

RESEARCH

Open Access



The effects of the administration sequence and the type of hypnotics on the development of remifentanil-induced chest wall rigidity: a randomized controlled trial

Yu Jin Oh¹, Yesull Kim^{1,2}, Chanhong Lee¹, Dong-Chan Kim^{1,2} and Aram Doo^{1,2*}

Abstract

Background Research on remifentanil-induced chest wall rigidity is limited. Furthermore, its incidence is unknown, and the clinical factors influencing its development remain unclear. This prospective, double-blind, randomized controlled trial aimed to investigate the effects of the administration sequence of hypnotics and remifentanil as well as the type of hypnotic administered on the development of remifentanil-induced chest wall rigidity.

Methods A total of 125 older patients aged ≥ 65 years, who were scheduled to undergo elective surgery under general anesthesia, were enrolled in this study. Participants were randomly assigned to one of four groups; Thio-Remi, Pro-Remi, Remi-Thio, or Remi-Pro. After confirming the loss of consciousness and achieving a target effect-site concentration of 3 ng/mL remifentanil, the development of remifentanil-induced chest wall rigidity was evaluated.

Results The incidence of chest wall rigidity was significantly higher in the remifentanil-hypnotic group than in the hypnotic-remifentanil (opposite sequence) group (55.0% vs. 21.7%, $P < 0.001$). Logistic regression analysis revealed that remifentanil-hypnotic administration was a significant predictor of the development of chest wall rigidity (crude odds ratio 4.42, 95% confidence interval 1.99; 9.81, $P < 0.001$).

Conclusions Pretreatment with hypnotics potentially reduces the development of chest wall rigidity during the induction of balanced anesthesia with remifentanil in older patients.

Trial registration This article was registered at WHO International Clinical Trials Registry Platform (Trial number: KCT0006542).

Keywords Complication, Elderly, General anesthesia, Hypoxemia, Opioids, Remifentanil, Respiratory failure, Rigidity

Background

Opioids have evidently been one of the major drugs for anesthetic induction and maintenance. They provide intra- and post-operative analgesia and promote hemodynamic stability during surgery and airway manipulation by blocking sympathetic stimulation [1]. Remifentanil is an ultra-short-acting synthetic opioid, which is a widely used adjuvant for balanced anesthesia. Remifentanil may improve the quality of anesthesia by reducing hypnotic dose requirements and

*Correspondence:

Aram Doo
ruiwin3518@gmail.com

¹ Department of Anesthesiology and Pain Medicine, Jeonbuk National University Medical School and Hospital, 20, Geonji-Ro, Deokjin-Gu, Jeonju, Jeollabuk-Do 54907, South Korea

² Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, South Korea



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

shortening the onset of anesthesia during anesthesia induction [2]. Its pharmacokinetic characteristics and short context-sensitive half-life potentially enhance rapid recovery from anesthesia compared with other opioids, such as fentanyl [2]. These characteristics render it more favorable for fast-track anesthesia and surgery. In addition, remifentanyl is metabolized by nonspecific tissue esterase; therefore, it can be safely used in patients with underlying diseases, such as hepatic or renal dysfunction [3].

Intravenous administration of a bolus of opioids during anesthesia induction frequently elicits unexpected adverse effects, including cough, muscle rigidity, laryngospasm, and resultant respiratory failure [4–6]. In particular, opioid-related muscle rigidity is most prominent in the chest and abdomen. Chest wall rigidity followed by opioid administration, also called “wooden chest syndrome” may be one of the most serious complications [7]. Opioid-induced chest wall rigidity may worsen lung compliance, thereby causing ineffective ventilation. It potentially leads to life-threatening hypoxemia, hypercarbia, and desaturation [5, 8]. Although it is clinically important for patient safety, there have been few well-designed clinical trials that characterized it. Potential risk factors includes high-dose opioids administration and extremes of age (neonate or elderly), and critical neurologic or metabolic illness [8–11].

A few studies have investigated chest wall rigidity due to remifentanyl administration [6, 12, 13]. However, its incidence is unknown, and the clinical factors that affect it remain unclear. Meanwhile, older patients present with hypoxemia and desaturation during anesthesia more frequently because this population has reduced pulmonary reserve [14]. Therefore, the consequences resulting from the abrupt development of chest wall rigidity are potentially more complicated in this population.

This prospective, double-blind, randomized controlled trial aimed to investigate the development of remifentanyl-induced chest wall rigidity in older patients (≥ 65 years) undergoing general anesthesia. We hypothesized that the administration sequence of hypnotics and remifentanyl (order of administration: hypnotic-remifentanyl versus remifentanyl-hypnotic) during anesthesia induction potentially affects the development of remifentanyl-induced chest wall rigidity. We also compared the effects of different types of hypnotics, including thiopental sodium and propofol, which are the most commonly administered intravenous anesthetics. This study also aimed to determine the predictive factors for chest wall rigidity in older patients.

Methods

This study was approved by the Institutional Review Board of the authors' hospital and registered with the WHO International Clinical Trials Registry Platform (Trial number: KCT0006542, Date of registration: 03/09/2021). The protocol is available by reasonable request from the corresponding author. This manuscript adheres to the applicable CONSORT guidelines. Participants were recruited from a tertiary care teaching hospital. After obtaining written informed consent, 125 older patients aged ≥ 65 years with American Society of Anesthesiologists physical status 1 or 2, who were scheduled to undergo elective surgery under general anesthesia, were enrolled in this study. Participants who had a history of allergy to propofol or thiopental; severe pulmonary disease including asthma, chronic obstructive pulmonary disease or interstitial lung disease; severe hepatorenal impairment; or had taken opioid analgesics within 3 months prior to surgery were excluded from the study.

All participants enrolled in the study underwent body composition measurements using a body composition analyzer (Inbody S10[®] Biospace, Seoul, Korea) the day before surgery. Body composition measures, such as body fat mass (kg), percent body fat (%), skeletal muscle mass (kg), skeletal muscle mass index (kg/m^2), and the amount of total body water (L), were evaluated.

Group allocation

Participant group allocation was based on the administration sequence of hypnotics and remifentanyl (hypnotic-remifentanyl and remifentanyl-hypnotic groups), and further subdivision was based on the type of hypnotic administered, that is, thiopental or propofol. Consequently, participants were randomly assigned to one of four groups in a 1:1:1:1 ratio using computer-generated random numbers. In the Thio-Remi group, thiopental was administered first until loss of consciousness (LOC), followed by remifentanyl infusion via target-controlled infusion (TCI) at an effect-site concentration (Ce) of 3 ng/mL. In the Pro-Remi group, propofol was administered first until LOC, followed by remifentanyl at a Ce of 3 ng/mL. In the Remi-Thio group, remifentanyl was first infused at a Ce of 3 ng/mL using a TCI pump, followed by thiopental until LOC. In the Remi-Pro group, remifentanyl and propofol were administered in that order and in the same manner.

Drug preparation, blinding, and randomization

Thiopental sodium (500 mg), diluted with 20 ml of normal saline at a concentration of 25 mg/mL, was prepared in a 20-ml syringe. Twenty milliliters of propofol (1%) was prepared in a 20-ml syringe. Remifentanyl (1 mg)

was diluted with normal saline to a concentration of 50 ug/mL (final volume, 20 ml). To maintain blinding of the outcome assessor (an experienced anesthesiologist, Y. J. Oh), syringe contents (thiopental, propofol and remifentanyl) were concealed with an opaque syringe and giving sets. All anesthetic drug infusions during the intervention were blinded to both the patient and outcome assessor, and all drugs used for the intervention were prepared by a single anesthetic nurse. Randomization was performed using computer-generated random numbers by an anesthesiologist who was not involved in the anesthetic intervention and data collection.

Anesthetic regimen

The anesthetic regimen was standardized for all participants. None of the patients received any preanesthetic medication. Standard anesthetic monitoring, including electrocardiography, noninvasive blood pressure, pulse oximetry, capnography, and bispectral index, was implemented.

In the hypnotic-remifentanyl groups, that is, the Thio-Remi and Pro-Remi groups, thiopental sodium or propofol was initially infused at a rate of 350 mL/h using an infusion pump (Agilia®, Fresenius Vial, France) until LOC was achieved (no response to verbal command “open your eyes”). Thereafter, the target Ce was set at 3 ng/mL using a TCI pump (Orchestra® Base Primea,

Fresenius Vial, France), in which the Minto model was pre-programmed, in effect-site targeting mode. Remifentanyl was initially infused using a TCI pump in the remifentanyl-hypnotic groups (Remi-Thio and Remi-Pro groups). When a predetermined Ce of 3 ng/mL was achieved, thiopental or propofol was administered in the same manner as in the hypnotic-remifentanyl groups.

The total dose of hypnotics administered until LOC and elapsed time to LOC were recorded. Moreover, vital signs, including peripheral oxygen saturation (SpO₂), blood pressure, heart rate, and bispectral index, were monitored during the intervention.

Evaluation of chest wall rigidity

After confirming loss of spontaneous breathing and achieving a target Ce of 3 ng/mL remifentanyl, the development of remifentanyl-induced chest wall rigidity was evaluated for 120 s while providing manual positive pressure ventilation without administration of a neuromuscular blocking agent. During the assessment, the fresh gas flow rate and inspired fraction of oxygen were set at 6 L/min and 0.5, respectively. An experienced anesthesiologist (Y. J. Oh) blinded to the study groups assessed the patients using a 3-point Likert scale (1=Unlikely, 2=Probable, and 3=Definite) as follows: Grade 1 (Unlikely); no signs of chest wall rigidity during positive pressure ventilation; Grade 2 (Probable); increased

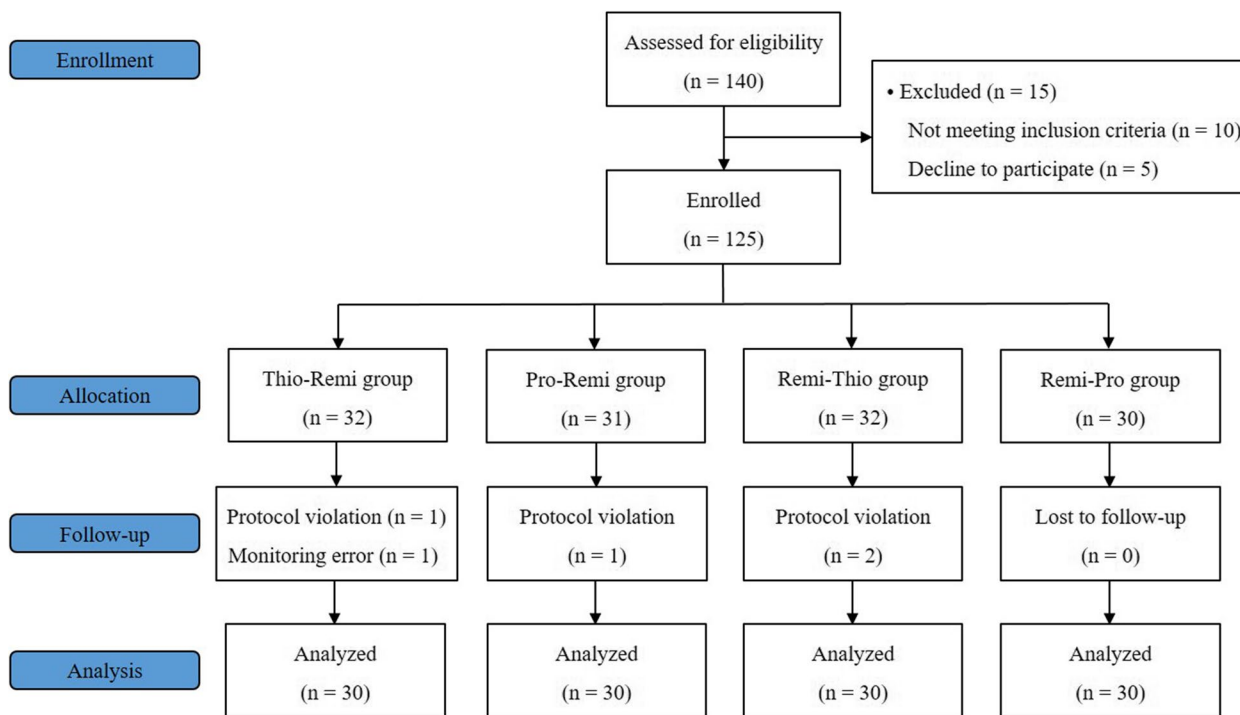


Fig. 1 The CONSORT flow diagram

Table 1 Patient characteristics and body composition measures among the four groups

	Thio-Remi (n = 30)	Pro-Remi (n = 30)	Remi-Thio (n = 30)	Remi-Pro (n = 30)	P value
Age (years)	68.7 (4.7)	71.4 (5.9)	70.5 (5.2)	71.0 (6.1)	0.257
65–75 years	26	24	24	23	0.796
≥ 75 years	4	6	6	7	
Female [n (%)]	14 (46.7%)	22 (73.3%)	18 (60.0%)	19 (63.3%)	0.205
Height (cm)	159.0 (9.3)	156.2 (6.0)	156.7 (9.5)	158.2 (7.7)	0.523
Weight (kg)	65.5 (9.9)	60.1 (9.1)	59.6 (9.8)	60.9 (11.7)	0.099
BMI (kg/m ²)	25.9 (3.2)	24.7 (3.6)	24.2 (2.4)	24.2 (3.6)	0.134
Body fat mass (kg)	18.1 (6.3)	16.8 (6.7)	16.2 (4.9)	16.2 (7.1)	0.657
Percent body fat (%)	27.4 (9.3)	27.7 (7.9)	27.8 (8.6)	26.1 (9.0)	0.858
Skeletal muscle mass (kg)	26.6 (6.0)	23.3 (4.4)	23.4 (6.2)	24.3 (5.1)	0.098
Skeletal muscle index (kg/m ²)	8.4 (1.2)	7.7 (1.2)	7.5 (1.5)	7.7 (1.2)	0.049*
Total body water (L)	35.6 (7.2)	31.7 (5.5)	31.8 (7.7)	32.9 (6.3)	0.110
Underlying diseases [n (%)]					
Hypertension	15 (50.0%)	11 (36.7%)	16 (53.3%)	13 (43.3%)	0.576
Diabetes mellitus	4 (13.3%)	4 (13.3%)	8 (26.7%)	4 (13.3%)	0.410

Values are presented as means (SD), numbers, or numbers (percentages)

BMI Body mass index

* There were no significant differences based on multiple comparisons with Tukey's post-hoc test

Table 2 Hypnotic requirements and elapsed time to loss of consciousness

	Thio-Remi (n = 30)	Pro-Remi (n = 30)	Remi-Thio (n = 30)	Remi-Pro (n = 30)	P value
Administered dose of thiopental (mg)	244.4 (77.0)	N/A	222.0 (60.2)	N/A	0.215
Administered dose of propofol (mg)	N/A	99.3 (14.7)	N/A	92.4 (25.0)	0.201
Elapsed time to LOC (s)	106.6 (26.4)	101.7 (15.2)	91.5 (24.5)	94.6 (25.8)	0.059

Values are presented as means (SD)

N/A Not applicable, LOC Loss of consciousness

Table 3 Incidence of remifentanyl-induced chest wall rigidity and other adverse effects

	Thio-Remi (n = 30)	Pro-Remi (n = 30)	Remi-Thio (n = 30)	Remi-Pro (n = 30)	P value
Chest wall rigidity	9 (30%)	4 (13.3%)	16 (53.3%)	17 (56.7%)	0.001*
Desaturation	2 (6.7%)	2 (6.7%)	8 (26.7%)	8 (26.7%)	0.034*
Cough	2 (6.7%)	4 (13.3%)	1 (3.3%)	2 (6.7%)	0.516

Categorical variables are presented as numbers (%)

Desaturation is indicated by a SpO₂ < 94%

* P < 0.05 by chi-square test comparisons among the four groups

inspiratory airway pressures required to deliver appropriate tidal volumes (6–8 mL/kg *ideal body weight*), with SpO₂ maintained at or above 94%; and Grade 3 (Definite); decreased tidal volumes (< 6 mL/kg *ideal body weight*), despite an increased peak inspiratory airway pressure of up to 35 cmH₂O and the development of SpO₂

desaturation < 94%. To qualify as an event, the development of chest wall rigidity had to be evaluated for at least five consecutive ventilatory cycles. After the assessment was completed, rocuronium (1 mg/kg) was administered to facilitate endotracheal intubation. If SpO₂ desaturation < 94% did not resolve after successful endotracheal

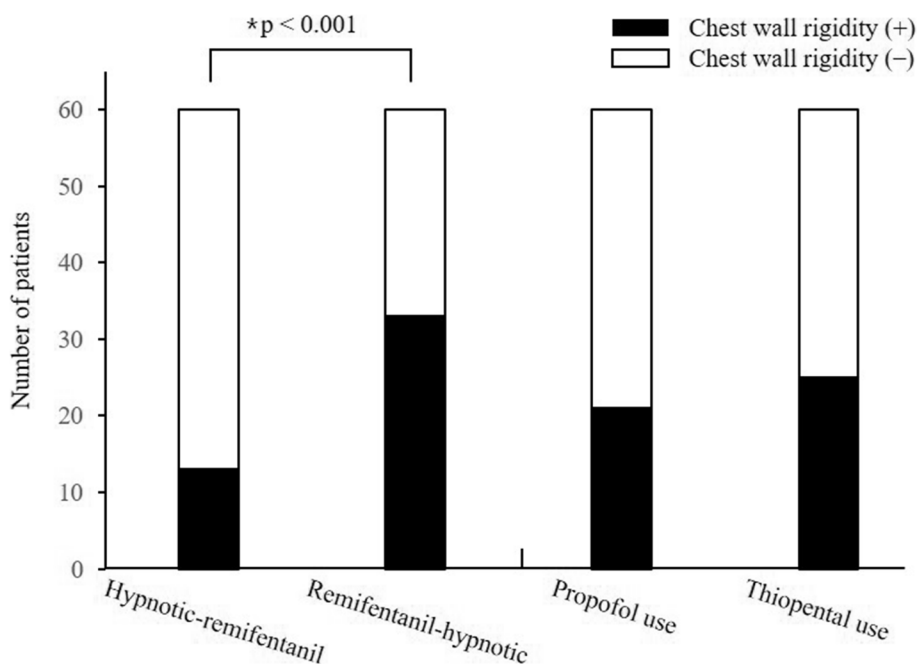


Fig. 2 The number of patients experiencing chest wall rigidity according to the administration sequence of the hypnotics and remifentanyl as well as the type of hypnotic. *The numbers of patients who exhibited chest wall rigidity were 13/60 (21.7%) and 33/60 (55.0%) in the hypnotic-remifentanyl and remifentanyl-hypnotic groups, respectively ($P < 0.001$). There was no significant difference in the development of chest wall rigidity between propofol and thiopental sodium use

Table 4 Possible risk factors for remifentanyl-induced chest wall rigidity based on logistic regression analysis

	Univariate analysis	
	Crude OR [95% CI]	P value
≥ 75 years	1.85 [0.77–4.45]	0.170
Female sex	1.10 [0.52–2.35]	0.807
Remifentanyl-hypnotic order	4.42 [1.99–9.81]	< 0.001*
Propofol usage	0.751 [0.36–1.58]	0.453
BMI (kg/m ²)	1.06 [0.95–1.19]	0.315
Percent body fat (%)	1.00 [0.96–1.05]	0.848
Skeletal muscle index (kg/m ²)	1.12 [0.84–1.50]	0.437

* Compared with the hypnotic-remifentanyl sequence

intubation, an incremental dose of naloxone 0.1 mg was intravenously administered. Grade 2 or 3 was defined as the development of remifentanyl-induced chest wall rigidity.

The primary outcome was the incidence of remifentanyl-induced chest wall rigidity. The development of other adverse effects, such as desaturation and cough, during the intervention was also compared as secondary outcomes. Potential risk factors for the development of remifentanyl-induced chest wall rigidity were also identified.

Statistical analysis

The sample size was predetermined by the Chi-square Sample Size calculation using SigmaPlot 14.5 (Systat Software Inc. San Jose, USA) based on the assumption that the incidence of remifentanyl-induced chest wall rigidity, which was considered the primary endpoint, would be 15% and 45% in the hypnotic-remifentanyl and remifentanyl-hypnotic group, respectively. A total of 103 patients were required, with a significance level of 0.05 ($\alpha = 0.05$) and power of 80% ($\beta = 0.20$). To allow attrition, the total sample size was increased to 125.

All statistical analyses were performed using SigmaPlot 14.5. Continuous variables were compared using one-way analysis of variance (ANOVA) with Tukey post-hoc test after normality test using Shapiro–Wilk test. Categorical variables were analyzed using chi-square test. Vital signs, including mean arterial pressures and heart rate, were analyzed using two-way repeated measures ANOVA. The Holm-Sidak method and Bonferroni correction were used for multiple comparisons. Based on the statistical comparison, univariate logistic regression analysis was performed to identify possible risk factors for the development of chest wall rigidity, with the odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for each variable. All data are expressed as the number of patients, means (SD), or numbers (percentages).

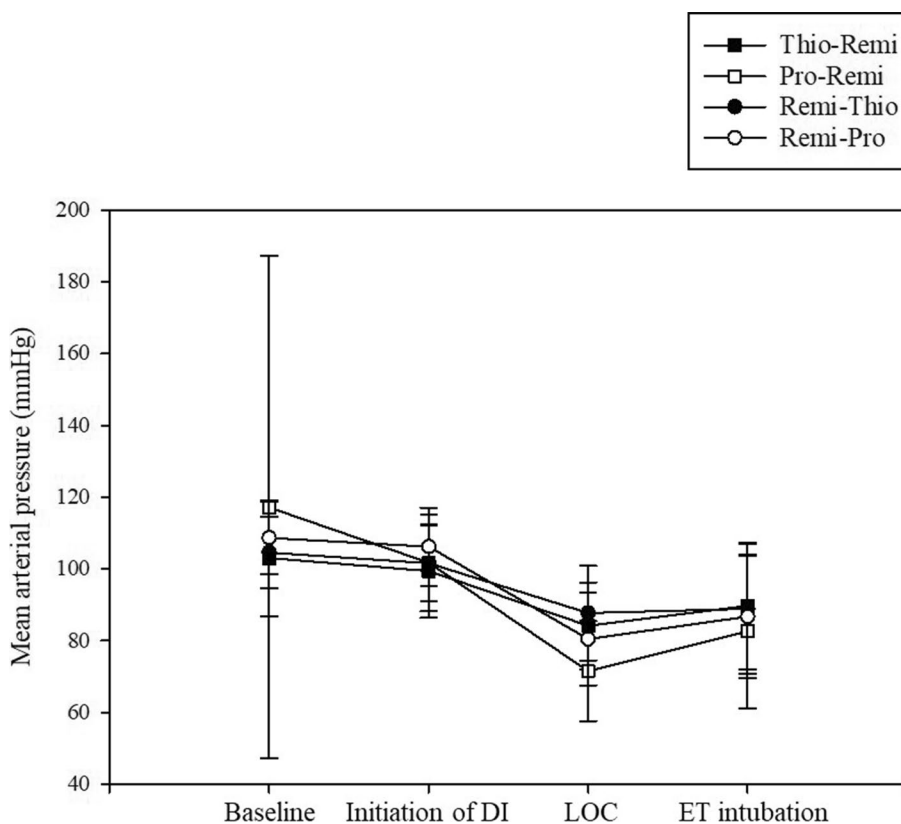


Fig. 3 The changes in mean arterial pressures among the four groups. DI; drug infusion, LOC; loss of consciousness, ET; endotracheal

A *P* value less than 0.05 was considered statistically significant.

Results

Among the 125 enrolled participants, 120 (30 in each group) were analyzed in the current study. The five participants who failed to complete the study included four who violated the study protocol and one with a SpO₂ monitoring error from pulse oximetry. The CONSORT flow diagram is shown in Fig. 1.

Patient characteristics, including body composition measures, were compared among the Thio-Remi, Pro-Remi, Remi-Thio, and Remi-Pro groups (Table 1). No significant differences in patient age, gender, height, weight, or body mass index (BMI) were noted. Body composition measures, such as body fat mass, percent body fat, skeletal muscle mass, and total body water, were also not statistically different among the four groups. The hypnotic dose required for LOC and elapsed time to LOC were comparable among the groups (Table 2).

The incidence of chest wall rigidity and other adverse effects is presented in Table 3. Significant differences in the incidence of chest wall rigidity and desaturation were noted among the four groups (*P*=0.001 and *P*=0.034,

respectively). The incidence of chest wall rigidity was significantly higher in the remifentanyl-hypnotics groups than in the hypnotic-remifentanyl groups (55.0% vs. 21.7%, *P*<0.001 according to the Chi-square test) when compared according to the administration sequence of the hypnotics and remifentanyl (Fig. 2). However, no significant difference in the development of chest wall rigidity was observed between propofol and thiopental sodium use. The univariate logistic regression analysis revealed that remifentanyl-hypnotic administration was a significant predictor of the development of chest wall rigidity (crude OR 4.42, 95% CI 1.99; 9.81, *P*<0.001) (Table 4).

Changes in vital signs, such as mean arterial pressure and heart rate, are shown in Figs. 3 and 4. Although no differences in heart rate were noted among the groups, the heart rate was significantly lower at LOC than at baseline in both the Pro-Remi and Remi-Pro groups (*P*<0.001 and *P*=0.001, respectively).

Discussions

The current study characterized remifentanyl-induced chest wall rigidity in older patients in usual clinical practice. In this study, the overall incidence of

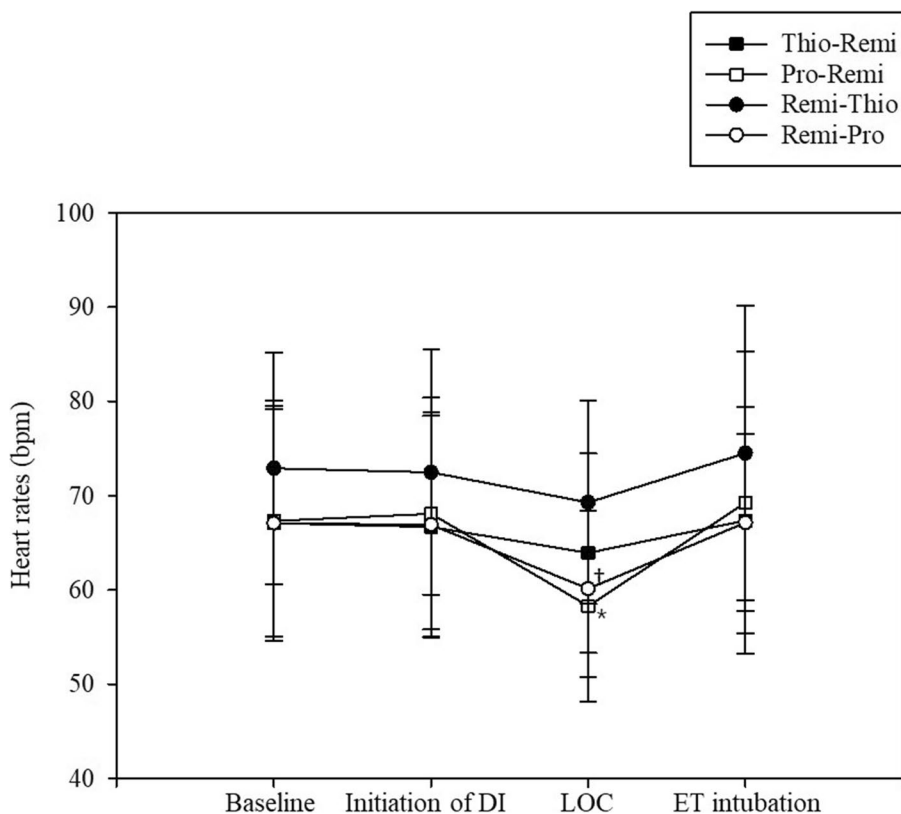


Fig. 4 The changes in heart rates among the four groups. DI; drug infusion, LOC; loss of consciousness, ET; endotracheal. *Compared with that at baseline, the heart rate was significantly lower at LOC ($P < 0.001$) in the Pro-Remi group. †The heart rate was also significantly lower at LOC ($P = 0.001$) than at baseline in the Remi-Pro group

remifentanyl-induced chest wall rigidity were 38% (46/120) in older patients (≥ 65 years), and SpO_2 desaturation $< 94\%$ developed in 16.7% (20/120). Careful anesthetic management and close monitoring are required in older patients because they are more vulnerable to perioperative morbidity. This study demonstrated that remifentanyl administration at a relatively low and conventional dosage potentially leads to severe chest wall rigidity in older patients, although it is commonly accepted that opioid-induced muscle rigidity develops more frequently when larger doses are administered rapidly.

The result of a healthy volunteer study showed that muscle rigidity developed in 50% of subjects who were administered high-dose fentanyl (15 $\mu\text{g}/\text{kg}$) [15]. Another study reported the incidence of difficult ventilation and respiratory failure to be 46% and 9.1%, respectively, in patients treated with high-dose remifentanyl (0.7 $\mu\text{g}/\text{kg}/\text{min}$) during anesthesia induction. Moreover, they suggested that a relatively lower dose of remifentanyl (0.2 $\mu\text{g}/\text{kg}/\text{min}$) resulted in significantly reduced incidence of them [6]. In the current study, 3 ng/ml of remifentanyl via TCI system, which is the conventional dosage for

anesthesia induction, was selected for the investigation. This concentration approximately corresponds to a bolus dosing of 0.75 $\mu\text{g}/\text{kg}$, followed by 0.1–0.15 $\mu\text{g}/\text{kg}/\text{min}$, which is not a high dosage, when the pre-programmed Minto model and effect-site targeting mode are used [16]. Nevertheless, the incidence of remifentanyl-induced chest wall rigidity was similar to that in other previous studies [6, 15]. The authors suggest that the development of remifentanyl-induced chest wall rigidity may not occur in a dose-dependent manner.

Furthermore, the order of administration of hypnotics and opioids predominantly depends on the anesthesiologists' preference, based on their anesthetic experiences. Propofol, the most commonly used hypnotic, is known to cause injection pain [17]. Therefore, the administration of remifentanyl before the injection of propofol is a commonly performed method to reduce the incidence and severity of propofol injection-related pain during anesthesia induction [17–19]. Several studies have suggested that the TCI of remifentanyl at a C_e of 3–6 ng/ml may be safely used for this purpose without serious respiratory complications, such as respiratory depression

[18, 20]. However, it is remarkable that pretreatment with remifentanyl prior to hypnotic administration was potentially associated with a higher probability of chest wall rigidity compared with the opposite sequence (crude OR 4.42, 95% CI 1.99; 9.81, $P < 0.001$) in the current study. Furthermore, this study aimed to clarify the effects of the body composition characteristics, such as BMI, percent body fat, or skeletal muscle index on it. No significant association between body composition and the development of remifentanyl-induced chest wall rigidity was observed.

Although the precise pathophysiologic mechanism underlying opioid-induced chest wall rigidity has not yet been completely elucidated, centrally mediated noradrenergic and cholinergic actions are considered to be the most explainable underlying molecular mechanism [21–23]. An animal study indicated that the activation of μ -opioid receptors in the locus coeruleus appeared to increase noradrenergic outflow by activating $\alpha 1$ -adrenergic receptor [21]. In addition, the inhibition of gamma-aminobutyric acid (GABA) interneuron signaling in the locus coeruleus potentially plays a partial role in the increased muscle rigidity [24–26]. Other experimental and clinical studies have suggested that pretreatment of hypnotics, including barbiturates and benzodiazepine, could mitigate the severity of opioid-induced chest wall rigidity by enhancing GABAergic activation [21, 27]. The current study demonstrated that both propofol and thiopental sodium have beneficial effects in preventing remifentanyl-induced chest wall rigidity when administered as premedication (hypnotic-remifentanyl administration).

The study has certain limitations. First, quantitative and objective measurements for evaluating chest wall rigidity are limited. Esophageal pressure, as a useful surrogate of pleural and intrathoracic pressure, can be used to estimate lung and chest wall mechanics. However, the measurements are complicated by several technical factors, such as the appropriate placement of the esophageal balloon catheter [28, 29], and are often unavailable because chest wall rigidity might develop shortly after opioid administration [23]. In the current study, the authors attempted to detect the development of opioid-induced chest wall rigidity based on bedside clinical signs and symptoms. There is scarce evidence on that issue, and that clinical evaluation might introduce a bias. An integrated qualitative and quantitative methodological approach may be necessary and can contribute to improving future research practices. Second, we did not investigate the possibility of remifentanyl-induced chest wall rigidity and resultant hypoxemia affecting perioperative outcomes. Although the decreased SpO_2 was simultaneously resolved following endotracheal intubation

and neuromuscular relaxation in the current study, cerebral desaturation in older patients may be an important issue because of its possible association with neurologic complications, such as postoperative delirium and cognitive dysfunction [30, 31]. The clinical significance of cerebral desaturation in perioperative neurologic outcomes should be investigated in future studies.

Conclusions

In conclusion, older patients frequently experience remifentanyl-induced chest wall rigidity during anesthesia induction. The authors suggest that pretreatment with hypnotics may reduce the possibility of chest wall rigidity during the induction of balanced anesthesia with remifentanyl in older patients.

Abbreviations

LOC	Loss of consciousness
TCI	Target-controlled infusion
Ce	Effect-site concentration
SpO_2	Peripheral oxygen saturation
ANOVA	Analysis of variance
BMI	Body mass index
GABA	Gamma-aminobutyric acid

Acknowledgements

Not applicable.

Authors' contributions

Y.J.O.: This author helped perform the research and wrote the original draft. Y.K.: This author helped collect data and perform statistical analysis. C.L.: This author helped collect data and perform statistical analysis. D.C.K.: This author helped design and supervise the research. A.D.: This author helped design the research and edit and revise the manuscript. The author(s) read and approved the final manuscript.

Funding

No external funding declared.

Availability of data and materials

The data analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was performed in accordance with the Good Clinical Practice regulations and guidelines and in conformity with the ethical principles of the Declaration of Helsinki. Institutional Review Board of Jeonbuk National University Hospital approved the study (IRB number; CUH 2019–12-021). Informed consent was obtained from all the participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 10 March 2023 Accepted: 26 May 2023
Published online: 08 June 2023

References

- Gemma M, Tommasino C, Cozzi S, Narcisi S, Mortini P, Losa M, et al. Remifentanyl provides hemodynamic stability and faster awakening time in transsphenoidal surgery. *Anesth Analg*. 2002;94:163–8 table of contents.
- Sridharan K, Sivaramakrishnan G. Comparison of fentanyl, remifentanyl, sufentanil and alfentanil in combination with propofol for general anesthesia: a systematic review and meta-analysis of randomized controlled trials. *Curr Clin Pharmacol*. 2019;14:116–24.
- Scott LJ, Perry CM. Remifentanyl: a review of its use during the induction and maintenance of general anaesthesia. *Drugs*. 2005;65:1793–823.
- Shuying L, Ping L, Juan N, Dong L. Different interventions in preventing opioid-induced cough: A meta-analysis. *J Clin Anesth*. 2016;34:440–7.
- Dimitriou V, Zogogiannis I, Liotiri D, Wambi F, Tawfeeq N, Koumi A, et al. Impossible mask ventilation after an unusually low dose fentanyl-induced muscle rigidity in a patient with essential tremor: a case report and review of the literature. *Middle East J Anaesthesiol*. 2014;22:619–22.
- Nakada J, Nishira M, Hosoda R, Funaki K, Takahashi S, Matsura T, et al. Priming with rocuronium or vecuronium prevents remifentanyl-mediated muscle rigidity and difficult ventilation. *J Anesth*. 2009;23:323–8.
- Levine R, Veliz S, Singer D. Wooden chest syndrome: Beware of opioid antagonists, not just agonists. *Am J Emerg Med*. 2020;38(411):e5–6.
- Comstock MK, Carter JG, Moyers JR, Stevens WC. Rigidity and hypercarbia associated with high dose fentanyl induction of anesthesia. *Anesth Analg*. 1981;60:362–3.
- Dewhurst E, Naguib A, Tobias JD. Chest wall rigidity in two infants after low-dose fentanyl administration. *Pediatr Emerg Care*. 2012;28:465–8.
- Roan JP, Bajaj N, Davis FA, Kandinata N. Opioids and Chest Wall Rigidity During Mechanical Ventilation. *Ann Intern Med*. 2018;168:678.
- Fahnestich H, Steffan J, Kau N, Bartmann P. Fentanyl-induced chest wall rigidity and laryngospasm in preterm and term infants. *Crit Care Med*. 2000;28:836–9.
- Carvalho B, Mirikitani EJ, Lyell D, Evans DA, Druzin M, Riley ET. Neonatal chest wall rigidity following the use of remifentanyl for cesarean delivery in a patient with autoimmune hepatitis and thrombocytopenia. *Int J Obstet Anesth*. 2004;13:53–6.
- Honda T, Takenami T, Itou N, Suzuki K, Okamoto T, Hoka S. increased dose of remifentanyl caused difficult ventilation at emergence from general anesthesia. *Masui*. 2009;58(8):980–3.
- Sprung J, Gajic O, Warner DO. Review article: Age related alterations in respiratory function - anesthetic considerations. *Can J Anaesth*. 2006;53:1244–57.
- Streisand JB, Bailey PL, LeMaire L, Ashburn MA, Tarver SD, Varvel J, et al. Fentanyl-induced rigidity and unconsciousness in human volunteers. Incidence, duration, and plasma concentrations. *Anesthesiology*. 1993;78:629–34.
- Eleveld DJ, Colin P, Absalom AR, Struys M. Target-controlled-infusion models for remifentanyl dosing consistent with approved recommendations. *Br J Anaesth*. 2020;125:483–91.
- Picard P, Tramèr MR. Prevention of pain on injection with propofol: a quantitative systematic review. *Anesth Analg*. 2000;90:963–9.
- Kim J, Kim D, Lee HG. Effect-site concentration of remifentanyl for preventing propofol injection pain during induction of balanced anesthesia. *Anesth Pain Med (Seoul)*. 2020;15:152–6.
- Iyilikci L, Balkan BK, Gökel E, Günerli A, Ellidokuz H. The effects of alfentanil or remifentanyl pretreatment on propofol injection pain. *J Clin Anesth*. 2004;16:499–502.
- Lee JR, Jung CW, Lee YH. Reduction of pain during induction with target-controlled propofol and remifentanyl. *Br J Anaesth*. 2007;99:876–80.
- Lui PW, Lee TY, Chan SH. Fentanyl-induced muscle rigidity in unanesthetized and ketamine- or thiopental-anesthetized rats. *Anesthesiology*. 1989;70:984–90.
- Turski L, Havemann U, Kuschinsky K. Role of muscarinic cholinergic mechanisms in the substantia nigra pars reticulata in mediating muscular rigidity in rats. *Naunyn Schmiedeberg's Arch Pharmacol*. 1984;327:14–7.
- Torralva R, Janowsky A. Noradrenergic mechanisms in fentanyl-mediated rapid death explain failure of naloxone in the opioid crisis. *J Pharmacol Exp Ther*. 2019;371:453–75.
- Turski L, Havemann U, Kuschinsky K. Gabaergic mechanisms in mediating muscular rigidity, catalepsy and postural asymmetry in rats: Differences between dorsal and ventral striatum. *Brain Res*. 1984;322:49–57.
- Griffioen KJ, Venkatesan P, Huang ZG, Wang X, Bouairi E, Evans C, et al. Fentanyl inhibits gabaergic neurotransmission to cardiac vagal neurons in the nucleus ambiguus. *Brain Res*. 2004;1007:109–15.
- Jin X, Li S, Bondy B, Zhong W, Oginsky MF, Wu Y, et al. Identification of a group of gabaergic neurons in the dorsomedial area of the locus coeruleus. *PLoS One*. 2016;11:e0146470.
- Sanford TJ Jr, Weinger MB, Smith NT, Benthuysen JL, Head N, Silver H, et al. Pretreatment with sedative-hypnotics, but not with nondepolarizing muscle relaxants, attenuates alfentanil-induced muscle rigidity. *J Clin Anesth*. 1994;6:473–80.
- Soares JH, Brosnan RJ, Smith A, Mayhew PD. Rabbit model of chest wall rigidity induced by fentanyl and the effects of apomorphine. *Respir Physiol Neurobiol*. 2014;202:50–2.
- Persson P, Ahlstrand R, Gudmundsson M, de Leon A, Lundin S. Detailed measurements of oesophageal pressure during mechanical ventilation with an advanced high-resolution manometry catheter. *Crit Care*. 2019;23:217.
- Bendahan N, Neal O, Ross-White A, Muscedere J, Boyd JG. Relationship between near-infrared spectroscopy-derived cerebral oxygenation and delirium in critically ill patients: a systematic review. *J Intensive Care Med*. 2019;34:514–20.
- Ballard C, Jones E, Gauge N, Aarsland D, Nilsen OB, Saxby BK, et al. Optimised anaesthesia to reduce post-operative cognitive decline (pocd) in older patients undergoing elective surgery, a randomised controlled trial. *PLoS One*. 2012;7: e37410.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

