and T4, there were no significant differences in HR, MAP, and BIS between the two groups ($p > 0.05$), while the levels of Glu, Ang II, and Cor in study group were significantly lower ($p < 0.05$). At 3, 12 and 24 h after surgery, VAS score in the study group was significantly lower, while Ramsay's analgesia score was significantly higher ($p < 0.05$). Total effectiveness was significantly higher in the study group ($p < 0.05$). Recovery time for orientation, spontaneous breathing, awakening, stay in the recovery room, and incidence of adverse reactions were significantly lower in study group ($p < 0.05$).*
Conclusion: *The use of remifentanil for postoperative intravenous analgesia significantly lowers stress response, sedation and improves recovery time. It is, therefore, effective, and produces lower adverse effects than fentanyl. Large-scale investigation to determine the impact of confounding factors on the outcome of fentanyl/remifentanil combination is required.*

Keywords: *Anesthesia, Postoperative intravenous analgesia, Fentanyl, Remifentanil, Vital signs, Stress response, Adverse reactions*

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INTRODUCTION

In the surgical process, anesthesia is of utmost importance. In recent years, clinical practice has embraced surgical treatments for a majority of illnesses, which often bring significant pain to patients. Therefore, it becomes necessary to administer anesthesia to all patients before surgery to achieve analgesic and sedative effects. This results in reversible, transient loss of consciousness in patients, ultimately alleviating

their pain and distress and enabling them to complete the surgery smoothly and safely [1,2].

Clinical practice utilizes various anesthetic drugs such as fentanyl, remifentanil, and morphine, all of which effectively anesthetize and alleviate the pain of patients during and after surgery [3]. However, improper and non-standard application of these drugs negatively impacts anesthesia outcomes, leads to adverse reactions, severely affects patient health, and has a detrimental impact on quality of life and prognosis [4].

This study was a retrospective analysis that investigated the effect of remifentanil and postoperative intravenous analgesia.

METHODS

General information

A retrospective study was carried out on the medical records of 100 patients who received remifentanil for anesthesia and postoperative intravenous analgesia at Zibo Center Hospital, Zibo, China from February 2020 to February 2023. Based on the postoperative intravenous analgesia and clinical anesthesia methods, they were divided into study and control groups comprising 50 patients each. This study received ethical approval from the institutional review board of Zibo Center Hospital (approval no. Z17589231) and was performed following the guidelines of Declaration of Helsinki [7]. Written informed consent was obtained from the patients before the study.

Inclusion criteria

Patients who exhibited good compliance, had surgical indications, with complete medical records.

Exclusion criteria

History of drug allergies, respiratory tract diseases, and mental disorders.

Treatment

After patients entered the operating room, they were administered oxygen via a face mask, and venous access was established. Anesthesia induction was initiated, and close monitoring of vital signs such as temperature and blood pressure was performed. Once the patient exhibited stable vital signs, intravenous injection of 0.1 mg/kg vecuronium bromide and 0.04 mg/kg midazolam and 2-3 mg/kg propofol was administered. The control group was subsequently administered intravenous injection of 3-4 μg/kg fentanyl, and postoperatively, 0.4 μg/kg fentanyl was continued for 10 min for patient analgesia [5]. Study group received 8 g/kg remifentanil intravenously, and postoperatively, 0.1 μg/kg fentanyl was continued for 10 min for patient analgesia [6].

Evaluation of parameters/indices

Follow-up was conducted one month after surgery.

Vital signs

Heart rate (HR), mean arterial pressure (MAP), and Bispectral index (BIS) were monitored 5 min before anesthesia (T1), 10 min after (T2), 40 min after (T3), and 5 min before the end of surgery (T4).

Stress response

Levels of blood glucose (Glu), angiotensin II (Ang Ⅱ), and cortisol (Cor) were measured at T1, T2, T3, and T4.

Analgesic and sedative effects

Analgesic and sedative effects were evaluated at 3, 12 and 24 h after surgery using the visual analog scale (VAS) [8] and Ramsay sedation score [9]. VAS scores ranged from 0 to 10, with 0 representing no pain and 10 representing severe pain. Ramsay sedation scores ranged from 1 to 6, with 1 representing restlessness and 6 representing deep sleep.

Anesthesia recovery time

Orientation recovery time, spontaneous breathing recovery time, time to full consciousness, and duration of stay in the recovery room were evaluated.

Adverse reactions

Adverse reactions were investigated in both groups and compared.

Therapeutic efficacy

The visual analog scale (VAS) is a widely used subjective pain assessment tool that allows individuals to rate their pain intensity on a continuous scale. The VAS consists of a horizontal line, typically 10 centimeters in length, with anchor points representing the extremes of pain intensity. The VAS pain scoring criteria are as follows: 0 (no pain) found at the extreme left

end of the line, 1 - 3 (mild pain), 4 - 6 (moderate pain), 7 - 9 (severe pain), 10 (worst pain). At the extreme right end of the line is labeled "Worst Possible Pain." Participants mark this point if they experience the most severe pain imaginable. Participants are instructed to place a vertical mark on the line to indicate their level of pain intensity. The distance in millimeters from the left end of the line to the participant's mark is measured and recorded as the VAS pain score, ranging from 0 to 10, with higher scores indicating greater pain intensity. Based on this grading, participants with VAS points of 0 - 3, 4 - 6, and 7 - 10 were identified as significantly effective, effective, and ineffective respectively.

Statistical analysis

Data were analyzed using Statistical Packages for Social Sciences (SPSS 28.0 IBM, Armonk, NY, USA). Count data were expressed as percentages and analyzed using chi-squared test. Normally distributed continuous data were expressed as mean ± standard deviation (SD) and analyzed using the t-test. $P < 0.05$ was considered statistically significant.

RESULTS

General information

In study group, the age ranged from 25 to 65 years, with an average of 45.85 ± 7.13 years. There were 24 females and 26 males, the majority had BMI between 18-24 kg/m² gallbladder and spinal surgeries. In control group the age ranged from 26 to 66 years, with an average age of 46.23 ± 7.20 years. There were 23 females and 27 males, majority had BMI between 18 - 24 kg/m², and 16 gallbladder surgeries. There were no significant differences in general information between the two groups *(p* > 0.05) (Table 1).

Vital signs and stress responses

At T1, T2, T3, and T4, there were no significant differences in HR, MAP, and BIS in study and control groups *(p* > 0.05; Table 2). Glucose (Glu), angiotensin II (Ang Ⅱ), and cortisol (Cor) levels gradually increased over time from T1 to T4 and Glu, Ang Ⅱ, and Cor levels in study group were significantly lower compared to control group at T1, T2, T3 and T4 ($p < 0.05$; Table 3).

Analgesic and sedative effects

Visual analogue score (VAS) 3 h after surgery was significantly lower compared to 12 h after surgery in both groups ($p < 0.05$), and VAS score at 12 h after surgery was significantly compared to 24 h after surgery ($p < 0.05$). Ramsay sedation scores at 3, 12, and 24 h after surgery gradually decreased significantly ($p < 0.05$) in both groups. Furthermore, at 3, 12, and 24 h after surgery, VAS scores in study group were lower than those in control group, while Ramsay sedation scores were higher (Table 4).

Table 1: General information (n = 50 in each group)

Variable	Categorization	Study group	Control group	t/χ^2	*P*-value
Age (years)		45.85±7.13	46.23±7.20	0.265	0.791
Gender	Female	24(48)	23(46)	0.040	0.841
	Male	26(52)	27(54)		
Body mass index	18-24 kg/m^2	28(56)	27(54)	0.040	0.841
	25-31 kg/m^2	22(44)	23(46)		
Surgical types	Gallbladder	15(30)	16(32)	0.181	0.981
	Spinal	15(30)	14(28)		
	Colon	13(26)	14(28)		
	Uterine	7(14)	6(12)		

Table 2: Vital signs (n = 50 in each group)

Group	Time	HR (beats/min)	MAP (mmHg)	BIS
Study	T1	66.04±12.13	87.31±12.34	45.04±5.31
	T2	71.34±14.44	87.24±10.55	48.04±6.07
	T3	71.14±12.74	85.41±10.05	49.04±6.34
	T4	70.24±12.05	88.25±12.77	52.41±5.57
Control	T1	69.64±10.14	87.04±12.22	45.05±6.24
	T2	69.51±13.34	86.13±11.64	49.24±5.53
	T3	71.74±11.61	86.44±11.27	49.05±5.74
	T4	72.13±11.07	88.25±12.74	51.04±7.07

Heart rate (HR), mean arterial pressure (MAP), Bispectral index (BIS)

Table 3: Stress responses (n = 50 in each group)

Group	Time	Glu (mmol/L)	Ang Ⅱ (ng/L)	Cor (nmol/L)
Study	T1	4.74±1.11*	245.25±21.46*	428.05±72.05*
	T2	5.01±1.34*	302.04±45.05*	831.74±103.53*
	T3	5.13±1.24*	397.25±62.13*	953.25±105.53*
	T4	5.25±1.33*	556.24±95.33*	1018.04±104.55*
Control	T1	5.05±1.23	253.55±36.37	435.04±71.45
	T2	5.44±1.25	345.04±52.27	1013.64±101.55
	T3	5.57±1.31	457.45±73.07	1159.64±202.03
	T4	5.63±1.31	639.04±105.55	1427.77±201.55

Blood glucose (Glu), angiotensin II (Ang Ⅱ), cortisol (Cor). *P < 0.05 compared to control group

Table 3: Analgesic and sedative effects (n = 50 in each group)

Group	Post-surgery (h)	VAS scores	Ramsay sedation scores
Study	3	$3.18±0.97^{a}$	$4.11±0.87^{a}$
	12	$3.68±1.11^{b}$	$3.70±0.93^{b}$
	24	$2.77±0.50^{c}$	$3.30±1.07^{c}$
Control	3	$3.22±1.01^{a}$	$4.08±0.72^{a}$
	12	$3.86±1.20^{b}$	$3.66±1.01^{b}$
	24	$2.95±0.42^{c}$	$3.23±1.10^{c}$

$^{a,b,c}P$ < 0.05 significantly different from each other

Table 4: Clinical efficacy (n = 50, {n %})

Group	Remarkably effective	Effective	Ineffective	Total effectiveness
Study	22(44)	27(54)	1(2)	49(98)
Control	16(32)	26(52)	8(16)	42(84)
χ^2				4.396
P-value				0.036

Table 5: Anesthesia recovery time (min) (n = 50)

Group	Orientation recovery time	Spontaneous breathing recovery time	Time to full consciousness	Duration of stay in the recovery room
Study	12.08±1.20	13.92±2.22	9.51±1.51	33.66±5.45
Control	22.57±1.61	18.37±3.37	18.55±2.10	43.92±6.26
T-value	36.940	7.797	24.714	8.741
P-value	< 0.001	< 0.001	< 0.001	< 0.001

Note: Values are presented as mean ± standard deviation (min)

Table 6: Incidence of adverse reactions (n = 50 {n, %})

Group	Nausea and vomiting	Dizziness and headache	Restlessness	Cognitive impairment	Bradycardia	Total occurrence
Study	1(2)	1(2)	1(2)	0(0)	0(0)	3(6)
Control	3(6)	3(6)	2(4)	2(4)	1(2)	11(22)
χ^2						5.316
P-value						0.021

Clinical efficacy

Total effective rate in study group was significantly higher compared to control group (χ^2 = 4.396, p < 0.05; Table 4).

Anesthesia recovery time

The orientation recovery time, spontaneous breathing recovery time, time to full consciousness, and duration of stay in the recovery room were significantly shorter in study group compared to control group (p < 0.05; Table 5).

Incidence of adverse reactions

The incidence of adverse reactions in study group was significantly lower compared to control group (p < 0.05) (Table 6).

DISCUSSION

In recent years, surgical safety and management of postoperative pain have gained increasing

attention in China, driven by advances in medical technology [9]. Clinical practice has seen the use of surgery as a treatment for many severe and complex diseases. Anesthesia plays an indispensable role in ensuring smooth progress of surgery. Anesthesia involves the use of drugs or other methods to suppress the functions of the central or peripheral nervous system in a reversible manner, primarily inhibiting sensation, especially pain perception, allowing surgery to be performed painlessly. This ensures safety during surgery and allows for the sedative and calming effects of anesthesia to take effect [10,11]. Therefore, when selecting anesthesia drugs, a comprehensive consideration of factors such as analgesia, sedation, and safety should be considered. This guarantees the effectiveness of surgical anesthesia and also emphasizes the impact of anesthesia drugs on patients. Selection of anesthesia drugs should be based on factors such as age, specific condition, and type of surgery, and it should be made by professional anesthesiologists to avoid harm, thereby enhancing safety of the surgery [12,13].

Postoperative pain management involves choosing from a range of analgesic medications based on the preferred method of pain control. Intravenous analgesia commonly utilizes opioids like fentanyl, sufentanil, or morphine, as well as nonsteroidal anti-inflammatory drugs (NSAIDs) and antiemetics to alleviate surgical site pain and prevent nausea and vomiting. Alternatively, spinal or epidural analgesia employs local anesthetics and potent opioids to block sensory nerves, providing targeted pain relief. Subcutaneous analgesics and continuous nerve blocks are also options for managing postoperative pain, often using opioids as the primary choice for relief. Fentanyl and sufentanil are widely used anesthetic agents in clinical practice [12]. Fentanyl, in particular, finds extensive application in postoperative analgesia for various pain conditions and surgical procedures, including gynecological surgeries. Fentanyl is classified as an opioid receptor agonist and possesses potent analgesic properties. It exhibits a rapid onset of action, typically within 1 min after injection, reaching peak concentrations within 4 mins. Additionally, it has a relatively short duration of action, allowing for repeated administration [14]. However, the safety profile is less favorable, as it can contribute to the occurrence of adverse reactions such as nausea and dizziness [15].

Fentanyl belongs to the same class as morphine and meperidine. It rapidly takes effect when administered intravenously, with analgesia typically achieved within 1 min and peaks within 4 mins, lasting for approximately 30 mins. Fentanyl provides significant analgesia, with a potency of approximately 80 times that of morphine [16]. Importantly, it has a milder respiratory depressant effect and a lower likelihood of adverse reactions and addiction, making it a common choice in clinical practice. Fentanyl-type drugs are used for general anesthesia induction and maintenance and as an adjunct in spinal anesthesia. These fentanyl-type drugs exert minimal respiratory and circulatory depression, allowing safe use in patients with unstable circulatory function, including those undergoing major cardiovascular surgeries [16]. Typical doses range from 0.001 to 0.004 mg/kg. Rapid injection of fentanyl leads to chest wall rigidity, while excessive dosing may result in delayed respiratory depression and respiratory amnesia.

Sufentanil is also an opioid receptor agonist known for its potent analgesic effects. Compared to fentanyl, remifentanil exhibits significantly higher lipophilicity, with a ratio of approximately 1:2. This increased lipophilicity facilitates its passage through the blood-brain barrier and binding to plasma proteins. Consequently, sufentanil not only offers more robust analgesia but also has a longer duration of action compared to fentanyl, with a ratio of approximately 1:2 [17]. However, it should be noted that in patients who abuse alcohol, the use of sufentanil may have adverse effects on anesthesia outcomes and postoperative recovery, potentially affecting prognosis [18]. Remifentanil is structurally derived from fentanyl. It provides significantly stronger analgesic effects than fentanyl and achieves maximum efficacy within minutes of administration.

Remifentanil is known for its hemodynamic stability and the potential to ensure adequate myocardial oxygen supply [18]. It is primarily used for pain management, particularly during surgical procedures, as an induction and maintenance agent for endotracheal intubation and controlled mechanical ventilation. It is also employed as an adjunct in balanced anesthesia. Sufentanil is classified as a controlled substance with specific regulatory restrictions, limiting its use to necessary medical situations within healthcare institutions. Consequently, the primary role of sufentanil lies in potent analgesia, making it a strong candidate for pain management during various medical procedures. There is usually no comparison between sufentanil citrate and remifentanil hydrochloride in terms of which one has stronger analgesic effects, as they are used in different clinical contexts [19].

Remifentanil citrate is categorized as an opioid receptor agonist and is often used as an adjuvant in general anesthesia, while remifentanil hydrochloride is primarily used for the induction and maintenance of general anesthesia [18]. Both medications typically have potent analgesic and sedative effects. The results of this study showed that there were no significant differences in HR, MAP, and BIS between the two groups at 5 mins before anesthesia (T1), 10 mins after (T2), 40 mins after (T3), and 5 mins before the end of surgery (T4). Study group had lower levels of Glu, AngⅡ, and Cor compared to control group. At 3, 12, and 24 h after surgery, study group had a lower VAS score compared to control group, while Ramsay's sedation score was higher. Total effective rate was higher in study group. Recovery times for orientation, spontaneous breathing, awakening, and recovery room stay were shorter in study group. A study has indicated that remifentanil offers advantages such as strong analgesic effects, rapid onset, and fewer adverse reactions in clinical surgical anesthesia [16]. It also significantly reduces recovery room stay, and time to regain spontaneous breathing, and decreases the incidence of adverse reactions, thus demonstrating a high level of safety. Additionally, the results demonstrated a lower incidence of adverse reactions in study group, likely due to its minimal residual accumulation in the body and rapid clearance through the kidneys [20].

Limitations of this study

The study is limited by the small sample size used, the presence of selection or measurement bias and methodological factors that may impact the validity of the results. For example, there may be potential confounding factors that were not adequately controlled or limitations in the measurement tools or techniques used.

CONCLUSION

Administration of remifentanil and intravenous postoperative analgesia is more effective than fentanyl, with fewer adverse effects. It would be necessary to carry out a large-scale investigation to determine the impact of confounding and other related factors on the outcome of the combination of the two agents and the probable mechanisms of action involved.

DECLARATIONS

Acknowledgements

None provided.

Funding

None provided.

Ethical approval

This study was approved by the institutional review board of Zibo Center Hospital (approval no. Z17589231).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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