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Review

Remifentanil PCIA for labor analgesia: Does it work? Is it safe?

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Abstract

Background: **Patient-controlled intravenous analgesia with remifentanil (RPCA) is increasingly considered as an alternative to epidural analgesia during labor. Its pharmacological profile—ultrashort half-life, rapid metabolism, and ease of titration—offers theoretical advantages in terms of speed, autonomy, and clearance. Nevertheless, questions remain regarding its pharmacodynamic profiles, especially related to its analgesic potential and safety.**
Objective: **To evaluate whether RPCA is an effective and safe method for intrapartum analgesia.**
Methods: **A structured PubMed search (2000–2025) yielded 130 articles. After applying predefined selection criteria, 74 studies were included. These comprised randomized controlled trials, systematic reviews, guidelines, and both prospective and retrospective observational studies. Due to heterogeneity in protocols and outcomes, no meta-analysis was performed.**
Results: **RPCA was more effective than systemic opioids like pethidine in terms of pain relief and maternal satisfaction. Compared to epidural analgesia, RPCA provided less potent pain relief but similar satisfaction in selected patients. Conversion rates to neuraxial techniques ranged from 19% to 41%. Respiratory depression—mostly mild desaturation—was common. Severe maternal complications have been reported, particularly in association with inadequate monitoring or concurrent sedatives. Neonatal outcomes, including Apgar scores and umbilical cord pH, were generally comparable to other analgesic methods.**
Conclusion: **RPCA provides superior pain relief to systemic opioids and may offer a valuable alternative when neuraxial techniques are not feasible. While less effective than epidural analgesia, it can yield high maternal satisfaction. Respiratory events are common and sometimes severe, requiring strict safety measures including uninterrupted midwifery care, continuous saturation and respiratory monitoring, written protocols, a dedicated IV line, and staff trained in cardiorespiratory resuscitation.**

Key words: **Remifentanil, Analgesia, Patient-Controlled, Pain, Obstetric, Labor, Obstetric, Anesthesia, Epidural.**

Introduction

Labor pain ranks among the most severe pain experiences in clinical practice. Effective pain relief is therefore essential in perinatal care. Epidural analgesia is generally considered the gold standard for intrapartum pain relief due to its consistent and profound analgesic effect. However, neuraxial techniques such as epidural analgesia are not suitable or feasible for all women[1]. Medical contraindications—such as coagulopathies, spinal abnormalities, or localized infections—may prevent their use. Additionally, rapid labor progression or temporary unavailability of anesthesia staff can interfere with timely administration. Some women also decline neuraxial analgesia for personal reasons.

In such cases, systemic analgesic alternatives are often used, including intramuscular opioids such

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as pethidine or the use of nitrous oxide. However, these approaches offer only limited pain relief and are frequently associated with maternal and neonatal side effects[2]. Within this context, patient-controlled intravenous analgesia with remifentanil (RPCA) has gained attention as a potential alternative3,4. Remifentanil is a potent, ultra-short-acting μ-opioid receptor agonist with rapid clearance and favorable pharmacokinetics for use during labor. Administered via a patient-controlled analgesia pump, it enables the laboring woman to self-administer small boluses in response to contractions, potentially increasing her sense of control with pain management[5].

Despite growing interest, RPCA is not widely adopted as a standard option. Its analgesic efficacy remains under discussion—particularly in comparison with epidural analgesia—and concerns about maternal safety, especially regarding respiratory depression, persist.

This review addresses two key questions: (1) How effective is remifentanil-PCA in terms of pain reduction, maternal satisfaction, and the need for conversion to epidural analgesia? and (2) How safe is the technique, considering both maternal adverse events (e.g., sedation, hypoxemia, respiratory depression) and neonatal outcomes (e.g., Apgar scores, umbilical cord pH, NICU admission)?

Background

Labor Pain Mechanisms

Labor pain results from a combination of physiological and psychological factors. In the first stage, pain is mainly visceral, caused by uterine contractions and cervical dilation. In the second stage, somatic pain becomes dominant due to distension of the pelvic floor, vagina, and perineum. Pain intensity increases with stronger contractions, fetal descent, and maternal fatigue. Anxiety, parity, and previous childbirth experiences further influence pain perception.

Analgesic Options and Limitations

Pain relief during labor is essential. Current strategies include both pharmacological and non-pharmacological methods. Among pharmacological options, neuraxial techniques—particularly epidural analgesia—are widely accepted as the most effective method of analgesia[6,7]. Epidural analgesia involves the administration of local anesthetics, often in combination with opioids, into the epidural space. This approach provides profound and segmental analgesia, but may be associated with motor blockade, hypotension, urinary retention, and prolonged second-stage labor. It is not always feasible due to contraindications such as coagulopathy or spinal abnormalities, or because of limited anesthesia availability or rapid labor.

When neuraxial techniques are not available or declined, systemic analgesia is often used. Intramuscular opioids like pethidine (meperidine) have historically been the mainstay. These agents offer modest pain relief but are often associated with side effects such as maternal sedation, nausea, and vomiting. Furthermore, pethidine crosses the placenta and may lead to neonatal respiratory depression or reduced alertness postpartum. Inhaled nitrous oxide is another option used in some countries. It is easy to administer and has a fast onset, but its analgesic effect is modest, and side effects like dizziness and nausea are common[8,9].

Pharmacology of Remifentanil

Within this therapeutic landscape, patient-controlled intravenous analgesia with remifentanil (RPCA) has emerged as a potential alternative[10]. It has rapid onset and offset due to metabolism by non-specific plasma and tissue esterases. Its pharmacokinetics allow for fast titration and minimal accumulation. Early pharmacological studies, such as Evron et al. (2005), identified remifentanil as a promising agent due to its rapid onset and short duration[11]. Studies show that remifentanil crosses the placenta but is quickly metabolized in the fetus, with umbilical artery levels often undetectable. Volikas et al. (2005) reported cord blood levels of 2–7 ng/ml in the umbilical vein but often undetectable levels in the umbilical artery[12]. A Swedish cohort study suggested that RPCA may shorten labor and increase spontaneous delivery rates compared to epidural analgesia, supporting its use in selected populations[13].

Rationale for RPCA

RPCA enables the laboring woman to self-administer timed remifentanil boluses, typically before a contraction. This modality offers an individualized approach to analgesia and may enhance the mother's sense of control[14].

Despite its potential, RPCA is not widely implemented. Concerns remain about efficacy, safety, and the need for continuous monitoring. Early interest was fueled by its pharmacokinetic profile and patient control. Yet as Van de Velde (2008) noted, most early trials were small and inconsistent, with moderate analgesia at best. Visual analog scale (VAS) scores typically ranged from 30–60 mm, and many women needed epidural conversion. These concerns emphasized the need

for more rigorous evidence before RPCA could be broadly recommended[15]. The current review therefore aims to critically examine the available literature on RPCA's effectiveness and safety during labor.

Methodology

This review was conducted as a narrative synthesis of the available literature on patient-controlled intravenous remifentanil analgesia (RPCA) during labor. A systematic search was performed in PubMed to identify studies published between January 1, 2000, and March 1, 2025. The goal was to retrieve publications evaluating either the effectiveness or safety of RPCA in obstetric settings.

The search strategy combined the following terms: ("remifentanil" [MeSH] OR remifentanil [Title/Abstract]) AND ("Patient-Controlled" [Title/Abstract] AND analgesia [Title/Abstract]) AND ("Labor, Obstetric" [MeSH] OR labor OR childbirth [Title/Abstract]) AND (analgesia [MeSH] OR analgesia [Title/Abstract]). The search was executed on April 9, 2025.

In total, 130 records were identified. After title and abstract screening, full texts were reviewed for relevance. Seventy-four studies met the predefined inclusion and exclusion criteria and were retained for qualitative analysis. Data were extracted manually and organized thematically according to study design, focus, and outcome type.

Studies were included if they met the following criteria:

- Focused specifically on RPCA as a method for labor pain relief.
- Reported outcomes on analgesic efficacy (e.g., pain scores, maternal satisfaction, epidural conversion) or safety (e.g., respiratory events, sedation, Apgar scores, cord pH, NICU admission).
- Included a comparator group (e.g., epidural, systemic opioids) or provided meaningful clinical context (e.g., implementation protocols, safety guidelines).
- Included guidelines or expert commentaries that informed clinical use or described rare but serious complications (e.g., maternal respiratory depression or cardiac arrest).

Most selected studies consisted of randomized controlled trials, cohort studies, systematic reviews, or clinical guidelines. A small number of case reports and expert editorials were also included when they contributed unique insights or highlighted safety concerns.

Due to considerable heterogeneity in study design, dosing protocols, monitoring standards, and outcome definitions, no meta-analysis was performed. Formal risk-of-bias tools (e.g., Cochrane RoB, GRADE) were not applied. However, limitations noted by the original authors were considered during interpretation.

To provide a clear overview of the nature of the included evidence, the 74 retained studies were further categorized by study type: 27 were randomized controlled trials (RCTs), 10 were systematic reviews or meta-analyses, 14 were prospective observational studies, 9 were retrospective observational studies, 11 were case reports or expert opinion articles, and 3 were audits or registry-based analyses.

Efficacy of patient-controlled intravenous remifentanil analgesia (RPCA)

Rationale for the use of RPCA

In clinical practice, neuraxial analgesia—particularly epidural techniques—may not always be feasible due to medical contraindications, rapid labor progression, institutional constraints, or maternal preference[8,9]. Therefore, alternative systemically administered analgesic methods have gained increasing attention.

Remifentanil is a potent, ultra-short-acting μ-opioid receptor agonist that undergoes rapid metabolism by non-specific plasma and tissue esterases, resulting in a context-independent half-life of approximately 3–5 minutes[16]. Its pharmacokinetic profile allows for rapid onset and offset, enabling flexible titration during labor. These characteristics make remifentanil well suited for use in a patient-controlled intravenous analgesia system, specifically referred to as remifentanil-PCIA (RPCA).

RPCA enables the laboring woman to self-administer bolus doses in anticipation of uterine contractions. This approach offers both pharmacological and psychological advantages.

Early clinical studies and audits reported growing interest in RPCA as a viable alternative for women who cannot or do not wish to receive neuraxial analgesia. Hill (2008) and Cai et al. (2023) observed that RPCA can offer effective analgesia while maintaining maternal alertness and respiratory drive, provided it is administered with appropriate dosing protocols and continuous monitoring[17,18].

The NICE guideline (2023) supports RPCA as a clinically acceptable second-line option in well-equipped centers. In contrast, Van de Velde & Carvalho (2016) urge caution, citing frequent

maternal respiratory events and the necessity for continuous one-to-one monitoring[8,9].

Mechanism of action and administration

Remifentanil is a μ-opioid receptor agonist with ultra-short duration of action due to rapid metabolism by non-specific plasma and tissue esterases[16]. This pharmacokinetic profile allows for rapid onset and offset of effect, enabling titrated bolus administration in response to uterine contractions. Li et al. (2023) reported significantly faster analgesic onset with RPCA (0.97 minutes) compared to epidural analgesia (15.7 minutes), which may be advantageous during rapid labor[19].

In labor settings, RPCA allows the woman to activate pre-programmed boluses at the onset of contractions. Peak analgesic effect typically occurs 60–90 seconds after administration[20,21]. Accurate timing is essential, requiring anticipatory use and coaching to synchronize dosing with contractions.

Effective use of RPCA depends on individualized titration and protocol adherence[22]. Common regimens include 20–40 μg boluses with 2–3 minute lockout intervals, without background infusion. Higher doses may improve analgesia but increase the risk of desaturation[8,18,23]. Background infusions are generally avoided due to cumulative opioid exposure and the risk of respiratory depression.

Jost et al. (2013) found slightly lower pain scores using a dynamic bolus-infusion regimen versus a fixed-bolus approach. The modified protocol required fewer additional requests and no dose adjustments[24]. In a randomized trial, Balcioglu et al. (2008) compared two regimens differing in background infusion rate. The 0.15 μg/kg/min group reported lower pain scores than the 0.1 μg/kg/min group, despite identical bolus dosing, suggesting that modest background infusion may enhance efficacy[25].

Pain reduction

RPCA versus systemic opioids

Several studies have compared the analgesic effectiveness of RPCA with systemic opioids, mainly intramuscular pethidine and intravenous fentanyl.

Blair et al. (2005) reported significantly lower VAS pain scores and higher maternal satisfaction with RPCA compared to pethidine, particularly during the first stage of labor[2]. RPCA also showed faster onset of action and less neonatal sedation. Ng et al. (2011) confirmed these findings, reporting lower pain scores and a higher percentage of successful PCA demands with RPCA[4].

In the multicenter RESPITE trial, Wilson et al. (2018) similarly found that RPCA led to lower pain scores, fewer conversions to neuraxial analgesia, and higher maternal satisfaction compared to pethidine[26].

Comparisons between RPCA and fentanyl PCIA have yielded more variable results. Marwah et al. (2012) found no significant difference in pain scores, but RPCA had a higher percentage of successful demands, suggesting improved titration[27]. Douma et al. (2010) observed better early pain relief with RPCA during the first hour, though this benefit was not sustained over time[20].

In summary, RPCA provides superior analgesia compared to pethidine and appears at least as effective—if not more efficient—than fentanyl PCIA in early labor.

RPCA versus epidural analgesia

Several studies have compared RPCA to epidural analgesia for labor pain relief. Across trials, RPCA consistently resulted in higher pain scores, though maternal satisfaction often remained acceptable.
In a randomized trial, Douma et al. (2011) reported significantly higher pain scores with RPCA, especially during the second stage of labor, despite relatively high satisfaction[20].

Logtenberg et al. (2017) confirmed this pattern: RPCA produced more pain but was still considered acceptable by many women[21].

Stocki et al. (2014) also observed higher VAS scores in the RPCA group during active labor, while satisfaction levels were comparable[28]. In a prospective study, Süğür et al. (2020) found that from the second hour onward, VAS scores peaked at 4 with RPCA versus 1 with epidural, indicating inferior analgesia despite general adequacy[29].

Observational reports by Hill (2008) and Frauenfelder et al. (2015) supported these findings, concluding that while RPCA offers weaker pain control, it may still provide a positive birth experience in selected patients[18,30].

Overall, epidural analgesia remains superior to RPCA in analgesic efficacy, particularly in advanced labor. However, RPCA can offer satisfactory pain relief when carefully administered and supported.

Maternal satisfaction

Maternal satisfaction with RPCA varies depending on the comparator and clinical context.

Compared to intramuscular pethidine, RPCA consistently results in higher satisfaction scores. Blair et al. (2005) and Ng et al. (2011) attributed this to faster onset, improved autonomy, and reduced neonatal sedation[2,4]. The ability to self-administer analgesia contributed strongly to women's sense of control.

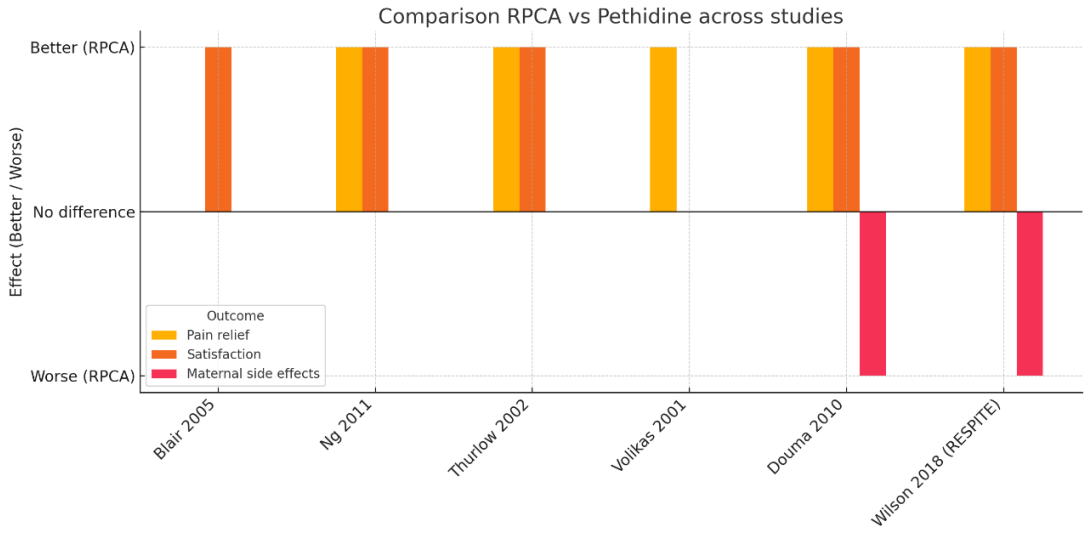

Fig. 1 — Comparative effectiveness of remifentanil PCA versus pethidine across key outcomes. Remifentanil PCA provided significantly better pain relief and higher maternal satisfaction compared to pethidine in most studies. Maternal desaturation was more frequent with remifentanil PCA in some studies. "No difference" indicates no statistically significant difference between groups.

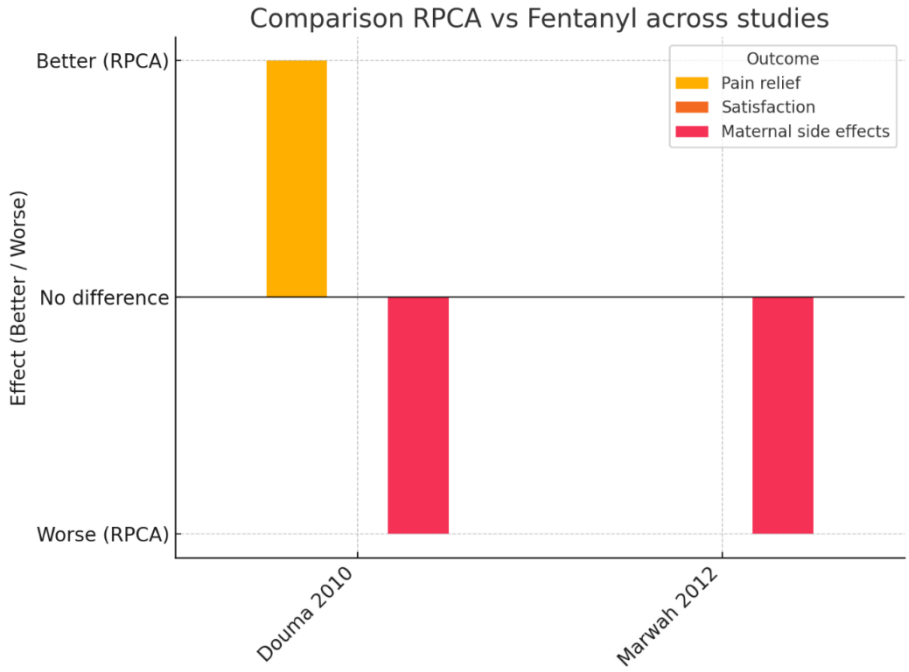

Fig. 2 — Comparative effectiveness of remifentanil PCA versus fentanyl across key outcomes. Remifentanil PCA resulted in better early pain relief in one study, but maternal side effects, particularly desaturation episodes, were more common compared to fentanyl. "No difference" indicates no statistically significant difference between groups.

When compared to epidural analgesia, findings are less uniform. Logtenberg et al. (2017) and Stocki et al. (2014) reported comparable satisfaction despite higher pain scores in the RPCA group[21,28]. This suggests that satisfaction is not solely dependent on pain intensity but may also reflect factors such as autonomy and mobility preservation.

However, other studies observed significantly lower satisfaction with RPCA. Douma et al. (2011) and Frauenfelder et al. (2015) linked this to suboptimal pain control and unmet expectations[6,30]. In a large multicenter trial, Freeman et al. (2015) confirmed this trend: RPCA scored significantly lower than epidural analgesia across both hourly and global satisfaction ratings[31]. In summary, although RPCA can yield acceptable satisfaction—especially in motivated or well-supported patients—epidural analgesia more reliably achieves high satisfaction levels.

Conversion to neuraxial analgesia

Initial feasibility studies, such as that by Blair et al. (2001), demonstrated that RPCA could provide

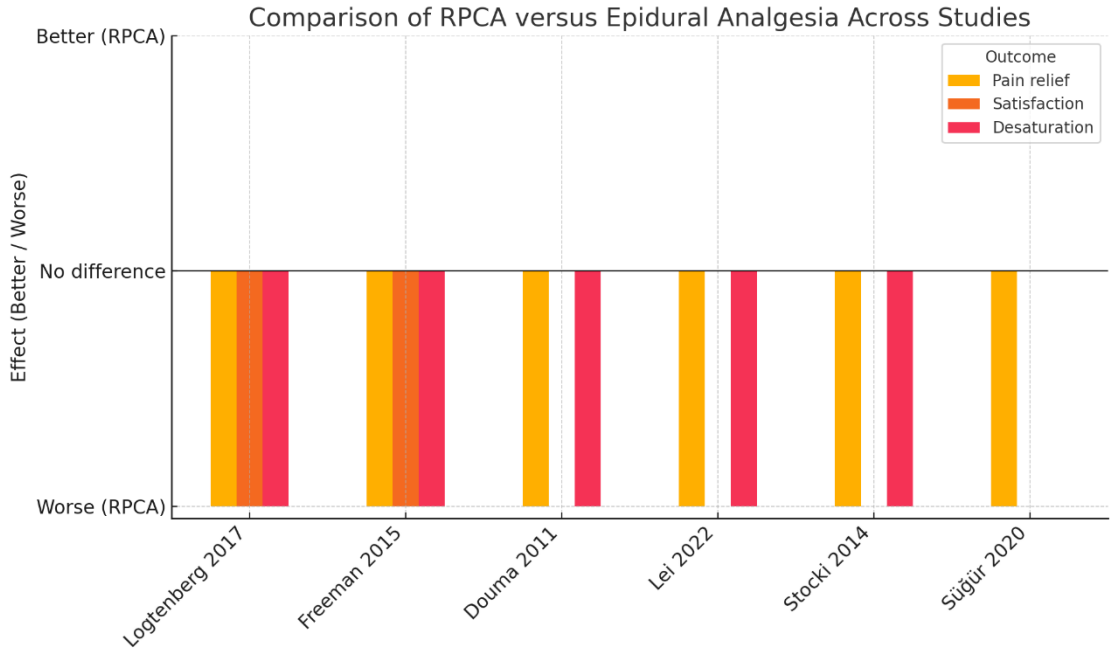

Fig. 3 — Comparative effectiveness of remifentanil PCA versus epidural analgesia across included studies.
Pain relief was consistently worse with remifentanil PCA compared to epidural analgesia, while maternal oxygen desaturation was more frequent with remifentanil PCA.
No significant difference in maternal satisfaction was observed in several studies.
"No difference" indicates no statistically significant difference between groups.

adequate labor analgesia, although conversion rates were not yet clearly established[32].

Since then, multiple studies have reported conversion rates from RPCA to neuraxial analgesia. In the RESPITE trial, Wilson et al. (2018) observed a conversion rate of 19% 26. Blair et al. (2005) reported a similar incidence, while observational studies by Hill (2008) and Logtenberg et al. (2017) described higher rates ranging from 25% to over 40%[2,18,21].

Reasons for conversion are often multifactorial. Most commonly, women requested neuraxial techniques in the second stage of labor due to insufficient analgesia, maternal fatigue, or changing preferences[33].

Importantly, as Freeman et al. (2018) noted in the RAVEL trial, conversion to epidural does not equate to failure but reflects dynamic, patient-centered analgesia planning[34].

Some studies allowed adjunct use of nitrous oxide, although this was not part of the standardized RPCA protocol, further complicating interpretation of conversion data.

Comparison of study designs and limitations

The evidence base for RPCA during labor is marked by substantial heterogeneity in study design, dosing strategies, monitoring protocols, and outcome measures[35]. This variability hinders comparability across studies and precludes high-quality meta-analyses.

Included studies range from randomized controlled trials (Wilson et al., 2018; Lei et al., 2022; Ismail et al., 2012) to observational cohorts and single-center audits (Hill, 2008; Logtenberg et al., 2017; Cai et al., 2023)[17,18,21,26,36,37]. While RCTs provide methodological robustness, their generalizability may be limited due to narrow eligibility criteria and tightly controlled conditions. Observational studies better reflect real-world practice but are more susceptible to confounding and bias.

Dosing protocols differ considerably. Some trials administered conservative boluses of 20–30 µg with 2–3 minute lockouts, while others allowed higher boluses up to 50–60 µg or used background infusions[17,38]. Monitoring standards also vary: some studies required continuous supervision and pulse oximetry, whereas others offered minimal detail on safety procedures. As highlighted by Wydall et al. (2023), this inconsistency limits synthesis and emphasizes the need for transparent reporting standards[39].

Outcome definitions are equally inconsistent. Pain relief is measured using diverse VAS metrics—peak vs. mean scores, or stage-specific assessments. Respiratory events are variably defined, using different desaturation thresholds, sedation scores, or apnea reporting. Neonatal outcomes such as Apgar scores or cord pH are often incomplete or inconsistently reported[40].

These methodological discrepancies increase the risk of outcome reporting bias and impair meaningful interpretation. Systematic reviews, including those by Weibel et al. (2017) and the

NICE Evidence Review (2023), have acknowledged these limitations and graded the certainty of RPCA-related evidence as low to very low across most outcomes[9,41].

In conclusion, although RPCA appears promising as a second-line analgesic technique, future studies must adopt consistent dosing schemes, unified outcome definitions, and clearly documented safety protocols. Improved methodological rigor is essential for valid comparisons and safe implementation.

Safety of patient-controlled intravenous remifentanil analgesia (RPCA)

Maternal safety

The main maternal adverse effects associated with remifentanil-PCIA (RPCA) are dose-dependent respiratory depression and sedation. Mild oxygen desaturation ($SpO_2 < 94\%$) is common, particularly at higher bolus doses or in the absence of supplemental oxygen, with reported incidence ranging from 25% to over 50%[20,42,43]. Sedation is also frequently observed, though typically mild and self-limiting.

A randomized trial comparing RPCA regimens found that escalating bolus doses increased sedation rates, despite similar analgesic outcomes[44]. This highlights the importance of cautious dosing and continuous monitoring during administration.

Apneic episodes have been reported but are inconsistently defined across studies. Definitions range from the absence of respiratory effort for more than 10 seconds to various clinical or surrogate criteria[28,45]. While most episodes resolve spontaneously, any occurrence of apnea during labor is clinically relevant. Therefore, one-to-one supervision and continuous respiratory monitoring are mandatory.

Compared to neuraxial techniques, RPCA is associated with a higher rate of maternal desaturation events[46]. However, under strict monitoring protocols, most events remain manageable. Despite remifentanil's favorable pharmacokinetic profile, the risk of respiratory depression necessitates uninterrupted supervision8.

Other adverse effects such as nausea, vomiting, dizziness, and bradycardia have been reported, though less frequently and typically mild[20,36,47].

Severe maternal complications are rare but documented. Marr et al. (2013) reported a cardiorespiratory arrest related to RPCA without monitoring or oxygen supplementation48. A similar case was described by Bonner & McClymont (2012), again involving inadequate supervision[45]. These cases underline the need for continuous bedside presence by trained personnel.

Recent data suggest that RPCA can be used in selected high-risk populations, such as patients with obesity or pre-existing respiratory vulnerability, provided that enhanced monitoring is ensured[49]. However, this use remains off-label and should be limited to experienced centers with immediate access to resuscitation resources.

Neonatal outcomes

Apgar scores and respiratory adaptation

Most studies report no significant differences in Apgar scores between neonates exposed to remifentanil-PCIA (RPCA) and those whose mothers received neuraxial analgesia. Stocki et al. (2014) found no increased incidence of Apgar scores below 7 at five minutes in the RPCA group compared to the epidural group[28]. These findings were supported by two systematic reviews (Weibel et al., 2017; Lei et al., 2022), which both concluded that RPCA was not associated with a higher risk of poor Apgar outcomes compared to other analgesic options[36,41].

RPCA may even offer advantages over traditional systemic opioids. Volikas et al. (2001) reported significantly higher Apgar scores and a reduced need for neonatal stimulation following RPCA compared to intramuscular pethidine[50]. Similarly, Tveit et al. (2013) observed no deterioration in Apgar scores or umbilical cord pH after maternal use of RPCA, further supporting its safety in routine obstetric settings[51].

Need for resuscitation or NICU admission

Available data on the need for neonatal resuscitation or admission to a neonatal intensive care unit (NICU) following maternal RPCA use are generally reassuring. In a cohort of over 1500 women, Hill (2008) reported an immediate intubation rate of 0.1%, which was comparable to that seen after epidural analgesia and intramuscular pethidine18. Murray et al. (2019) conducted a retrospective analysis and observed a lower NICU admission rate following RPCA (1.6%) compared to epidural analgesia (3.6%)[52]. However, this result should be interpreted cautiously. In that study, women receiving epidural analgesia more often had complicated labors or required operative delivery, which could confound neonatal outcomes. The observational design also precludes any firm conclusions regarding causality.

Umbilical cord pH and acid-base status

Umbilical cord pH is a key parameter for assessing neonatal metabolic status at birth. Across most studies, no significant differences have been reported in cord pH values between neonates

exposed to RPCA and those exposed to alternative analgesic methods. Knapp et al. (2023) specifically examined a cohort of women with significant cardiac comorbidities and found normal umbilical cord blood gas values in all cases, without evidence of neonatal acidemia[49]. These findings support the view that, under strict monitoring conditions, RPCA does not adversely impact neonatal acid-base balance.

Mild sedation and neonatal tone

Rare cases of mild neonatal sedation or hypotonia have been reported when RPCA was administered up to the time of delivery. These effects were transient, resolved spontaneously, and did not require active intervention. Jia et al. (2020) assessed neonatal adaptation after maternal RPCA and found no severe adverse outcomes. Subtle, short-lived reductions in neonatal tone or responsiveness were occasionally observed[53]. The rapid metabolism of remifentanil by both placenta and fetus is believed to explain the brief neonatal exposure.

Monitoring of neonatal vital parameters

Available studies have not identified concerning trends in neonatal cardiovascular or respiratory parameters following maternal RPCA. In a prospective observational study, Konefał et al. (2013) found that neonatal heart rate, blood pressure, and oxygen saturation during the first 24 hours postpartum were comparable between RPCA and epidural groups[54]. These data support the physiological stability of neonates when RPCA is used with appropriate monitoring and timing.

Neurological assessment

Neonatal neurobehavioral outcomes following maternal use of RPCA appear to be reassuring. In a prospective trial, Douma et al. (2010) evaluated early neurological adaptation using the Neonatal Adaptive Capacity Score (NACS), and found no significant differences between neonates exposed to RPCA, fentanyl-PCIA, or intramuscular meperidine[20]. More recent observational data by Lucovnik et al. (2023) supported these findings, reporting no adverse neurodevelopmental effects even in high-risk deliveries such as breech or twin gestations[55]. These results suggest that RPCA does not negatively impact early neonatal neurological function, although longer-term neurodevelopmental follow-up data remain limited.

Summary

When administered with adequate monitoring and supervision, RPCA does not adversely affect key neonatal outcomes. Studies consistently report comparable Apgar scores, umbilical cord pH, and need for resuscitation or NICU admission relative to neuraxial or systemic opioid analgesia. The rapid metabolism and limited placental transfer of remifentanil likely underpin this favorable neonatal safety profile. Although rare cases of mild sedation or transient hypotonia have been observed when RPCA continued until delivery, these events were self-limiting and did not require intervention. Overall, current evidence suggests that RPCA, when used under strict safety protocols, is comparable to other analgesic techniques in terms of neonatal well-being.

Monitoring and safety protocols

Clinical monitoring requirements

The safe administration of RPCA during labor requires continuous monitoring and the presence of trained staff. Maternal respiratory depression is the primary risk, and use without direct observation is not aligned with best clinical practice[56].

Pulse oximetry must be used in all patients receiving RPCA[57]. However, its limitations are well established: apneic episodes and hypoventilation may occur without immediate oxygen desaturation, potentially delaying detection[28,58].

Therefore, exclusive reliance on pulse oximetry is inadequate. Real-time assessment of respiratory rate, level of consciousness, and sedation must be included in the monitoring protocol. Capnography enables earlier detection of respiratory compromise and is particularly recommended when background infusions are used, although availability varies between centers[58].

Neonatal preparedness

Due to the rapid placental transfer of remifentanil, neonatal exposure may lead to transient respiratory depression, especially if RPCA is continued until delivery[9]. If RPCA remains active near the time of birth, a pediatrician or neonatologist must be readily available, and naloxone should be prepared in advance.

Dosing strategies and respiratory risk management

A conservative starting dose of 20–30 µg with a minimum lockout interval of two minutes is commonly recommended to minimize respiratory adverse events without sacrificing analgesic efficacy[9,59]. Bolus doses exceeding 40 µg have been linked to higher rates of desaturation and sedation[28,60,61].

Several trials suggest that adding a background infusion to bolus administration may enhance analgesic consistency without substantially

increasing total remifentanil use or desaturation risk[62,63]. However, no prospective trials have validated low-dose regimens in labor, and dosing strategies remain a subject of debate.

Institutional standards and team readiness

RPCA must be restricted to settings with continuous bedside monitoring and immediate access to advanced airway support. NICE (2023) guidelines require the presence of an onsite anesthetist during RPCA administration.

Evidence from Tveit et al. (2012) indicates that in the absence of proper monitoring and dosing, RPCA carries a higher risk of maternal desaturation than epidural analgesia[64].

Furthermore, Kranke et al. (2013) warned against considering RPCA a "poor man's epidural," highlighting that its apparent simplicity belies serious risks if implemented without the same institutional vigilance, staff expertise, and emergency readiness required for neuraxial analgesia[65]. Clinical use of RPCA demands the same infrastructural safeguards as epidural techniques.

Labor ward staff must be trained to promptly identify and manage opioid-induced respiratory depression. This includes sedation scoring, oxygen administration, airway maneuvers, and troubleshooting of PCA devices[66].

Technology-assisted administration and its limitations

Technological innovations, such as variable positive infusion analgesia (VPIA) systems, aim to automate remifentanil delivery and reduce bolus errors[42]. However, while promising, such technologies cannot replace vigilant clinical supervision.

Rehberg et al. (2015) demonstrated that anticipatory bolus algorithms alone are insufficient: human presence remains the critical safety factor[16].

Practical examples of structured implementation

- A dedicated intravenous line for remifentanil,
- Continuous bedside monitoring,
- Documentation of vital signs every 30 minutes,
- Immediate availability of resuscitation equipment.

Similarly, the RemiPCA SAFE Network emphasized standardized safety protocols and emphasized conservative dosing as the cornerstone of safe RPCA practice[59].

Summary

The use of RPCA in labor requires strict adherence to safety protocols, including continuous respiratory monitoring, bedside presence of trained staff, and immediate access to emergency support. Conservative dosing and careful patient selection further reduce risk. While technological systems may help standardize drug delivery, they cannot replace active human supervision.

However, consistently applying these measures in clinical practice presents logistical challenges. The level of monitoring required goes beyond standard one-to-one midwifery care and may be difficult to achieve in all settings. This discrepancy between theoretical standards and real-world feasibility must be acknowledged: ethical justification for RPCA depends on actual, not assumed, compliance with safety requirements.

Without adequate infrastructure and continuous clinical oversight, the use of RPCA during labor cannot be considered safe or appropriate.

Discussion

Interpretation of effectiveness

Remifentanil patient-controlled intravenous analgesia (RPCA) has garnered increased attention in recent years as a second-line analgesic option during labor, particularly in scenarios where neuraxial analgesia is contraindicated or unavailable. This section synthesizes findings on RPCA's effectiveness regarding pain reduction, maternal satisfaction, and conversion to neuraxial analgesia.

Available evidence consistently demonstrates that RPCA provides superior analgesia compared to conventional systemic opioids. A randomized study by Douma et al. (2010) showed significantly lower pain scores and higher maternal satisfaction with RPCA than with intravenous fentanyl PCIA or intramuscular pethidine[20]. Similarly, the multicenter RESPITE trial reported that RPCA resulted in less pain and reduced need for epidural rescue analgesia compared to pethidine, although epidural analgesia remained absolutely superior[26]. A Cochrane review by Weibel et al. (2017) confirmed that RPCA offers better pain relief than conventional opioids, although the certainty of evidence was rated low 41. These findings align with expert classifications, such as that by Van de Velde & Carvalho (2016), who awarded RPCA a higher evidence grade than pethidine (Class I-A)[8].

However, RPCA consistently provides less potent analgesia compared to epidural techniques. Several RCTs (e.g., Lei et al., 2022; Logtenberg et al., 2017) and meta-analyses (e.g., Liu et al., 2014) reported significantly higher VAS pain scores with RPCA, particularly during the second stage of labor[21,36,67]. This limitation in analgesic

depth remains a key reason why guidelines do not recommend RPCA as a first-line technique[8,67].

Despite inferior analgesia compared to epidural techniques, maternal satisfaction with RPCA remains notably high. In the study by Douma et al. (2010), women reported greater satisfaction with RPCA compared to fentanyl PCIA or pethidine, even when pain scores were moderate 20. Similarly, a retrospective study by Cai et al. (2023) found that higher remifentanil bolus doses (50 μg) improved both pain scores and satisfaction without increasing side effects[17]. The ability to self-administer analgesia likely enhances the sense of autonomy and control, which positively impacts maternal satisfaction even when pain relief is incomplete[20,68]. Qualitative findings support this : a sub-analysis of the RESPITE trial found that most women appreciated the autonomy RPCA provided and would opt for RPCA again in future labor, despite acknowledging incomplete analgesia (Moran et al., 2019)[68]. Logtenberg et al. (2017) also reported that multiparous women were as satisfied or even more satisfied with RPCA than with epidural analgesia, whereas primiparous women were more likely to prefer epidurals[21]. These observations highlight that maternal satisfaction is multidimensional and influenced by autonomy, expectations, and support—not merely pain intensity.

The rate of conversion from RPCA to neuraxial analgesia (usually epidural) is often used as an indicator of RPCA's limitations. In the RESPITE trial, 19% of women initially assigned to RPCA ultimately requested an epidural 26. In observational cohort studies, conversion rates are higher; Logtenberg et al. (2017) and Hill (2008) reported conversion rates of approximately 25% and over 40%, respectively[18,21]. This variability likely reflects differences in dosing protocols, patient populations, and institutional practices. Importantly, conversion should not be automatically viewed as RPCA failure. Freeman et al. (2018), analyzing RAVEL trial data, emphasized that switching to epidural analgesia often results from a complex interplay of patient preferences, clinical course, and institutional norms rather than from intrinsic inadequacy of RPCA. Conversely, the fact that approximately 60–80% of women do not require conversion demonstrates that RPCA can provide sufficient analgesia for the majority[34].

Although overall findings consistently show that RPCA reduces pain (especially compared to opioids) and results in high satisfaction, the quality of evidence remains limited by study heterogeneity. Both Liu et al. (2014) and the NICE Evidence Review (2023) rated the certainty of evidence as low to moderate due to variability in study designs, populations, and outcome definitions[9,67]. Nonetheless, the totality of available data supports that RPCA can offer clinically meaningful analgesia and high satisfaction for selected patients. When administered and monitored appropriately, RPCA constitutes a valid second-line analgesic strategy, particularly in cases where neuraxial techniques are not feasible.

Interpretation of safety

RPCA can be safely administered for both mother and neonate when delivered under highly controlled conditions with continuous monitoring. Without stringent safeguards, this technique carries meaningful clinical risks. Frequent but generally mild maternal respiratory effects are observed, and although rare, serious complications have been reported. Strict adherence to safety protocols is therefore essential.

Respiratory depression remains the most prominent risk for mothers receiving RPCA. Sedation and oxygen desaturation occur frequently—reported in approximately 25–50% of women—and are more pronounced with higher bolus doses or when supplemental oxygen is not provided[20,43]. Messmer et al. (2016) observed transient SpO_2 drops below 90% in 70% of women (median minimum 87%), despite appropriate supervision[43]. Similarly, Leong et al. (2021) reported desaturation events in all patients, with prolonged episodes (>60 seconds) occurring in 68%[42]. These hypoxemic episodes were generally brief and without lasting clinical consequences. Apneas have also been described, although their definitions vary among studies. Stocki et al. (2014) noted occasional brief respiratory pauses without clinical impact[28], while Thurlow (2002) demonstrated that respiratory depression can occur even at low remifentanil doses, suggesting individual susceptibility[69].

Aside from respiratory effects, some evidence suggests that RPCA might induce less intrapartum fever than epidural analgesia, though findings remain inconclusive[36,70].

Serious maternal complications during RPCA are exceedingly rare but underscore the critical importance of monitoring. Marr et al. (2013) described a maternal cardiopulmonary arrest during labor induction with RPCA, in a setting without continuous monitoring or supplemental oxygen[48]. Bonner & McClymont (2012) reported a similar respiratory arrest under conditions of inadequate supervision[45]. Ohashi et al. (2016) described respiratory arrest when RPCA was combined with other opioids, highlighting risks of drug interactions[71]. All these cases involved deviations

from recommended protocols. Conversely, large registry data (e.g., the RemiPCA SAFE initiative with over 6000 cases) reported no maternal mortality or irreversible harm under strict protocol adherence[59]. Most recorded complications occurred in centers with limited experience or inadequate staffing, emphasizing the necessity of expert supervision[59].

Neonatal outcomes after maternal RPCA use are generally reassuring. Key parameters such as Apgar scores and umbilical cord pH are comparable to those seen with conventional analgesia. Stocki et al. (2014) found no differences in the number of neonates with 5-minute Apgar scores below 7 between RPCA and epidural groups[28]. Similarly, Knapp et al. (2023) reported no cases of neonatal acidosis among high-risk pregnant women who received RPCA[49]. Although mild neonatal sedation or hypotonia has occasionally been observed when remifentanil administration occurred close to delivery, these effects are transient and resolve spontaneously without intervention. Rapid placental and neonatal metabolism of remifentanil limits neonatal exposure duration and intensity.

There is a strong consensus that RPCA must be administered cautiously. Van de Velde & Carvalho[8] recognized that RPCA offers superior pain relief and satisfaction compared to pethidine but emphasized its narrow safety margin and high incidence of maternal respiratory events. Accordingly, they advised against routine RPCA use unless one-on-one continuous monitoring and emergency protocols are guaranteed. This view is echoed by the latest NICE guideline (2023), which states that RPCA should only be offered where continuous specialist monitoring and immediate intervention capabilities are available[9]. Such recommendations highlight that RPCA, while valuable, must remain reserved for settings where strict safety standards can be assured.

Broader implications and future directions

The findings of this literature review suggest that RPCA can serve as a useful alternative for labor analgesia under appropriate conditions. Although RPCA cannot match epidural analgesia in terms of analgesic potency, it fills an important niche for women who cannot or do not wish to undergo neuraxial techniques.

Evidence shows that RPCA outperforms traditional systemic opioids while falling short of epidural analgesia. Multiple studies confirm that remifentanil PCIA achieves better pain relief and higher satisfaction than intramuscular pethidine[20,26]. However, meta-analyses, such as Liu et al. (2014), conclude that RPCA cannot provide analgesia equivalent to epidurals but offers an acceptable alternative when neuraxial analgesia is not feasible[67]. Van de Velde & Carvalho (2016) similarly classified RPCA as superior to pethidine (evidence Class I-A) but inferior to epidurals, explicitly cautioning against widespread RPCA adoption due to its safety and staffing requirements[8].

Despite its limited analgesic depth, many women remain highly satisfied with RPCA for reasons including autonomy and less invasiveness. In a post-RESPITE trial survey, most women indicated willingness to choose RPCA again in future deliveries, even when pain relief was incomplete[68].

Implementing RPCA demands careful organization and resource allocation. Continuous one-on-one monitoring by trained personnel, strict respiratory surveillance, and clearly defined protocols are mandatory. The study by Logtenberg et al. (2019) illustrates that serious adverse events, including apnea, desaturation and even cardiac arrest, continue to occur despite national SOPs and training efforts. Although all cases resolved without lasting harm, the authors stress that RPCA entails a non-negligible risk of severe respiratory compromise, especially when protocols are not strictly followed. These findings reinforce the position that RPCA should only be used in facilities with the capacity to provide continuous bedside monitoring, trained personnel, and immediate respiratory support[72]. As Van de Velde & Carvalho (2016) noted, such infrastructure is not universally available, and without it, risks increase substantially[8]. Financially, while NICE (2023) suggests that RPCA might be cost-effective under certain conditions (e.g., fewer antiemetics, NICU admissions), accounting for necessary staffing and monitoring may bring its overall cost closer to that of epidural programs[9,34].

Despite considerable progress, several areas require further study. First, large, high-quality trials are needed to directly compare RPCA with epidural analgesia and other PCA methods across diverse populations. Identifying subgroups (e.g., multiparous women, women with prior cesareans) who might benefit most from RPCA remains an important goal. Preliminary findings in special populations (e.g., preeclamptic women, El-Kerdawy et al., 2010) are encouraging but underpowered[73].

Second, optimal RPCA dosing strategies remain to be established. Cai et al. (2023) suggested that higher bolus doses (50 µg) might improve analgesia without increasing adverse events, but additional data are needed to confirm this[17].

Third, implementation research is essential to develop best practices for RPCA[74]. Initiatives

like the RemiPCA SAFE project advocate for standardized auditing and reporting. Technological innovations—such as "smart" pumps adjusting doses based on vital signs—may further enhance safety, although vigilance by skilled personnel remains irreplaceable[16,41].

Conclusion

Based on current evidence, remifentanil patient-controlled analgesia (RPCA) provides superior pain relief and higher maternal satisfaction than traditional intramuscular opioids, though it remains inferior to neuraxial techniques in terms of analgesic depth. Satisfaction may nonetheless be high in certain patients—for example, those valuing autonomy, rapid onset of analgesia, and self-management. In selected populations, RPCA can reduce the need for epidural conversion, underscoring its utility as a second-line option. While maternal respiratory events are frequent, they are typically self-limiting; however, rare cases of severe respiratory depression with maternal cardiac arrest and emergency peri-mortem caesarean delivery have been reported. Neonatal outcomes appear comparable to those observed with other analgesic methods, although caution remains warranted when RPCA is used close to delivery. RPCA should not be viewed as interchangeable with neuraxial techniques nor as universally applicable, but when implemented with rigorous safety protocols, it can serve as a valuable alternative in well-equipped obstetric settings.

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