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Managing Post-Episiotomy Pain: A GRADE-Qualified Meta-Analysis of Diclofenac Rectal Suppository Compared with Other NSAIDs

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ABSTRACT

Background & aim: Pain management following episiotomy—a surgical cut made in the perineum during childbirth—is a vital component of postpartum care. This study aimed to rigorously synthesize available evidence regarding the efficacy of diclofenac rectal suppository compared to the placebo or other NSAIDs in managing post-episiotomy pain.

Methods: This review followed the PRISMA 2020 guidelines. Randomized controlled trials comparing diclofenac rectal suppository with placebo or other NSAIDs in women with mediolateral episiotomy were identified through a comprehensive database search up to August 14, 2025. Risk of bias was assessed using the Cochrane RoB 2 tool. Meta-analyses were conducted using RevMan 5.4, and the quality of evidence was evaluated with GRADE.

Results: Eleven articles were included in the systematic review, with nine RCTs involving 1577 women included in the meta-analysis. Overall risk of bias ranged from low to high Overall, diclofenac rectal suppository consistently reduced pain compared with both placebo and other NSAIDs, with effect sizes varying by comparator. Diclofenac rectal suppository significantly reduced post-episiotomy pain at 24 hours compared with placebo (SMD = −1.49, 95% CI −2.45 to −0.53; p = 0.002) and oral diclofenac (MD = −1.64, 95% CI −2.80 to −0.49; p = 0.005). No significant difference was observed compared with rectal indomethacin (MD = −0.89, 95% CI −2.28 to 0.50; p = 0.21). The quality of evidence ranged from very low to moderate.

Conclusion: This study provides insights into using diclofenac rectal suppository for post-episiotomy pain management. However, further high-quality RCTs are needed to confirm these findings.

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Introduction

Pain management following episiotomy, in which a surgical incision is made in the perineum during childbirth, is a critical aspect of postpartum care. This procedure, while often necessary to facilitate delivery, can result in significant discomfort and pain for the new mother (1-2). This pain can interfere with her ability to care for her newborn and herself, impacting her overall quality of life and potentially leading to long-term complications (3-4). Among the pharmacological interventions available, nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used to manage post-episiotomy pain because of their analgesic and anti-inflammatory properties (5-7). Among these, diclofenac has been widely used in various forms, including rectal suppository,

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owing to its proven efficacy and safety profile (8-9).

However, the comparative effectiveness of diclofenac in rectal suppository with that of other NSAIDs in managing post-episiotomy pain remains unclear. Previous studies have provided conflicting results, and a comprehensive comparison is lacking (5, 10). For instance, a systematic review evaluated the effectiveness of NSAIDs rectal suppository (such as indomethacin, diclofenac, and naproxen) in comparison to a placebo for alleviating perineal pain following an episiotomy. The findings indicated that women who were administered NSAIDs suppository had a reduced need for extra analgesics 24 hours after giving birth (11). Another study showed that diclofenac given per rectum is the simplest method that is rapidly effective for a long duration and is safe and very promising for decreasing the degree of pain that women feel after the trauma of the perineum within the first 24 hours after delivery (10). Despite these findings, important gaps remain in the existing literature. Previous studies have primarily compared NSAIDs suppository with placebo, while direct head-to-head comparisons between diclofenac and other NSAIDs are limited. In addition, earlier reviews have often pooled different NSAIDs together, limiting conclusions about the relative efficacy of diclofenac rectal suppository specifically, and the certainty of evidence has not been evaluated using the GRADE framework. These limitations hinder clear clinical decision-making regarding optimal NSAID selection for post-episiotomy pain management. Therefore, this study aims to systematically review and Meta-analyze the available randomized controlled trials to compare the efficacy of diclofenac rectal suppository with other NSAIDs for managing post-episiotomy pain.

Methods

This systematic review and meta-analysis was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (12).

Search strategy

We performed a thorough literature search across several databases, including Medline/PubMed, Web of Science, Scopus, ScienceDirect, the Cochrane Library, and Google Scholar, covering all entries up to August 14, 2025. The search strategy incorporated a mix of MeSH terms and relevant free-text keywords associated with “episiotomy” and “diclofenac” (see Table 1).

Table 1. Search strategies in databases

PubMed	
((((((((((Diclofenac[Title/Abstract]) OR (Diclophenac[Title/Abstract])) OR (Dicrofenac[Title/Abstract])) OR (Dichlofenal[Title/Abstract])) OR (Diclonate[Title/Abstract])) OR (Feloran[Title/Abstract])) OR (Voltarol[Title/Abstract])) OR (Novapirina[Title/Abstract])) OR (Orthofen[Title/Abstract])) OR (Ortofen[Title/Abstract])) OR (Orthophen[Title/Abstract])) OR (Voltaren[Title/Abstract])) AND (episiotom*[Title/Abstract])	10 results
Web of Science	
# Web of Science Search Strategy (v0.1) # Database: Web of Science Core Collection # Entitlements: - WOS.SCI: 1945 to 2025 - WOS.AHCI: 1975 to 2025 - WOS.BHCI: 2005 to 2025 - WOS.BSCI: 2005 to 2025 - WOS.ESCI: 2005 to 2025 - WOS.ISTP: 1990 to 2025 - WOS.SSCI: 1956 to 2025 - WOS.ISSHP: 1990 to 2025 # Searches: 1: Diclofenac (Topic) OR Diclophenac (Topic) OR Dicrofenac (Topic) OR Dichlofenal (Topic) OR Diclonate (Topic) OR Feloran (Topic) OR Voltarol (Topic) OR Novapirina (Topic) OR	12 results

Voltaren (Topic) Date Run: Aug 14 2025 01:49:57 GMT+0330 (Iran Standard Time) Results: 24380 2: (TS=(episiotomy)) OR TS=(episiotomies) Date Run: Aug 14 2025 01:51:09 GMT+0330 (Iran Standard Time) Results: 3858 3: #1 AND #2 Date Run: Aug 14 2025 01:51:39 GMT+0330 (Iran Standard Time) Results: 12	
Scopus	
TITLE-ABS-KEY(Diclofenac OR Diclophenac OR Dicrofenac OR Dichlofenal OR Diclonate OR Voltarol OR Voltaren OR Orthophen) AND TITLE-ABS-KEY(episiotomy OR episiotomies) AND DOCTYPE(ar)	38 results
Cochrane Library	
Hits Search ID 2289 MeSH descriptor: [Diclofenac] explode all trees #1 6576 Diclofenac #2 57 Diclophenac #3 11 Dicrofenac #4 4 Dichlofenal #5 5 Diclonate #6 363 Voltaren #7 1652 episiotom* #8 386 MeSH descriptor: [Episiotomy] explode all trees #9 6677 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 #10 1652 #8 OR #9 #11 70 #10 AND #11 #12	70 results
ScienceDirect	
(diclofenac OR Diclophenac OR Voltaren OR Dicrofenac OR Orthofen) AND (episiotomy OR episiotomies)	2 results

We also extensively reviewed gray literature by screening conference abstracts and manually examining the reference lists of included studies to identify additional relevant or unpublished evidence, thereby enhancing the comprehensiveness of the review. Importantly, no restrictions related to language or publication date were imposed during the search process.

Study Selection

Studies were included in this systematic review based on the following PICO criteria:

- Population (P): Women who underwent mediolateral episiotomy during childbirth.
- Intervention (I): Diclofenac rectal suppository.
- Comparator (C): Placebo or other NSAIDs.
- Outcome (O): Pain management, assessed via validated scales or the need for additional analgesia (e.g., proportion of participants requiring extra pain relief).
- Study design: Only randomized controlled trials (RCTs) were included. Cluster trials were eligible, but none were found.
- Publication criteria: Only full-text articles published in peer-reviewed journals were considered, and no abstracts met the inclusion criteria.

Studies were excluded if they utilized non-randomized designs, lacked a control group, did not report relevant pain-related outcomes, or involved participants with preexisting conditions that could confound pain results (such as chronic pain disorders or a history of substance abuse). Crossover trials and quasi-randomized trials were excluded. No language restrictions were applied in our inclusion criteria.

Two independent reviewers (MA, MS) evaluated the titles and abstracts of the identified studies to determine their eligibility. Full texts of potentially eligible studies were sourced and examined for inclusion. Any disagreements between the reviewers were addressed through discussion or by consulting a third reviewer (SMa).

Data Extraction

Data extraction was independently performed by two researchers (MS, MN). Any discrepancies were resolved through discussion between them or, if needed, consultation with a third researcher (SMa).

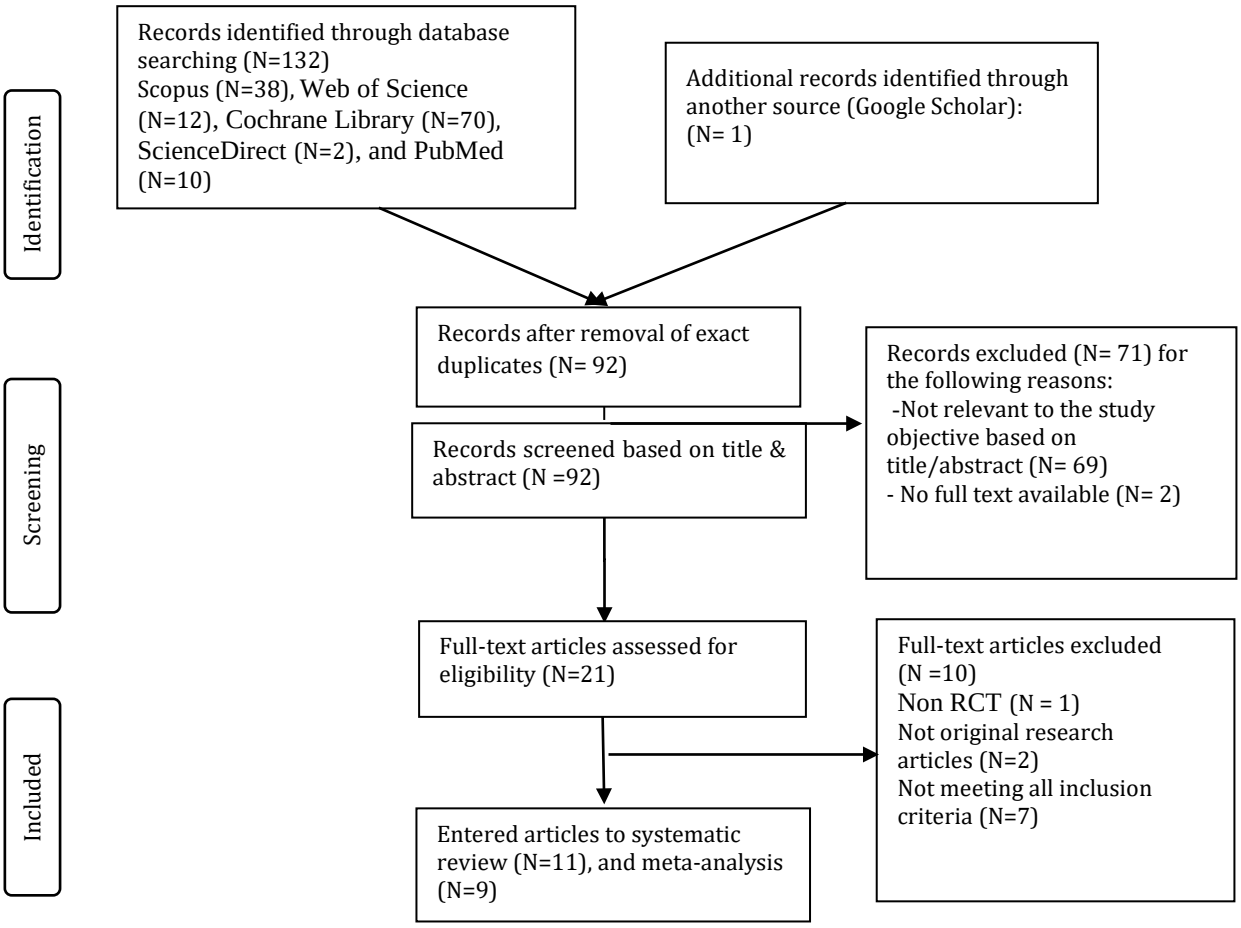


Figure 1. PRISMA 2020 flow diagram of the systematic search strategy

Risk of bias assessment

The quality of the included RCTs was evaluated using the Cochrane risk of bias tool (RoB2) (13). This tool analyzes the risk of bias across five specific domains.

1. **Bias Arising from the Randomization Process**: Assesses whether the randomization process was adequately implemented to prevent selection bias.
2. **Bias Due to Deviations from Intended Interventions**: Evaluates if participants adhered to the assigned interventions and considers the potential impact of any deviations.
3. **Bias Due to Missing Outcome Data**: Investigates whether missing data could influence the overall results and conclusions of the study.
4. **Bias in the Measurement of the Outcome**: Assesses the accuracy and consistency of outcome measurements and whether they were influenced by the knowledge of the allocated interventions.
5. **Bias in Selection of the Reported Result**: Evaluates whether the results reported were selected among multiple outcomes in a way that could skew the findings.

The assessments of risk in each domain were categorized as low risk, high risk, or some concerns. To ensure the reliability of our evaluations, two independent reviewers (SMa, SMo) conducted the assessments. In cases of disagreement, consensus was reached through discussion and mutual agreement.

Data Synthesis and Analysis

We conducted a meta-analysis to estimate pooled effect sizes and their 95% confidence intervals. For three trials (14-16), we derived

the sample mean and standard deviation based on the sample size, median, range, and/or interquartile range (17-18). The mean difference (MD) or standardized mean difference (SMD) was calculated for outcomes reported across all studies. To visually present the estimated effect sizes, we created forest plots, setting a p-value threshold of 0.05 to determine statistical significance. The I^2 statistic was used to assess heterogeneity among the studies. Given the significant differences indicated by the heterogeneity test ($I^2 \geq 50\%$, $P < 0.05$), we applied a random-effects model for our analysis. Additionally, we performed a sensitivity analysis using leave-one-out methods to identify any individual study that might disproportionately influence the overall results. Due to the limited number of RCTs (fewer than 10 articles), we did not assess publication bias. All analyses were carried out using Review Manager (RevMan) version 5.4.

Assessment of Evidence Certainty

To evaluate the quality of evidence for outcomes, we employed the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool. This framework categorizes systematic reviews and meta-analyses into four levels: 'high,' 'moderate,' 'low,' and 'very low.' We initiated the assessment with a 'high' grade and subsequently downgraded it based on the presence of bias, inconsistency (I^2 statistics > 50%), indirectness (differences in interventions), imprecision (when the 95% confidence interval includes 1.0), or publication bias. Conversely, the rating could be upgraded if there was strong evidence of a significant intervention effect or if the presence of reasonable biases would likely diminish the intervention's effect, particularly in the case of a dose-response association (19). Two researchers (SMa, SMo) independently conducted the GRADE assessment and resolved any discrepancies through discussion to ensure consistency and accuracy in the evaluation process.

Ethical considerations

Ethical considerations in this systematic review and meta-analysis were addressed in accordance with best practices for conducting and reporting such studies. As no primary data were collected from human participants, formal ethical approval was not required. We ensured ethical integrity by systematically and transparently searching, selecting, and analyzing all eligible studies, accurately reporting results, and appropriately citing all sources.

Results

Of the 133 articles initially identified by the search, 41 were selected for a full-text review (Figure 1). Ultimately, 11 articles were included in the systematic review, and 9 RCTs, including 1577 women with mediolateral episiotomy, were included in the meta-analysis. Two studies were not included in the meta-analysis: one study did not report sufficient data to calculate effect sizes, and the other investigated mefenamic acid, which was represented by a single trial; therefore, its findings were described narratively rather than quantitatively.

Characteristics of the included studies

The characteristics of the included studies are shown in Table 2. The included studies were conducted in the UK (15, 16), Pakistan (9, 10), Sri Lanka (20), Australia (21), Iran (22), Thailand (14), Turkey (23, 24), and Egypt (8). The included RCTs were published between 1997 (15) and 2023 (8). All the articles were published in English. The sample size in the studies varied from 70 (23) to 230 women (8) per study. One study was designed as a three-arm RCT (22), and the remaining ten RCTs had two arms. In 5 studies, the rectal suppository of diclofenac was compared with the rectal placebo (14-16, 20, 21). Altungül et al. (2012) and Yildizhan et al. (2009) compared the effects of two rectal suppositories, diclofenac and indomethacin, on post-episiotomy pain (23, 24). Oral and rectal diclofenac were also compared in two trials (8, 9). Rezaei et al. (2014) also compared rectal diclofenac and indomethacin with a placebo (22).

Description of risk of bias

The overall risk of bias for the included trials varied across trials (Table 3 and Figure 2). Five trials had a low risk of bias (14-16, 21, 22). Three trials were rated as high-risk (9, 10, 23), and three trials were rated as high-risk (8, 20, 24). Six trials were assessed as having a low risk of bias in the randomization domain (8, 14-16, 21, 22). Most trials were designed as placebo

Table 2. Characteristics of the included RCTs

First author, year	Country	Age (MD±SD)	Intervention	Control	pain measurement too	Results	Risk of bias
Achariyapota, 2008 (14)	Thailand	IG: 23.39±6.3 CG: 24.28±4.8	N=36 Two tablets of 50 mg rectal diclofenac	N=36 Two placebo rectal suppositories	VAS	Median pain scores were significantly lower in the IG at both 12- and 24-hours post-administration compared to the CG, with scores of 4.5 versus 0.0 (P<0.001) at 12 hours and 2.0 versus 0.0 (p=0.02) at 24 hours.	Low
Yoong, 1997 (15)	United Kingdom	No data	N=56 A single dose of 100 mg diclofenac sodium rectal suppository	N=54 Placebo rectal suppository	VAS	Median (range) of VAS at 24 hours: IG: 2 (0-5), CG: 2.5 (0-7), P<0.05 At 24-48 hours: IG: 1 (0-5), CG: 1 (0-4.5), P=NS Mean±SD of additional paracetamol (g) at 24 hours: IG: 0.69±0.56, CG: 1.33±0.67, P<0.05, At 24-48 hours: IG: 0.6±.53), CG: 1.11±0.57, P<0.05	Low
Dasanayake, 2014 (20)	Sri Lanka	IG: 28.2 CG: 27.9 (Only mean)	N=84 A 100 mg diclofenac sodium rectal suppository was inserted when suturing was completed, and the second dose (50 mg) was used 12 hours after birth	N=85 Placebo rectal suppository in the same way	VAS	Pain Score at 24 hours after delivery: IG: 0.25±0.11, CG: 0.45±0.15, P<0.001	Some concerns
Dodd, 2004 (21)	Australia	IG: 29±5 CG: 30±6	N=67 2×100 mg diclofenac rectal suppository (The first suppository was inserted when suturing was completed, and the second was offered 12–24 hours	N=66 Two placebo rectal suppositories in the same way	VAS	Women in the IG demonstrated a significantly reduced likelihood of experiencing pain at 24 hours while walking (RR 0.8; 95% CI 0.6 to 1.0), sitting (RR 0.8; 95% CI 0.6 to 1.0), urinating (RR 0.6; 95% CI 0.4 to 1.0), and during bowel movements (RR 0.6; 95% CI 0.2 to 0.9) when compared to those in the CG. However, these differences were not sustained at 48 hours postpartum.	Low

First author, year	Country	Age (MD±SD)	Intervention	Control	pain measurement too	Results	Risk of bias
			after birth) N=45 2×100 mg diclofenac rectal suppository (The first suppository was inserted when suturing was completed, and the second was offered 12 hours after birth)	N=44 Two placebo rectal suppositories in the same way	NRS (0 to 5)	The average pain scores, assessed using a six-point numerical scoring system, showed a significant reduction for the IG at 24, 48, and 72 hours postpartum (0.86, 0.7, and 0.59, respectively) compared to the CG (1.64, 1.31, and 1.5; P<0.005). Additionally, the need for supplementary pain relief was considerably lower in the IG, with only 8 women requiring it at 72 hours, in contrast to 15 women in the CG	Low
Rezaei, 2014 (22)	Iran	IG1: 24.4±4.2 IG2: 24.9±4.4 CG: 25.6±4.4	N=30 A single dose of diclofenac suppository N=30 A single dose of an indomethacin suppository	N=30 Placebo	VAS	In the IG1 and IG2 reported pain levels were significantly lower than those in the CG (P<0.05). On comparison, diclofenac demonstrated superior efficacy to indomethacin at the 4-hour interval (P<0.05). However, due to diclofenac's shorter half-life, increased pain levels were reported in the diclofenac group at the 12th hour	Low
Altungül, 2012 (23)	Turkey	IG: 25±6 CG:24±4	N=35 Diclofenac sodium suppositories (Voltaren, 100 mg diclofenac sodium, Novartis, Istanbul, Turkey)	N=35 Indomethacin suppository (Endol, 10 mg indomethacin, Deva, Istanbul, Turkey)	VRS VAS	For the IG, the one-hour VRS score was 2.6 ± 0.5 points, and the VAS score was 4.9±0.8 points. For the CG the one-hour VRS score was 3.4±0.6 points, and the VAS score was 6.6±1.2 points (P<0.05). At 24 hours, the IG recorded a VRS of 1.2 ± 0.4 points and a VAS of 2.4±0.9 points, while the CG had a VRS of 2.0±0.7 points and a VAS of 4.0 ± 1.3 points (P<0.05). Both groups demonstrated a significant reduction in pain scores from the first to the 24th hour (VAS1-VAS24, VRS1-VRS24) (P<0.05). Additionally, a positive correlation was found between the first and 24th hour VRS and VAS scores (P=0.001).	High

First author, year	Country	Age (MD±SD)	Intervention	Control	pain measurement too	Results	Risk of bias
Yildizhan, 2009 (24)	Turkey	IG: 27.83±3.39 CG:29.08±3.27	N=100 A single dose of 100 mg of diclofenac suppository	N=100 2×100 mg indomethacin suppositories (one every 12 hours)	VAS	VAS at 24 h (mean± SD): IG: 1.89±1.79, CG: 2.07±1.82, p=NS Additional analgesic request at 24 hours: IG: 9/100, CG: 11/100, P=NS	Some concerns
Ahmed, 2023 (8)	Egypt	IG: 24.29±3.78 CG: 25.17±3.64	N=92 100 mg diclofenac sodium rectal suppository (1st dose was given immediately after perineal repair; 2nd dose was given after 12 hours and 3rd dose was given after 24 hours)	N=92 One tablet of diclofenac sodium 100 mg per oral (1st dose was given immediately after perineal repair; 2nd dose was given after 12 hours and 3rd dose was given after 24 hours)	VAS	Frequency of additional analgesia (IG: 1.1%, CG: 8.7%, p= 0.01). VAS at different times of assessment, either after one hour, 4-, 8-, 16- and 24-hours, was significantly lower among the rectal group in comparison to the oral group (P< 0.001).	Some concerns
Mushtaq, 2022 (9)	Pakistan	IG: 26.01±2.42 CG: 25.48±2.92	N=130 50 mg Diclofenac rectal suppository was placed at the time of episiotomy repair and was repeated after 12 hours	N=130 Oral tablet of 50 mg Diclofenac sodium after the completion of episiotomy repair, and it was repeated after 12 hours	VAS	Mean Pain Score at 24 hours: IG:2.93±0.74, CG:3.98±0.81, P=0.001	High
Ijaz, 2021 (10)	Pakistan	IG: 26.14±4.78 CG: 28.04±3.42	N=100 100 mg diclofenac rectal suppository, repeat dose was given after 8 hours	N=100 Oral mefenamic acid 500 mg, repeat dose was given after 8 hours	VAS	VAS at 6 hours after intervention IG: 2.99±1.00, CG: 3.68±0.875, P<0.001 VAS at 12 hours after intervention IG: 1.07±0.856, CG: 1.68±0.909, P<0.001	High

NRS: Numeric Rating Scale , VAS: visual analog scale, VRS: visual rating scale, IG: Intervention group, CG: control group

controls (14-16, 20-22). Eight trials were assessed as low risk in the domain of deviations from intended interventions (14-16, 20-24). Ten trials had a low risk of bias for attrition, with one trial assessed at some risk of bias (23). For all trials, we assessed the risk of selective reporting to be low risk because of sufficient reporting.

When rectal diclofenac was compared with other active analgesics, including oral diclofenac (9, 16), rectal indomethacin (23, 24), and oral mefenamic acid (10), results were more variable. Several studies showed significantly lower VAS scores in the rectal diclofenac group at early and intermediate time points (1, 4, 6, 8, 12, and 24 hours), as well as a lower frequency of additional analgesic requests. However, some trials reported non-significant differences at 24 hours, particularly when diclofenac was compared with indomethacin. Differences in drug pharmacokinetics were noted in individual studies, with one trial reporting superior early analgesic effects of diclofenac followed by increased pain scores at later time points, potentially related to its shorter half-life.

Meta-analysis findings

Overall, the meta-analysis demonstrated that diclofenac rectal suppository was associated with a significant reduction in post-episiotomy pain at 24 hours compared with placebo and oral diclofenac. In contrast, no statistically significant difference was observed when diclofenac rectal suppository were compared with rectal indomethacin. Although substantial heterogeneity was present across studies, sensitivity analyses confirmed the robustness of the main findings.

Descriptive findings of included studies

Overall, most studies reported lower perineal pain scores and/or reduced additional analgesic use in women receiving rectal diclofenac compared with control interventions. In placebo-controlled trials, median and mean pain scores were consistently lower in the intervention groups at 12 and 24 hours postpartum, with statistically significant differences reported in several studies. Some trials also demonstrated reduced pain-related functional limitations, including pain during walking, sitting, urination, and bowel movements at 24 hours, although these effects were not always sustained beyond 48 hours (21). Studies assessing pain over extended follow-up periods reported persistently lower pain scores up to 72 hours postpartum (16) and a reduced need for supplementary analgesics among women receiving rectal diclofenac (8, 16).

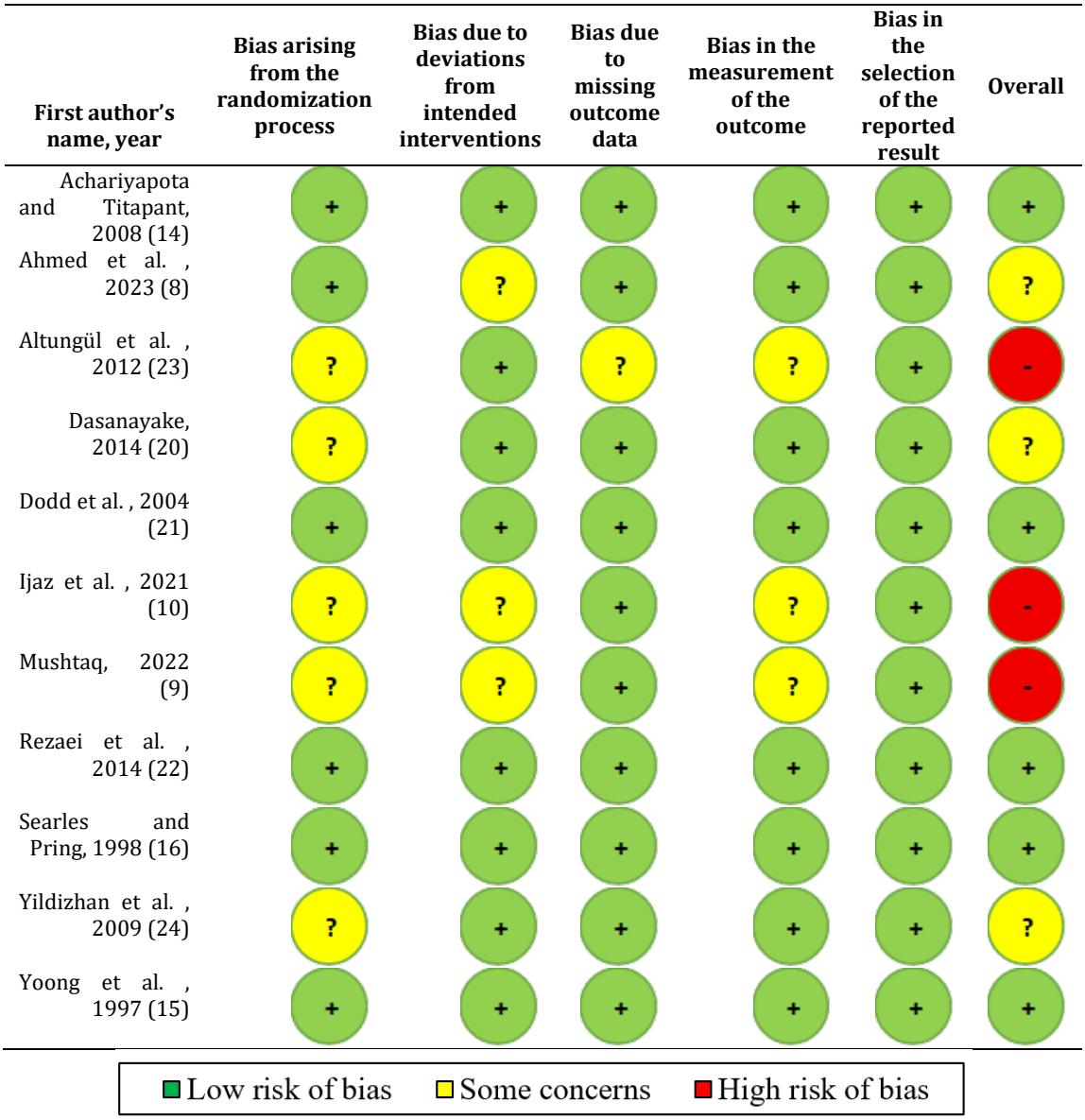
A. Diclofenac rectal suppository versus placebo:

Figure 3 shows the meta-analysis findings for 573 women from five studies (14-16, 20, 21). In the intervention group, post-episiotomy pain at 24 hours after delivery was 1.49 units lower than that in the placebo group (SMD=-1.49, 95% CI -2.45-- -0.53, p=0.002). Owing to the significant heterogeneity between the studies (I^2=96%, Chi^2=99.33, P<0.00001), a random effects model was used. Sensitivity analysis revealed that the overall effect size remained robust and did not substantially change after one study was excluded at a time, indicating the stability of the findings. The measurement of publication bias was not performed due to the limited number of studies.

B. Diclofenac rectal suppository versus oral diclofenac:

Figure 4 shows the forest plot of the pooled mean differences in the effect of rectal diclofenac versus that of oral diclofenac on post-episiotomy pain at 24 hours after delivery. The meta-analysis of data from two studies with 444 participants (8, 9) revealed that, in the diclofenac rectal group, the incidence of post-episiotomy perineal pain was 1.64 points lower than that in the comparison group, and this difference was statistically significant (MD=-1.64, 95% CI -2.80--0.49, p=0.005). A random effects model was used because of the significant heterogeneity between studies (I^2=99%, Chi^2=111.16, P<0.00001).

Table 3. Risk of bias judgment for each included studies based on the Cochran risk of bias tool



A. Diclofenac rectal suppository versus rectal indomethacin:

The forest plot of the pooled mean differences in the effect of rectal diclofenac versus that of rectal indomethacin on post-episiotomy pain at 24 hours after delivery is shown in Figure 5. The findings of the meta-analysis of 270 postdelivery women revealed that although the use of diclofenac rectal suppository resulted in less perineal pain than did the use of rectal indomethacin, this difference was not significant (MD=-0.89, 95% CI -2.28--0.50, p=0.21). A significant heterogeneity was found among the studies (I^2=93%, Chi^2=14.76, p=0.0001).

Other findings

Only one clinical trial compared diclofenac rectal suppository with oral mefenamic acid for reducing perineal pain after episiotomy(10). The analysis of a sample size of 200 post-delivery women revealed that rectal diclofenac was more effective than oral mefenamic acid in controlling perineal pain at 6 and 12 hours after episiotomy (P<0.001)(10).

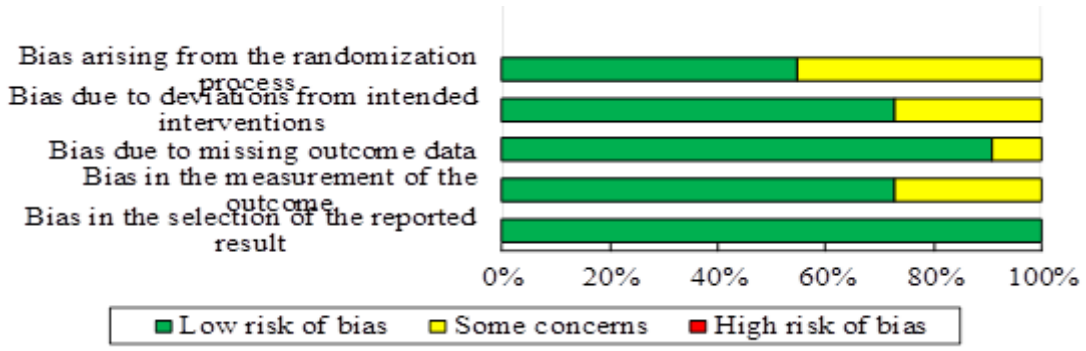


Figure2. Risk of bias graph across all included RCTs

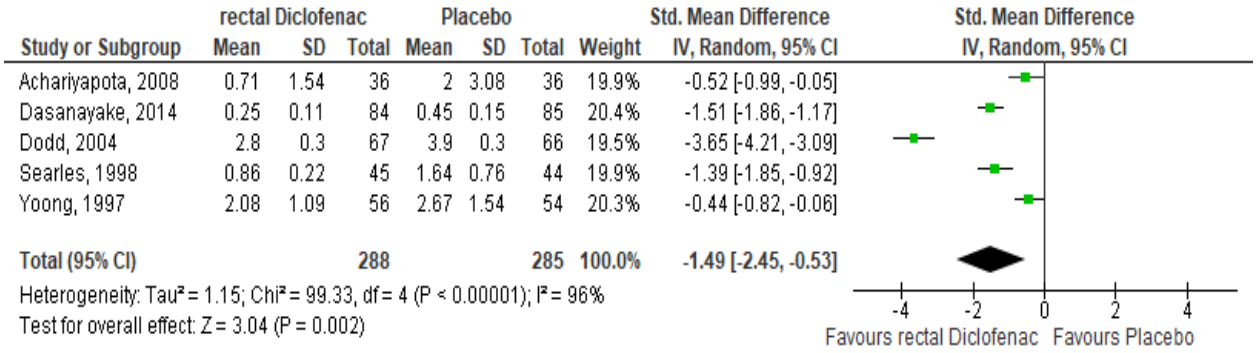


Figure3. Forest plots of the effects of rectal diclofenac versus placebo on post-episiotomy pain at 24 hours after delivery

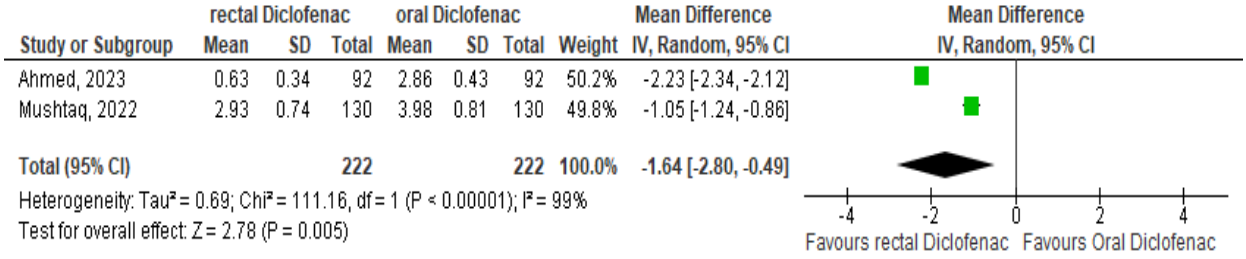


Figure4. Forest plots of the effects of rectal diclofenac versus oral diclofenac on post-episiotomy pain at 24 hours after delivery

Evidence grading

The GRADE-pro-GDT was utilized to assess the quality of evidence for the three main outcomes, and the results are presented in Table 4. The quality of evidence was moderate for the effect of rectal diclofenac versus placebo on perineal pain 24 hours after delivery. One downgrade was given because of a serious inconsistency. The quality of evidence for the effect of rectal diclofenac versus that of oral diclofenac or rectal indomethacin on perineal pain 24 hours after delivery was very low, and three studies with very serious limitations in the risk of bias, inconsistency, and imprecision were included.

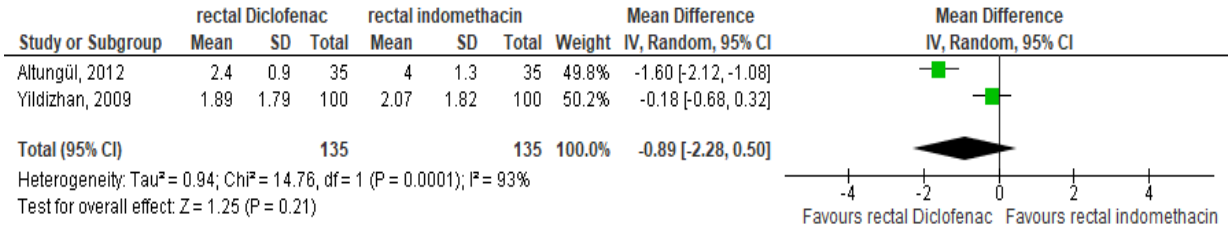


Figure5. Forest plots of the effects of rectal diclofenac versus rectal indomethacin on post-episiotomy pain at 24 hours after delivery

Table 4. GRADE evidence profiles for the main outcomes among the trials included in the meta-analysis

Certainty assessment							№ of patients		Effect			
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**[Diclofenac]**	**[comparison]**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
Rectal diclofenac effect versus placebo on post-episiotomy pain at 24 hours after delivery												
5	randomized trials	not serious	serious[a]	not serious	not serious	none	288	285	-	SMD **1.49 SD lower** (2.45 lower to 0.53 lower)	⊕⊕⊕◯ Moderate	CRITICAL
Rectal diclofenac effect versus oral diclofenac on post-episiotomy pain at 24 hours after delivery												
2	randomized trials	very serious[b]	serious[a]	not serious	not serious	none	222	222	-	MD **1.64 lower** (2.8 lower to 0.49 lower)	⊕◯◯◯ Very low	CRITICAL
Rectal diclofenac effect versus rectal Indomethacin on post-episiotomy pain at 24 hours after delivery												
2	randomized trials	very serious[b]	serious[a]	not serious	serious[c]	none	135	135	-	MD **0.89 lower** (2.28 lower to 0.5 higher)	⊕◯◯◯ Very low	CRITICAL

CI: confidence interval; MD: mean difference; SMD: standardized mean difference Explanations
a. Significant heterogeneity was found among the studies, b. Information is from studies at high risk of bias or some concerns, c. The optimal information size (OIS) criterion is not met

Discussion

To our knowledge, this study is the first meta-analysis to evaluate the efficacy of diclofenac rectal suppository compared with placebo and other NSAIDs for managing post-episiotomy pain. In this systematic review, 11 RCTs were included, of which 9 studies (involving 1,577 women) were eligible for the meta-analysis. Our findings showed that rectal diclofenac can reduce the episiotomy pain score 24 hours after delivery compared with placebo (14-16, 20-21) and other NSAIDs, including oral diclofenac (8, 9). In contrast to rectal suppository, oral

NSAIDs are metabolized in the liver and necessitate higher doses (26). Additionally, oral diclofenac may lead to gastric side effects in certain patients, which can be avoided when diclofenac is administered rectally (9).

Furthermore, the results of the study comparing rectal diclofenac suppository with rectal indomethacin, as examined in previous studies (23-24), revealed no statistically significant difference between the two drugs, with both having similar effects.

However, rectal diclofenac suppository was more effective than other NSAIDs, including indomethacin, in reducing episiotomy pain during the first 24 hours. A meta-analysis by Moore et al. (2015) demonstrated that diclofenac is more effective than other NSAIDs in reducing postoperative pain in adults. Additionally, diclofenac has been associated with a lower risk of stomach-related side effects than other drugs (27). Diclofenac, mefenamic acid, and indomethacin are all NSAIDs that inhibit the cyclooxygenase (COX) enzymes responsible for prostaglandin production, which are crucial in pain and inflammation (28). Diclofenac affects both COX-1 and COX-2, potentially enhancing their anti-inflammatory and analgesic effects (29), mefenamic acid, and indomethacin similarly block these enzymes to reduce pain temporarily (30, 31). Despite their common mechanism of action, diclofenac's broader spectrum may confer greater potency. The selection of an NSAID should be based on individual patient needs and the associated risks and side effects (29).

Few systematic reviews have investigated the safety and efficacy of diclofenac in the management of postpartum-related pain. In this context, in 2023, Jain et al. conducted a systematic review and meta-analysis of 8 studies to evaluate the effectiveness of NSAIDs for general postpartum pain management, including both cesarean and vaginal deliveries. The search period for these studies was up to 2020. They reported that NSAIDs were generally effective for postpartum pain, but an analysis of the data revealed inconclusive results regarding the risk of developing hypertension in those women (32). Notably, their review focused on the oral form of NSAIDs and did not specifically address perineal or post-episiotomy pain.

In another systematic review, Luxey et al. evaluated the literature until March 2023 to develop recommendations for pain management after a vaginal delivery with perineal trauma. After reviewing 79 studies, researchers reported that acetaminophen and NSAIDs were recommended as first-line treatments for the management of pain in cases of perineal trauma and episiotomy. They also recommended ice or chemical cold packs for the first-line treatment of postpartum pain because of their ease of use (1). In their study, no meta-analysis was performed. Our findings are generally in line with Luxey et al. (1) as we also found that NSAIDs, specifically rectal diclofenac, are effective in reducing post-episiotomy pain within 24 hours after delivery. Compared with the broader reviews by Jain et al. (32), our study provides more specific evidence for perineal pain and quantifies the effect of diclofenac relative to placebo and other NSAIDs, adding precision to the existing recommendations.

In a meta-analysis, Zang et al. (2016) assessed the analgesic efficacy of NSAIDs in postoperative cesarean delivery patients. In their study, 22 RCTs compared an NSAID to a control. They reported that patients in the NSAID group experienced less pain at 12 and 24 hours. When researchers performed subgroup analysis, the results revealed a significant difference in pain scores at 24 hours, with patients receiving NSAIDs via the intravenous–intramuscular route but not the oral or rectal route. Additionally, there was significantly less opioid consumption in the NSAID groups (33). In our meta-analysis, we specifically evaluated rectal diclofenac and found it to be significantly effective in reducing post-episiotomy perineal pain within 24 hours. This may be related to the local application and pharmacokinetic properties of rectal diclofenac, such as longer half-life and greater bioavailability (34). Diclofenac sodium, when taken orally, undergoes significant first-pass metabolism and can irritate the gastric mucosa, necessitating consumption with food. Some studies indicate that rectal administration improves absorption, bypasses the first-pass effect, and results in more of the drug being available in the bloodstream more quickly, providing faster pain relief and prolonged therapeutic action (16, 35).

Since there is no universally accepted method for evaluating the certainty of effect estimates produced by meta-analyses, we adhered to the recommendations of the GRADE working group, applying a rigorous methodology to assess the reliability of network evidence. As a result, the quality of evidence varied significantly. The quality of evidence was rated as moderate for the effect of rectal diclofenac compared to placebo on perineal pain 24 hours post-delivery. However, it was rated very low when comparing rectal diclofenac to oral diclofenac or rectal indomethacin for the same outcome, due to substantial limitations such as a high risk of bias in the included studies, inconsistency, and imprecision.

Based on the findings of this systematic review, the current evidence from indirect comparisons suggests that rectal diclofenac is more effective than other NSAIDs in managing pain from perineal tears and episiotomy. Nonetheless, further information is required regarding its effects on maternal well-being, breastfeeding, and long-term side effects.

The strengths of the present study include the inclusion of only RCTs in the meta-analysis, which enhances the validity of the findings, as RCTs are considered the gold standard in clinical research for minimizing bias and confounding factors. Additionally, employing the GRADE framework to assess the quality of evidence adds rigor, providing a systematic and transparent method for evaluating both the quality of evidence and the strength of recommendations in healthcare (36).

The current study has some notable limitations. One primary concern is the significant heterogeneity observed among the included studies, with I^2 values exceeding 90% in our meta-analysis. It is essential to point out that all studies considered in this analysis involved similar participant groups and were randomized controlled trials (RCTs). Consequently, the heterogeneity seen in the forest plots is likely attributed more to the variability of effect sizes reported by the individual studies rather than the random effects model itself. Also, due to the limited number of included RCTs (fewer than 10), tests for publication bias (e.g., Begg's or Egger's test) and subgroup analysis could not be performed. Additionally, some trials included in the analysis exhibited a high risk of bias, which could potentially impact the overall results of the meta-analysis. The number of studies comparing diclofenac rectal suppository with other NSAIDs is limited, which constrains the ability to draw definitive conclusions. Furthermore, the quality of evidence for some comparisons was rated as very low, diminishing confidence in the effect estimates. It is important to consider these strengths and limitations when interpreting the findings of this study. To enhance the robustness of the evidence, further high-quality studies are necessary.

Conclusion

In conclusion, this study offers insights into the use of diclofenac rectal suppository for post-episiotomy pain management. However, due to the varying risk of bias and the overall quality of evidence among the studies, there is a clear need for additional high-quality RCTs to confirm these findings and provide more robust evidence regarding the clinical application of diclofenac rectal suppository.

Declarations

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Conflicts of interest

Authors declared no conflicts of interest.

Ethical considerations

This study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Code of Ethics

Ref. No: IR.AJUMS.REC.1403.162.

Use of Artificial Intelligence (AI)

The authors declare that AI tools were used solely to assist with language refinement and clarity; all study design, data analysis, interpretation, and conclusions were performed by the authors.

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Authors' contribution

MA and MS conducted the search process, title screening, and full-text screening. MS and MN extracted data. SMa and SMo assessed potential bias and applied GRADE. SMa, MS, and MA

formulated the final tables and drafted the initial manuscript version. SMa conceived the study, provided methodological and content expertise, performed the meta-analysis, and supervised all its steps. All authors reviewed the article and approved its content.

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