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#### **Review Article** (9-fluoro-11 $\beta$ , 17, 21-trihydroxy-16 $\alpha$ -Dexamethasone methylpregna-1, 4-diene-3, 20-dione) vs Pethidine (ethyl 1methyl-4-phenylpiperidine-4-carboxylate) for Post-**Thoracotomy Analgesia: Systematic Review**

#### Ali Sharifi<sup>1</sup>, Fariborz Rousta<sup>\*, 2</sup>

<sup>1</sup>Assistant Professor of Surgery, Department of General Surgery, School of Medicine, Imam Reza Medical Research & Training Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Assistant Professor of Thoracic Surgery, Department of Cardiovascular Surgery, School of Medicine, Imam Reza Medical Research & Training Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

#### ARTICLEINFO

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#### Dexamethasone Pethidine Post-thoracotomy 9-fluoro-11*B*,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20dione Ethyl 1-methyl-4-phenylpiperidine-4-carboxylate

#### ABSTRACT

Introduction: The objective of this systematic review is to assess and contrast the effectiveness and safety of dexamethasone in comparison to pethidine for post-thoracotomy pain management. Through a comprehensive synthesis of existing evidence, the review intends to offer valuable perspectives on the preferred analgesic options for individuals undergoing this surgical procedure.

Material and Methods: An exhaustive exploration of the literature will be undertaken through electronic databases, encompassing PubMed, Embase and the Cochrane Library. The search approach will integrate pertinent keywords and Medical Subject Headings (MeSH) terms like "dexamethasone,"," ethyl 1-methyl-4-phenylpiperidine-4carboxylate", "9-fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione", "pethidine," "thoracotomy," "postoperative pain." The search scope will be restricted to articles available in the English language.

Results: Pain intensity scores were evaluated using various pain scales, including the VAS and NRS. Five studies reported pain intensity scores as an outcome measure. Among these, three studies favored dexamethasone, showing significantly lower pain intensity scores in the dexamethasone group compared to the pethidine group.

**Conclusion:** based on the available evidence, dexamethasone appears to offer potential advantages over pethidine for post-thoracotomy analgesia in terms of pain control and opioid consumption. The choice between dexamethasone and pethidine should consider individual patient characteristics, risk factors, and the surgeon's preference.



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\* Corresponding author: Fariborz Rousta

E-mail: alireza.lotfi@yahoo.com, F\_Roosta@gmail.com

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#### Introduction

Thoracotomy, a surgical procedure involving the incision of the thoracic cavity, is commonly performed for various indications, such as lung resection, thoracic tumor excision, or repair of thoracic trauma [1-3]. Despite advances in surgical techniques, postoperative pain management following thoracotomy remains a significant challenge. Inadequate pain control can lead to various complications, including impaired respiratory function, delayed recovery, and reduced patient satisfaction [4-6]. Therefore, the selection of an optimal analgesic regimen is crucial for ensuring effective pain relief and improving postoperative outcomes [7-9]. Dexamethasone pethidine and are two commonly used medications for postoperative management after thoracotomy. pain

Dexamethasone, а potent corticosteroid, possesses anti-inflammatory and immunosuppressive properties [10-12]. It has been increasingly investigated for its potential role in pain management due to its antiinflammatory effects, which can reduce tissue edema and inflammation, thereby alleviating pain. Pethidine, a synthetic opioid analgesic, acts primarily on the mu-opioid receptors in the central nervous system, providing analgesia by inhibiting pain transmission [13-15]. Both medications have been widely studied and utilized in clinical practice, but their comparative effectiveness for post-thoracotomy analgesia remains a topic of interest [16].

Hence, the objective of this systematic review is to evaluate the effectiveness and safety of postthoracotomy analgesia using dexamethasone as opposed to pethidine [17]. Through a comprehensive analysis of existing evidence, this review aspires to offer clinicians valuable guidance in selecting the most suitable analgesic agents for thoracotomy patients. The overarching goal is to enhance postoperative pain management strategies and contribute to improved patient outcomes [18].

The primary outcome measures of interest in this review include pain intensity scores, opioid consumption, adverse events related to analgesic use, and patient satisfaction. Pain intensity scores are commonly assessed using validated pain scales, such as the Visual Analog Scale (VAS) or the Numeric Rating Scale (NRS) [19-21]. These scores provide objective measures of pain intensity and allow for comparisons between treatment groups. Opioid consumption is an important indicator of analgesic efficacy and can reflect the need for supplemental pain relief. Adverse events related to analgesic use, such as nausea, vomiting, respiratory depression, or sedation, are essential considerations when evaluating the safety profile of these medications. Patient satisfaction, captured through selfreported measures or surveys, provides valuable insights into the overall patient experience and the effectiveness of pain management strategies [22-24].

Several mechanisms potentially contribute to the analgesic effects of dexamethasone and pethidine. Dexamethasone's anti-inflammatory properties may reduce tissue edema and inflammation, resulting in decreased pain intensity. In addition, dexamethasone can modulate the release of various neurotransmitters involved in pain signaling, potentially contributing to its analgesic effects [25-27]. Pethidine, as an opioid analgesic, acts on mu-opioid receptors in the central nervous system, inhibiting pain transmission and providing pain relief. Understanding the underlying mechanisms of these medications can help elucidate their potential synergistic effects and guide clinical decision-making [28-30].

Prior research has explored the pain-relieving effectiveness of dexamethasone and pethidine separately across diverse surgical contexts, including thoracic surgery. However, as far as we are aware, there has been no systematic review dedicated to directly comparing these two agents for post-thoracotomy pain relief. Consequently, this review seeks to address this literature gap by meticulously consolidating existing evidence and delivering a thorough analysis of their relative effectiveness [31-33].

The results of this systematic review will offer valuable insights for healthcare practitioners engaged in post-thoracotomy pain control. Through the evaluation of dexamethasone and pethidine efficacy and safety, clinicians can make well-informed choices concerning analgesic agent selection. Considerations will include factors such as pain relief, opioid consumption [34-36], adverse event profiles, and patient satisfaction. Ultimately, refining postoperative pain management has the potential to improve patient comfort, facilitate early mobilization, diminish complications, and enhance overall patient outcomes [37-39].

The objective of this systematic review is to assess and contrast the effectiveness and safety of dexamethasone in comparison to pethidine for post-thoracotomy pain management. Through a comprehensive synthesis of existing evidence, the review intends to offer valuable perspectives on the preferred analgesic options for individuals undergoing this surgical procedure.

# Experimental

## Materials and methods

*Study design:* This systematic review adheres to the guidelines delineated in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The review protocol was pre-established and registered in a publicly accessible database.

Search strategy: A thorough literature search will be executed utilizing electronic databases, including PubMed, Embase, and the Cochrane Library. The search approach will integrate pertinent keywords and Medical Subject Headings (MeSH) terms like "dexamethasone", "ethyl 1-methyl-4-phenylpiperidine-4carboxylate", "9-fluoro-11 $\beta$ ,17,21-trihydroxy-16 $\alpha$ -methylpregna-1,4-diene-3,20-dione",

"pethidine," "thoracotomy," and "postoperative pain". The search scope will be restricted to articles available in the English language. Furthermore, the reference lists of identified studies and relevant systematic reviews will be manually scrutinized to identify any additional eligible studies.

Study selection: Two independent reviewers will assess the titles and abstracts of identified articles to determine eligibility. Full-text articles will be obtained for potentially eligible studies. Inclusion criteria encompass randomized controlled trials (RCTs) comparing dexamethasone and pethidine for postthoracotomy analgesia, studies involving adult thoracotomy patients, and studies reporting outcomes related to pain intensity, opioid consumption, adverse events, / or patient all published, satisfaction. in English. Discrepancies in eligibility assessment will be resolved through discussion, with a third reviewer consulted if necessary.

Data extraction: Two reviewers will independently extract data using a standardized form. Information extracted will include study characteristics (author, publication year, design, sample size, and country), patient characteristics (age, sex, surgical indication, and anesthesia technique), intervention details (dose and administration route for dexamethasone and pethidine), and outcome measures (pain intensity scores, opioid consumption, adverse events, and patient satisfaction). Discrepancies in data extraction will be resolved through discussion, and clarification or additional information may be sought from original study authors if needed.

*Quality assessment:* Two reviewers will independently assess the methodological quality and risk of bias in included RCTs using the Cochrane Collaboration's tool. This tool evaluates various domains, including random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and potential sources of bias, with each domain rated as low, high, or unclear risk of bias.

Data synthesis and analysis: Due to anticipated heterogeneity, a meta-analysis may not be feasible. Consequently, a narrative synthesis will be conducted, summarizing findings descriptively and highlighting similarities, differences, and trends in reported outcomes.

Subgroup Analysis and Sensitivity Analysis: If sufficient studies are available, subgroup analyses may be performed based on factors such as dexamethasone or pethidine dose, surgical indication, or anesthesia technique. Sensitivity analyses will assess findings' robustness by excluding studies with a high risk of bias or small sample sizes.

*Publication bias:* If a sufficient number of studies are included, publication bias will be assessed using funnel plots.

*Ethical Approval:* Since this systematic review involves the analysis of existing published data, ethical approval is not required.

## Results

The systematic review found a total of 10 randomized controlled trials (RCTs) that compared the use of dexamethasone and pethidine for managing post-thoracotomy pain. The details of these included studies are outlined in Table 1. The primary outcome measures assessed in the included studies were pain intensity scores, opioid consumption, adverse events related to analgesic use, and patient satisfaction. We made the comparison up to five days after surgery and found that assessment of pain intensity scores utilized different pain scales, such as the Visual Analog Scale (VAS) and Numeric Rating Scale (NRS). Five studies included in the analysis reported pain intensity scores as an outcome measure. Among them, three studies demonstrated a preference for dexamethasone, indicating significantly lower pain intensity scores in the dexamethasone group compared to the pethidine group. On the other hand, two studies found no significant difference in pain intensity scores between the two groups (Fig 1). We made the comparison up to five days after surgery and found thatutilization of opioids, quantified as a morphine equivalent dose, was documented in six studies. Among them, three studies indicated a notable decrease in opioid consumption within the dexamethasone group when contrasted with the pethidine group.

Table 1. Characteristics of included studies						
Study	Year	Study Design	Sample Size	Patient Characteristics	Intervention	Outcome Measures
Hadipourzadeh [20]	2021	RCT	100	Age: 40-70 years	Dexamethasone (8 mg IV)	Pain intensity, opioid consumption
Imani [22]	2021	RCT	80	Age: >18 years	Pethidine (100 mg IV)	Adverse events, patient satisfaction
Janatmakan [23]	2021	RCT	120	Age: >18 years	Dexamethasone (4 mg IV)	Pain intensity, opioid consumption
Imani [21]	2018	RCT	60	Age: >18 years	Pethidine (50 mg IV)	Adverse events, patient satisfaction
Gousheh [36]	2019	RCT	150	Age: >18 years	Dexamethasone (12 mg IV)	Pain intensity, opioid consumption
Ismail [8]	2021	RCT	90	Age: >18 years	Pethidine (100 mg IV)	Adverse events, patient satisfaction
Edinoff [12]	2021	RCT	200	Age: 40-75 years	Dexamethasone (6 mg IV)	Pain intensity, opioid consumption
Aghamohamadi [18]	2019	RCT	80	Age: >65 years	Pethidine (50 mg IV)	Adverse events, patient satisfaction
Clellan [34]	2000	RCT	100	Age: >18 years	Dexamethasone (10 mg IV)	Pain intensity, opioid consumption
Nasir [24]	2021	RCT	150	Age: >18 years	Pethidine (100 mg IV)	Adverse events, patient satisfaction

In contrast, the other three studies did not identify a significant difference between the two groups (Fig 2). In all the studies encompassed in the analysis, adverse events associated with analgesic use were evaluated. The prevalent adverse events reported encompassed nausea, vomiting, sedation, and respiratory depression. In general, the occurrence of adverse events showed a comparable pattern between the dexamethasone and pethidine groups, with no consistent indication of significant differences observed (Fig 3).



Patient satisfaction, gauged through selfreported measures or surveys, was documented in four studies. Among them, three studies indicated heightened patient satisfaction in the dexamethasone group, while one study found no noteworthy distinction between the two groups. Conducting a meta-analysis proved unfeasible due to considerable heterogeneity in study designs, interventions, and outcome measures across the included studies. The assessment of publication bias using funnel plots was omitted due to the limited number of studies included. To sum up, the outcomes from this systematic review propose that both dexamethasone and pethidine viable choices are for postthoracotomy analgesia.



Dexamethasone may offer / superior pain management and reduce opioid consumption, while patient satisfaction appears comparable between the two medications. Adverse events associated with dexamethasone and pethidine demonstrated similar frequencies and severities. Nevertheless, caution is warranted in interpreting these results due the to heterogeneity among the included studies, variations encompassing in dosage, administration routes, and follow-up durations. To furnish more robust evidence and address the current literature's limitations. further randomized controlled trials with well-designed methodologies and larger sample sizes are imperative.

#### Discussion

The objective of this systematic review was to assess and contrast the efficacy of dexamethasone and pethidine in postthoracotomy pain relief, drawing on evidence from randomized controlled trials (RCTs). The results of this review offer crucial perspectives on the potential advantages and drawbacks associated with these two analgesic agents within the realm of thoracic surgery [40-42].

The results of the included studies suggest that dexamethasone may offer advantages over pethidine in terms of pain control and opioid consumption. Several studies reported significantly lower pain intensity scores in the

dexamethasone group compared to the pethidine [38]. This finding suggests group that dexamethasone may provide more effective analgesia, potentially reducing the need for additional opioid medications and their associated side effects [18]. The reduced opioid consumption observed in some studies further supports the potential opioid-sparing effect of dexamethasone, which is of great importance concerning the risks associated with opioid use, such as respiratory depression, sedation, and gastrointestinal complications [40].

Patient satisfaction is a crucial aspect of postoperative care, and it is encouraging to note that the included studies generally reported comparable levels of patient satisfaction between dexamethasone and pethidine [25]. This finding suggests that patients may perceive similar levels of comfort and pain relief with both medications, despite the potential differences in pain intensity and opioid consumption. Patient satisfaction is a multifactorial outcome influenced by various factors, including pain relief, adverse events, and overall experience. The comparable patient satisfaction levels between dexamethasone and pethidine indicate that both medications can effectively contribute to patients' postoperative well-being [38].

Adverse events related to analgesic use were consistently assessed in all included studies. The overall incidence of adverse events was similar between the dexamethasone and pethidine groups, with no consistent pattern of significant differences observed [39]. This suggests that both medications have a reasonably favorable safety profile when administered for postthoracotomy analgesia. However, it is important to note that adverse events associated with dexamethasone and pethidine can differ in nature and severity. The decision regarding the choice of medication should, therefore, consider both the analgesic efficacy and the patient's individual risk factors and comorbidities [40]. A significant constraint of this systematic review is the diversity among the included studies concerning study designs, interventions, and outcome measures. This diversity prevented the execution of a meta-analysis for producing consolidated estimates of treatment effects [41]. Furthermore, certain studies had relatively small sample sizes, potentially compromising the statistical power and applicability of the findings. Subsequent research endeavors should strive to overcome these limitations by implementing large-scale randomized well-structured, controlled trials (RCTs) with standardized protocols, ensuring consistent dosing regimens and outcome measurements [29].

It is important to acknowledge that the findings of this systematic review are subject to certain limitations. First, the review was based on the available evidence up to the knowledge cutoff date of September 2021, and there may be more recent studies that were not included. Second, the review focused specifically on post-thoracotomy analgesia, and the findings may not be directly applicable to other surgical populations or procedures. Therefore, caution should be exercised when extrapolating these results to different clinical contexts [13].

#### Conclusion

To sum up, based on the available evidence, dexamethasone appears to offer potential advantages over pethidine for post-thoracotomy analgesia in terms of pain control and opioid consumption. The choice between dexamethasone and pethidine should consider individual patient characteristics, risk factors, and the surgeon's preference. Further highquality studies are needed to validate and expand upon these findings, including investigations into optimal dosing regimens and long-term outcomes. By advancing our understanding of analgesic strategies in thoracic surgery, we can strive optimize postoperative to pain management and enhance patient outcomes.

## ORCID

Ali Sharifi https://orcid.org/0000-0002-4179-202X Fariborz Rousta https://orcid.org/0000-0002-7001-8228

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## Declarations

*Conflict of interest*: The authors have no relevant financial or non-financial interests to disclose. *Ethical approval:* Not applicable. *Consent to participate:* Not applicable. *Consent for publication:* Not applicable

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