Frontiers in Health Informatics www.healthinformaticsjournal.com
ISSN-Online: 2676-7104
2025; Vol: 14 Issue 2 Open Access

# Studying the effect of intravenous chlorpromazine injection to reduce the use of sedative drugs in patients under ventilation

**Mojgan chehrazad[1], fateme modjallal[2], Mohamadali Jafari[3], Ali Raee Ezzabadi[2], Faeze Zeinali.N[2], soheila Azimi Abarghouei[2], Naser Mohammadkarimi[*2]**

[1] Emergency Medicine Specialist, Department of Emergency Medicine, School of MEDICINE, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[2] Assistant Professor, Department of Emergency Medicine, School of MEDICINE, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[3] Associate Professor, Clinical Research Development Center, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[*]Correspond Author: nmkarimi1310@yahoo.com

**Cite this paper as:** Mojgan chehrazad, fateme modjallal, Mohamadali Jafari, Ali Raee Ezzabadi, Faeze Zeinali.N, soheila Azimi Abarghouei, Naser Mohammadkarimi* (2025), Studying the effect of intravenous chlorpromazine injection to reduce the use of sedative drugs in patients under ventilation. Frontiers in Health Informatics, 14(2) 2719-2725

## Abstract

**Introduction:** This study aimed to evaluate the sedation efficacy and drug requirements between the two groups.

**Method:** This randomized, double-blind clinical trial involved 50 ICU patients, divided into chlorpromazine and control groups. Both groups initially received fentanyl (1.5 mcg/kg) and midazolam (2 mg) bolus injections, with time recorded. The chlorpromazine group additionally received 50 mg intramuscular chlorpromazine by a blinded administrator. Sedation levels were assessed hourly up to 4 hours using the Richmond Agitation-Sedation Scale (RASS).

**Result:** According to the table above, the frequency distribution of sedative drug injections after the initial dose in patients indicates that in the control group, 86% of the subjects had two and three injections, respectively, while in the chlorpromazine group, only 24% of the subjects had two injections and no patient had three injections. With the intramuscular injection of chlorpromazine, there was no change in blood pressure in the short term (time 1). Nevertheless, after a longer time (time 4), a significant difference was observed between the blood pressure of the two groups. This pattern could indicate a strong and long-term effect of the drug.

**Conclusion:** intravenous chlorpromazine at usual doses can be used effectively and with acceptable safety as a treatment option for controlling agitation in adult patients hospitalized in the ICU.

**Key words:** Chlorpromazine, Sedation, Mechanical Ventilation, Intensive Care Units.

## Introduction

Tracheal intubation is a process that allows for mechanical ventilation(1). This method is mainly employed in critically ill patients, especially those who require artificial respiration. The main goal of intubation is to maintain optimal oxygenation of body tissues and prevent airway obstruction(2). However, this process

can also be associated with complications, one of the most important being the occurrence of irritability and agitation after intubation in patients (1).

Post-intubation agitation is a condition in which the patient experiences severe irritability, restlessness, and risky behaviors which can take place as a result of pain, anxiety, non-compliance with the breathing tube, or neurological problems(3). This condition not only reduces the patient's comfort but may also lead to accidental removal of the endotracheal tube, airway damage, and increased length of stay in the ICU. Thus, agitation control in intubated patients is of particular importance and is usually achieved by administering sedative drugs (4). In intubated patients, agitation control is of great importance to mitigate complications and increase patient safety. This treatment includes careful control of pain as the main cause of agitation, targeted and controlled use of sedative and anti-anxiety drugs such as benzodiazepines and haloperidol, as well as continuous monitoring of the level of consciousness(4). Maintaining adequate sedation with minimal use of appropriate drugs, shortening the duration of mechanical ventilation and ICU admission, and reducing associated complications are the main goals of treatment. This combined approach, while relieving symptoms, improves clinical outcomes in intubated patients (5).

This retrospective analysis of the National Emergency Airway Registry (NEAR) database, covering 11,748 emergency department intubations between 2016 and 2017, found that 77.5% of patients received post-intubation sedation within 15 minutes of endotracheal intubation (ETI). Factors associated with lower odds of post-intubation sedation included pre- and post-intubation hypotension (both with an odds ratio of 0.27). Patients intubated for medical reasons had higher odds (1.16) compared to those intubated for trauma. Also, those who underwent rapid sequence intubation (RSI) had significantly higher odds (15.15) of receiving sedation. Further, use of succinylcholine was linked to increased odds (1.89) of post-intubation sedation compared to longer-acting neuromuscular blockers such as rocuronium or vecuronium. Overall, post-intubation sedation rates in this cohort were higher than previously reported, with multiple clinical factors influencing sedation practices (6).

Chlorpromazine is a first-generation antipsychotic drug from the phenothiazine group exerting its therapeutic effect mainly by antagonizing postsynaptic dopamine D2 receptors in the central nervous system, especially in the mesolimbic and mesocortical pathways of the brain(7). This mechanism mitigates psychotic symptoms such as hallucinations and delusions. In addition to dopamine receptors, chlorpromazine also blocks muscarinic, histamine H1, serotonin, and alpha-adrenergic receptors, inducing sedative, antiemetic effects, as well as some side effects of the drug(8). This compound has diverse effects on nervous systems and has wide applications in the treatment of mental disorders, nausea, anxiety, and intractable hiccups (9).

## Method

This study was conducted as a double-blind, randomized clinical trial. Sampling was performed randomly. Considering similar studies and based on a confidence level of 95%, a power of 80%, and a standard deviation of S = 3.5 in the Richmond score, the minimum sample size in each group was confirmed to be 25 people.

Study inclusion criteria:

All patients hospitalized in the intensive care unit (ICU) who were intubated and therefore required sedation, and were within 18-75 years of age, were included in the study.

Study exclusion criteria:

Patients with hypotension, addicted or suspected addicted patients, patients with renal disorders (blood creatinine level > 2.4), level of consciousness (Glasgow Coma Scale: GCS) lower than 9, and patients taking drugs that would interact with chlorpromazine.

The present study was conducted as a randomized, double-blind clinical trial. After approval by the ethics committee and informed consent from the companions, 50 patients hospitalized in the intensive care units (ICUs) of Shahid Sadoughi and Rahnemoon hospitals in Yazd were enrolled in the study and divided into two groups: chlorpromazine and control based on a random number table.

Control group: 1.5 micrograms/kg fentanyl and 2 mg midazolam were injected as a bolus and the time was recorded by the nurse.

In the chlorpromazine group: First, 1.5 micrograms/kg fentanyl and 2 mg midazolam were injected as a bolus with the time recorded by the nurse. Then, 50 mg of chlorpromazine was injected intramuscularly by a person blinded to the study.

The level of sedation of each patient was measured hourly using the Richmond Agitation-Sedation Scale (RASS). In the case where the patient's score reached -2 (opens the eyes when called), 15 micrograms per kilogram of fentanyl and 2 mg of midazolam were injected. The frequency of injections and the amounts of sedative drugs needed per hour for up to 4 hours were calculated and recorded by an ICU nurse who was unaware of the patient group. The RASS tool is a standard tool and is recognized as valid for evaluating the level of agitation or sedation of patients admitted to the ICU. To determine the RASS score, the patient is first observed without any interaction, and if he is conscious, an appropriate score of 0 to -4 is considered for them. However, if the patient is not conscious, their name is called out loud and they are asked to look at the researcher. This can be repeated if necessary. If the patient responded to the sound, an appropriate score of -1 to -3 was recorded, but if there was no response, the patient's shoulder was shaken, and if there was still no response, the sternum was stimulated more vigorously and a score of -5 to -4 was considered for him.

Other patient information including age, gender, patient's previous history of intubation, time of intubation (if the patient had a history of intubation), history of the disease that led to intubation, and a questionnaire prepared in advance were recorded.

The dosage of fentanyl and midazolam, as well as side effects following chlorpromazine use, including hypotension (a 2-unit decrease in Systolic Blood Pressure (SBP), were also recorded in the questionnaire.

The obtained data were entered into SPSS version 21 and analyzed using appropriate statistical methods, including descriptive statistics (frequency indices and relative percentages) and suitable statistical tests (Chi-Square). The significance level was set at 0.05.

## Results

The mean age of patients in the chlorpromazine group was 44.68±17.7 years and in the control group was 42.28±14.73 years, which was not significantly different ($p>0.05$). Also, 56.7% of the patients in the

chlorpromazine group were male, 57.7% were male, and the rest were female, which was again not significantly different (p>0.05). Therefore, the two groups were similar in terms of age and gender.
The cause of intubation in the group chlorpromazine was trauma in 22 (24.8%) patients and in the control group in 23 (58.2%) patients, and in the other patients, the cause was other than trauma (p>0.05).
The mean duration of intubation in the chlorpromazine group was 49.2 ± 4.94 hours and in the control group was 38.4 ± 3.49 hours, showing no significant difference between the two groups (p>0.05).

Table 1: Frequency distribution of the need for sedative injection after the initial dose in the two studied groups

| Frequency | Chlropromazine[1] | Control[2] | Total | p-value |
|---|---|---|---|---|
| Zero | 9(24%) | 3(11.53%) | 9(18%) | 0.005 |
| Once | 14(52%) | 4(15.38%) | 17(34%) | |
| Twice | 7(24%) | 14(53.84%) | 20(40%) | |
| Three times | 0(0%) | 5(19.23%) | 4(8%) | |
| Total | 30(100%) | 26(100%) | 50(100%) | |

1. Fentanyl 1.5 micrograms/kg, midazolam 2 mg, chlorpromazine 50 mg intramuscular
2. Fentanyl 1.5 micrograms/kg, midazolam 2 mg

According to the table above, the frequency distribution of sedative drug injections after the initial dose in patients indicates that in the control group, 86% of the subjects had two and three injections, respectively, while in the chlorpromazine group, only 24% of the subjects had two injections and no patient had three injections.
Side effects: The following table presents the effect of the drug on the patient's hemodynamics:

Table 2. Determination and comparison of the average heart rate, mean arterial pressure (MAP), and body temperature of the patients in the two groups (independent t-test)

| **Time** | **Group** | **Average heart rate** | **p-value** | **Mean arterial pressure** | **p-value** | **Body temperature** | **p-value** |
|---|---|---|---|---|---|---|---|
| Zero | Chlropromazine[2] | 99.0±21.41 | 0.054 | 94.11± 2.03 | **0.595** | 37.11± 1.09 | **0.62** |
| | Control[1] | 88.2±17.17 | | 93.44± 2.83 | | 37.35± 1.10 | |
| 1 h later | Chlropromazine[2] | 106.8±21.24 | 0.086 | 93.11± 2.57 | **0.209** | 37.35± 2.30 | **0.65** |
| | Control[1] | 91.48±20.33 | | 94.56± 2.07 | | 37.23± 1.09 | |
| 4 h later | Chlropromazine[2] | 93.92±17.94 | 0.58 | 83.76± 6.55 | < **0.001** | 37.15± 2.00 | **0.58** |
| | Control[1] | 96.4±14.45 | | 94.56± 2.07 | | 37.13± 2.05 | |

1. Fentanyl 1.5 µg/kg, midazolam 2 mg, chlorpromazine 50 mg intramuscular
2. Fentanyl 1.5 µg/kg, midazolam 2 mg

According to Table 2, reporting the average heart rate and body temperature at different times in the two groups, no significant difference was observed between the two groups at any of the examined times.
With the intramuscular injection of chlorpromazine, there was no change in blood pressure in the short term (time 1). Nevertheless, after a longer time (time 4), a significant difference was observed between the blood pressure of the two groups. This pattern could indicate a strong and long-term effect of the drug.

**Discussion and Conclusion**

In a retrospective study of 39 ICU patients who received intravenous chlorpromazine at a dose of 1 mg/min for agitation control, mean arterial pressure (MAP) diminished significantly and returned to normal within 4 hours, while these patients did not require additional vasopressors or sedatives, and no symptomatic cardiac arrhythmias were reported. The results revealed that intravenous chlorpromazine at the usual dose is a safe drug to use despite transient hypotension (10). Another retrospective study of 97 terminal cancer patients treated with low-dose intravenous chlorpromazine (mean 17.9 mg/day) for irreversible delirium indicated a 48% response rate improvement in delirium scores by day three. Adverse events occurred in 11.3% of patients, all of whom survived less than two weeks and had shock index ≥1 (6). The findings of the above article are fully consistent with the present study.
In another retrospective study of 26 children with a mean age of 14.5 months who were hospitalized with chlorpromazine for the treatment of refractory agitation associated with hyperactive or mixed delirium (RAA-D), they concluded that the patients' agitation significantly improved 24 hours after treatment with chlorpromazine and no significant side effects were observed (11). This demonstrates that this drug can be used in a wide range of patients, although children were not studied in the present study.
In a study of 63 ICU patients with agitation, 25 mg of chlorpromazine was administered intravenously to two groups with baseline temperatures ≤ 38°C and > 38°C, where a significant decline in body temperature was observed in the groups 4 to 12 hours after treatment (12). However, in the present study, no finding was found in favor of lowering the patients' body temperature.
Berling, in a retrospective study of 218 patients poisoned with chlorpromazine at doses greater than 300 mg from 1987 to 2023, reported that the mean dose was 1250 mg. The dose in intubated patients was significantly higher than in the general population (mean 2000 mg). Common symptoms included central nervous system depression, delirium, hypotension, and seizures, and one death was reported(13). This suggests that the use of low doses of chlordiazepoxide is unlikely to cause severe adverse effects.
Watt et al in a retrospective study of 200 intubated patients found that those receiving rocuronium experienced a significantly longer delay in initiation of post-intubation sedation (27 vs. 15 minutes) compared to those given succinylcholine. All patients received etomidate, and most were sedated with propofol or midazolam(14). In the present study, succinylcholine was used for intubation of all patients.
Hoertel N et al in a retrospective multicenter study of 14,340 COVID-19 patients hospitalized outside ICUs found that chlorpromazine use (in 55 patients) was not significantly associated with reduced mortality. Primary analysis presented no significant mortality benefit (HR 2.01, p=0.163), while sensitivity analyses yielded mixed results, with one indicating a significant increased risk. Overall, chlorpromazine at an average daily dose of 70.8 mg did not lower mortality in these patients(15).

**Conclusion**

Based on the results of similar studies and the findings of the present study, it can be stated that intravenous chlorpromazine at usual doses can be used effectively and with acceptable safety as a treatment option for controlling agitation in adult patients hospitalized in the ICU. This drug does not cause significant and concerning changes in systolic blood pressure and heart rate nor does not cause significant cardiac complications, while also reducing the need for additional vasopressor and sedative drugs. Overall, chlorpromazine with controlled doses and under clinical supervision is an effective and safe option for mitigating agitation and managing associated symptoms in ICU patients.

**Referrences**

1. Bawazeer M, Amer M, Maghrabi K, Alshaikh K, Amin R, Rizwan M, et al. Adjunct low-dose ketamine infusion vs standard of care in mechanically ventilated critically ill patients at a Tertiary Saudi Hospital (ATTAINMENT Trial): study protocol for a randomized, prospective, pilot, feasibility trial. Trials. 2020;21(1):288.
2. Amer M, Maghrabi K, Bawazeer M, Alshaikh K, Shaban M, Rizwan M, et al. Adjunctive ketamine for sedation in critically ill mechanically ventilated patients: an active-controlled, pilot, feasibility clinical trial. Journal of Intensive Care. 2021;9(1):54.
3. Garber PM, Droege CA, Carter KE, Harger NJ, Mueller EW. Continuous infusion ketamine for adjunctive analgosedation in mechanically ventilated, critically ill patients. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2019;39(3):288-96.
4. Prendergast NT, Onyemekwu CA, Potter KM, Tiberio PJ, Turnbull AE, Girard TD. Agitation is a common barrier to recovery of ICU patients. Journal of intensive care medicine. 2023;38(2):208-14.
5. Adams AMN, Chamberlain D, Brun Thorup C, Maiden MJ, Waite C, Dafny HA, et al. Patient agitation in the intensive care unit: a concept analysis. Journal of Advanced Nursing. 2025.
6. Hasuo H, Kanbara K, Fujii R, Uchitani K, Sakuma H, Fukunaga M. Factors Associated with the Effectiveness of Intravenous Administration of Chlorpromazine for Delirium in Patients with Terminal Cancer. J Palliat Med. 2018;21(9):1257-64.
7. Kim SY, Simone S, Kishk OA, Graciano AL, Seung H, Edwards S. Chlorpromazine as treatment for refractory agitation associated with pediatric delirium. The Journal of Pediatric Pharmacology and Therapeutics. 2022;27(8):725-31.
8. SRINIVASAN M, YADAV G, SINGH Y, SAHU A, KUMARI S, SINGH A. Comparison of Efficacy of Combination Therapy with Chlorpromazine and Olanzapine with Chlorpromazine alone for Treatment of Hiccups in Traumatic Brain Injury Patients-A Randomised Control Trial. Journal of Clinical & Diagnostic Research. 2022;16(9).
9. Mousavi SG, Eghtesadi D, Mahaki B. Comparing the Velocity of Haloperidol, Chlorpromazine, Trifluoperazine, and Promethazine in Sedating of Aggressive Patients. Journal Of Isfahan Medical School. 2019;37(526):500-7.

10. Choi M, Barra ME, Newman K, Sin JH. Safety and Effectiveness of Intravenous Chlorpromazine for Agitation in Critically Ill Patients. J Intensive Care Med. 2020;35(10):1118-22.
11. Kim SY, Simone S, Kishk OA, Graciano AL, Seung H, Edwards S. Chlorpromazine as Treatment for Refractory Agitation Associated with Pediatric Delirium. J Pediatr Pharmacol Ther. 2022;27(8):725-31.
12. Muhammed Emin Z, Bülent A, Jale Ç E, Faruk ÇİÇ E, Ali B, Ateş D. The Acute Effect of Chlorpromazine on Body Temperature in Intensive Care Unit Patients. Genel Tıp Dergisi. 2022;32(6):658-65.
13. Berling I, Isbister GK. Chlorpromazine overdose: a case series. Clinical Toxicology. 2024;62(6):372-7.
14. Pankey JA, Christofferson S, Barrick G, Knettel BA, Knettel C. Effect of paralytic agents on post-intubation sedation in the emergency department. Hospital Pharmacy. 2022;57(6):759-66.
15. Hoertel N, Sanchez-Rico M, Vernet R, Jannot A-S, Neuraz A, Blanco C, et al. Observational study of chlorpromazine in hospitalized patients with COVID-19. Clinical drug investigation. 2021;41(3):221-33.