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Full length article

Efficacy of NSAIDs in reducing pain during intrauterine device Insertion: A systematic review

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ABSTRACT

Background: Intrauterine devices (IUD) are highly effective, but insertion pain deters many. While no consensus exists on gold standard analgesia, practitioners commonly recommend over-the-counter non-steroidal anti-inflammatory drugs (NSAIDs). This systematic review evaluates NSAID efficacy for pain reduction during IUD insertion. Methods: We searched PubMed, Embase, Web of Science, Scopus and Cochrane Library using (intrauterine device* OR IUD*) AND (NSAIDs OR non-steroidal anti-inflammatory drugs). The primary outcome was patient-reported pain during IUD insertion. The authors evaluated each publication for bias using the Centre for Evidenced-Based Medine Critical Appraisal Tool for Randomised Control Trials (CEBM). Results: The search yielded 6,529 studies, retrieving 29 full texts, with 20 meeting inclusion criteria. This review found limited evidence that prophylactic NSAIDs provide clinically significant pain relief for most women. The review included various NSAID types and dosages. Six studies demonstrated a statistically significant reduction in pain ($p < 0.05$) compared to placebo. Conclusion: Prophylactic NSAIDs show limited efficacy in reducing IUD insertion pain, with 70 % of studies reporting no significant benefit. These findings, suggesting lower overall effectiveness than previous research, underscore the need for standardized approaches and further research into meaningful pain relief. Heterogeneity in NSAID types, dosages, and pain assessment methods highlights the need for targeted research to improve patient-centered reproductive healthcare.

Introduction

Oligoanalgesia (the under treatment of pain) for women has been well-documented in recent research, and testimonials by patients [8]. Women presenting to physicians in emergent situations are less likely to receive appropriate treatment and are more likely to be diagnosed with a mental health condition when seeking care for a chronic pain condition [41]. Women experience moderate discomfort to severe pain during many in-office gynecologic procedures and are often offered little to no efficacious pain management [31]. The insertion of an intrauterine device (IUD) for the prevention of pregnancy is a key example of this. IUDs have a pregnancy rate of less than one percent (around 0.3 per 100 women) and last for up to ten years, making the device a first-line contraception option [28]. However, many women are hesitant, fearful, or abstain from the procedure due to the pain experienced during the device insertion [17]. Women and other supporters have petitioned and lobbied for better pain management during gynecological procedures [10], but the current U.S. clinical recommendations for pain management remain unclear or unspoken. Current guidelines suggest lidocaine may be useful for pain reduction during IUD insertion, but no standard pain management regime is currently advised [12]. Previous research evaluating paracervical blocks, topical analgesics, misoprostol, and NSAIDs for pain reduction during IUD insertion has not demonstrated consistent clinical and statistical efficacy. Other systematic reviews have analyzed various pain reduction methods at insertion, but none have limited their review to researching the efficacy of NSAIDs alone. The objective of this systematic review is to determine the efficacy of NSAID's for pain reduction during IUD insertion.

Methods

Search strategy

For our systematic search we followed the Preferred Reporting Items

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for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, with the exception of prior registration of the study. PubMed, Embase, Scopus, Cochrane Library and Web of Science databases were searched using the following search strategy: (intrauterine device* OR IUD*) AND (NSAIDs OR non-steroidal anti-inflammatory drugs) on March 4th, 2025. Additionally, experts at the authors' institution and at national conferences were consulted to inquire on unpublished studies.

Eligibility criteria

Studies were eligible for inclusion if they: 1) compared different methods of pain control during IUD insertion; 2) measured pain outcomes using visual analog scales (VAS); 3) included women of reproductive age eligible for IUD insertion; and 4) were published in peer-reviewed journals in English from the year 2000.

Studies were excluded if they: 1) did not have a control group or a clear comparison of pain control methods; 2) used subjective or unreliable measures of pain, such as verbal descriptors or facial expressions; 3) included women who were pregnant, had contraindications for IUD insertion, or had a history of pelvic inflammatory disease (PID) or endometriosis; or 4) were unpublished, no available English translation, or published before the year 2000.

Study selection

Titles and abstracts were uploaded into an AI-powered systematic review software (Rayyan) to aid in screening and is highly sensitive at detecting duplicate references [26]. Rayyan initially screened the studies for duplication, and the authors manually removed additional duplicates that Rayyan flagged for similarity. After the removal of duplicates, two reviewers independently screened the titles and abstracts for inclusion, with initial votes blinded. An article had to reach a unanimous decision to be included or excluded. Reviewers manually resolved discrepancies at the end of the initial screening process.

Critical Appraisal

The authors evaluated each publication for quality assessment using the Centre for Evidenced-Based Medine Critical Appraisal Tool for Randomised Control Trials [7]. This included assessing the validity of study design, methodology, and results in addition to the local impact of the studies. All included studies were found to have sound data after critical appraisal and external generalizability for our systematic review. See Table 2 for a summary of the appraisal.

Data Extraction

For each study, we extracted average VAS pain scores for the treatment, placebo, and comparator groups, the pharmacologic intervention used (including dosage and delivery method), and the number of participants in each group. Any discrepancies between reviewers were resolved through discussion or consultation with a third reviewer.

Results

Study selection

The initial search yielded 6,529 studies. 5,439 studies were excluded, yielding 29 full texts sought for retrieval. Full text articles were reviewed by two reviewers, yielding a total of 20 articles reached by unanimous decision to be included. The article selection process is illustrated in Fig. 1.

Pharmacological intervention

All pharmacological interventions were administered prior to IUD insertion to assess their prophylactic efficacy in reducing pain during the procedure. Of the 20 studies included, pharmacologic interventions included ibuprofen (400 mg orally and 800 mg orally), naproxen (375 mg orally and 550 mg orally), naproxen sodium (550 mg orally), etoricoxib (120 mg orally), ketorolac (20 mg orally, 50 mg orally, and 30 mg

Table 1
Summary of Studies. Overview of included studies, including the author and year, type of NSAID used, dosage, time given prior to IUD placement, number of participants in the NSAID and placebo and/or comparator groups, and the P value for NSAID versus placebo or comparator groups.

Study Author and Year	NSAID Type	Dose (mg)	Time (min)	N (NSAID)	Placebo or Comparator	N (placebo/ comparator)	P value
[19]	Ibuprofen	400	45	1011	Placebo	1008	*
[5]	Ibuprofen	800	30	101	Placebo	101	$p = 0.5$
[9]	Ibuprofen	800	45	47	Placebo	40	$p = 0.91$
[6]	Ibuprofen	400	60	48	Lidocaine	50	$p = 0.40$
[37]	Ibuprofen	400	60	40	Lidocaine	40	$p = 0.9$
[33]	Ibuprofen	400	45	70	Lidocaine	70	$p < 0.001$
[27]	Naproxen	375	60	40	Placebo	108	$p = 0.456$
[29]	Naproxen	550	60–90	59	Placebo	60	$p = 0.89$
[15]	Naproxen	550	30	49	Lidocaine	51	$p < 0.001$
[22]	Naproxen Sodium	550	60	34	Placebo, Tramadol	34/35	$p < 0.001$
[32]	Etoroxib	120	60	65	Placebo	65	$p = 0.873$
[11]	Ketorolac	20	40–60	35	Placebo	36	$p < 0.031$
[30]	Ketorolac	30	30	33	Placebo	34	$p = 0.99$
[24]	Ketorolac	20	60	60	Placebo, Dipyrone, Scopolamine, Hyoscyamine, Homatropine	60	*
[3]	Ketoprofen	150	60	70	Placebo	70	$p < 0.003$
[35]	Diclofenac	100	60	40	Misoprostol	39	$p < 0.039$
[1]	Diclofenac	50	30	53	Hyoscine-N-Butyl Bromide	54	$p = 0.104$
[40]	Diclofenac	100	60	33	Placebo, Lidocaine, Counseling	66	$p = 0.004$
[14]	Celecoxib	200	120	35	Placebo, Hyoscine-N-Butyl Bromide	70	$p < 0.001$
[2]	Indomethacin	50	30	48	Placebo	48	$p < 0.001$

*Reported as non-significant (no P-value).

Table 2
Summary of randomization, blinding, and validity characteristics in the included studies. The table was derived from answering the CEBM Critical Appraisal Tools for Randomized Control Trials.

Study Author and Year	Treatment Randomization	Baseline Characteristics Similarity	Treatment Similarity	Accounting Of Patients	Blinding	Statistical Significance	External Validity
[19]	Not reported	Not reported	Y	Y	Double	N	Y
[5]	Computer generated	Y	Y	Y	Double	N	Y
[9]	Computer generated	Age significant difference	Y	Y	Double	N	Y
[33]	Randomization table	Not reported	Y	Y	N	Y	Y
[27]	Computer generated	Prior c-section significant difference	Y	Y	Double	N	Y
[29]	Computer generated	Drug use significant difference	Y	Y	Double*	N	Y
[22]	Computer generated	Y	Y	Y	Double	Y	Y
[32]	Computer generated	Y	Y	Y	Double	N	Y
[11]	Computer generated	no	Y	Y	Double	Y	Y
[30]	Computer generated	Y	Y	Y	Double**	N	Y
[24]	Computer generated	Y	Y	Y	Double	N	Y
[3]	Computer generated	Y	Y	Y	Double	Y	Y
[35]	Computer generated	Y	Y	Y	Single(Investigators blinded)	Y	Y
[1]	Computer generated	Y	Y	Y	Double	N	Y
[40]	Computer generated	Y	Y	Y	Single(Investigators blinded)	Y	Y
[37]	Computer generated	Y	Y	Not reported	Single(Participants blinded,investigators unclear)	N	Y
[6]	Computer generated	Y	Y	Y	N	N	Y
[15]	Randomization was performed in block of five women each by the main researcher. Participants received a number according to the arrival order at the service. Then they were randomly drawn to one of two groups by cards stored in an envelope.	Y	Y	Y	N	Y	Y
[14]	Computer generated	Y	Y	Y	Double	Y	Y
[2]	Computer generated	Prior c-section significant difference	Y	Y	Double	Y	Y

*Nurses who administered medication were not blinded to intervention
*Not all Nurses who gave "study forms" were blinded due to staff issues.

intramuscularly), ketoprofen (150 mg orally), celecoxib (200 mg orally), indomethacin (50 mg rectal suppository) and diclofenac (100 mg orally and 100 mg vaginal suppository) (Table 1).

Parity and Mode of delivery Stratification

Only five studies stratified Visual Analog Scale (VAS) scores during intrauterine device (IUD) insertion by parity. In four studies, nulliparous women reported higher average VAS scores compared to their multiparous counterparts. One study did not find a significant difference between women with prior vaginal or cesarean deliveries but did find rectal suppository to be effective during the procedure [2]. None of the other four studies demonstrated significant pain relief with the use of NSAIDs, regardless of parity.

Nsaids vs placebo

Fig. 2 illustrates the VAS scores from all retrieved studies, where asterisks (*) on the figure indicate statistically significant differences from placebo ($p < 0.05$). Across the studies comparing NSAIDs to a true placebo (e.g., sugar pill, saline), the average VAS with NSAID use was 3.78 (range: 1.8–8.4). While several studies investigated the use of different NSAIDs (ibuprofen, naproxen, ketorolac, ketoprofen, etoricoxib, celecoxib and indomethacin), only six demonstrated a statistically significant reduction in pain compared to placebo. As can be seen in Fig. 2, these statistically significant reductions appear to be small. One study each using naproxen (Fig. 2B), ketorolac (Fig. 2C), ketoprofen (Fig. 2D) and diclofenac (Fig. 2G) demonstrated a statistically significant reduction in pain. However, other studies using naproxen and ketorolac did not find a statistically significant benefit. In one ketorolac study, subjects, on average, reported higher VAS scores than the placebo group (Fig. 2C).

NSAIDss vs comparator

Six of the studies did not compare NSAIDs to a placebo and instead ranked NSAIDs efficacy against other classes of medications or "comparators" (Table 1). Four used a combination of comparators and placebo groups. Comparators used differed across studies including tramadol, misoprostol, Hyoscine-N-Butyl Bromide, dipyrone, scopolamine, hyoscyamine, and homatropine. One study looked at the effects of counseling alone. The most used comparator was intracervical lidocaine. The average VAS score for the prophylactic NSAID groups in trials that did not include true placebos was 5.16, with a range of 3.66–7.3.

Efficacy of NSAIDs for pain control

Overall, six placebo-controlled studies reported that NSAIDs provided significant pain control during IUD insertion, although two of these noted adequate pain control were not achieved during tenaculum placement. Prophylactic NSAID usage was not clinically significant for pain control during IUD insertion in 14 studies (70 %). One of the studies that found NSAIDs were effective as a pain control method also analyzed the efficacy of two other treatment groups: tramadol and a placebo. While it noted the NSAIDs were more effective than the placebo as pain control, the tramadol control group outperformed NSAIDs for pain

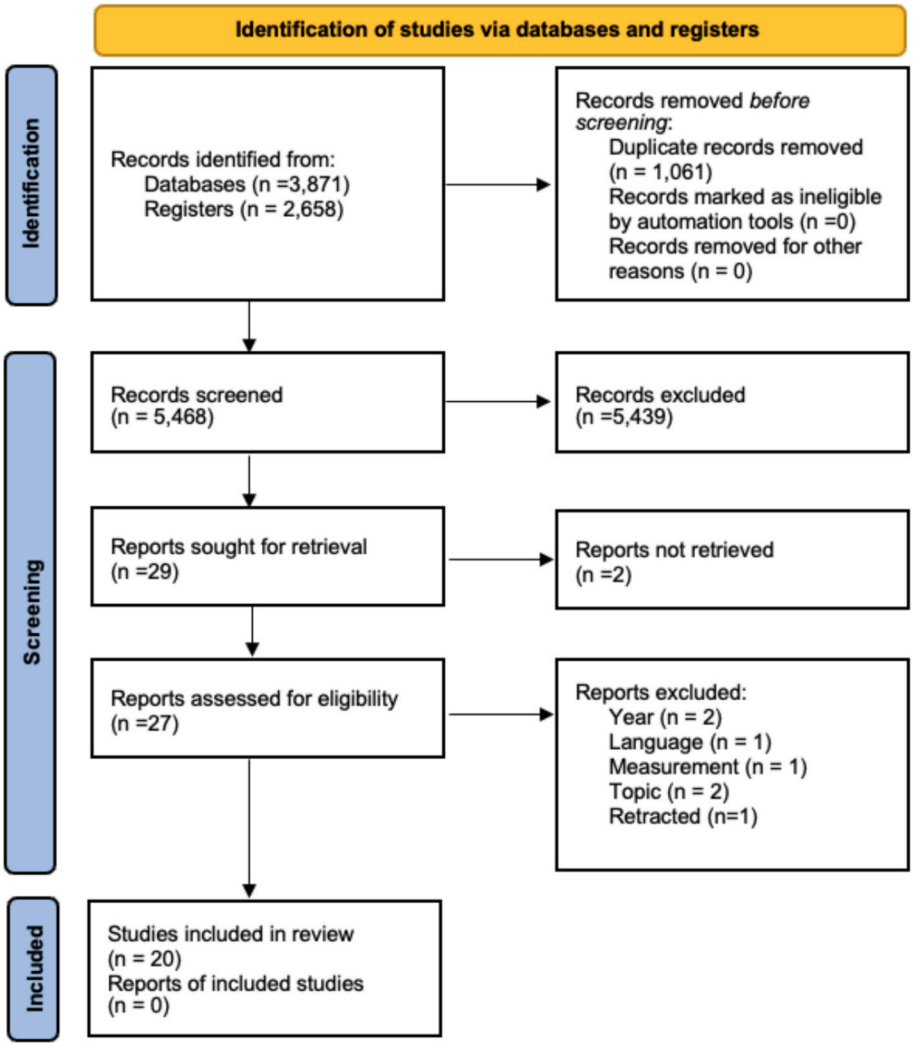

Fig. 1. Flowchart illustrating the study selection process.

control (VAS score 2.31 tramadol and 2.94 naproxen). Another study analyzed lidocaine and counseling in addition to NSAIDs (Fig. 2G), with VAS scores of 2.1, 3.4, and 2.2, respectively [40]. One study analyzed hyoscine butyl bromide (HBB) (Fig. 2F) in addition to the NSAID with VAS scores of 2.91 and 1.97, respectively [14].

Discussion

We found that the use of prophylactic NSAIDs does not provide clinically significant pain relief during IUD insertion for the majority of women undergoing the procedure. Among the 20 studies included in our review, 14 (70 %) showed no significant pain reduction with NSAID use. These findings underscore the need for further research into effective pain control methods and highlight the importance of evidence-based practices in women's reproductive health care.

Alignment and divergences from previous research

Our findings align with previous research indicating that NSAIDs generally lack consistent effectiveness for pain management, emphasizing the need for better therapeutic options. Lidocaine 2 % gel, misoprostol, and most NSAIDs do not significantly reduce pain, although naproxen shows moderate efficacy in multiparous women[23]. In our review, six controlled studies reported a statistically significant reduction in VAS scores—two with ketorolac, one with naproxen, one celecoxib, one indomethacin, one diclofenac. However, the results within each NSAID were inconsistent with other studies showing no meaningful difference. These findings underscore the limited reliability of NSAIDs as a solution.

An earlier systematic review similarly concluded that most NSAIDs were ineffective in reducing pain during IUD insertion, with ketorolac emerging as the most promising agent [34]. The research included in that study was limited to articles published during or before the year 2018. With the recent societal focus on pain during IUD insertion over the last five years, new studies continue to be published investigating the use of pain management strategies. However, the overall lack of consistent efficacy across NSAIDs remains, further highlighting their limitations in addressing pain. It is time to shift focus toward exploring alternative therapies and contemporary research that can offer more reliable and impactful pain relief for patients.

Lack of efficacy of NSAIDs hypothesis

NSAIDs work by inhibiting cyclooxygenase enzymes (COX 1, COX 2) and are directly involved in the production of prostaglandins, which are enzymes that trigger inflammation and contribute to pain. By inhibiting COX enzymes, this inflammatory cascade is reduced. The pain relief from NSAIDs, in inflammatory states, can be impressive, and, in severe inflammatory states can provide pain relief superior to opioids [38]. We argue that inflammation causes direct, physical activation of pain fibers

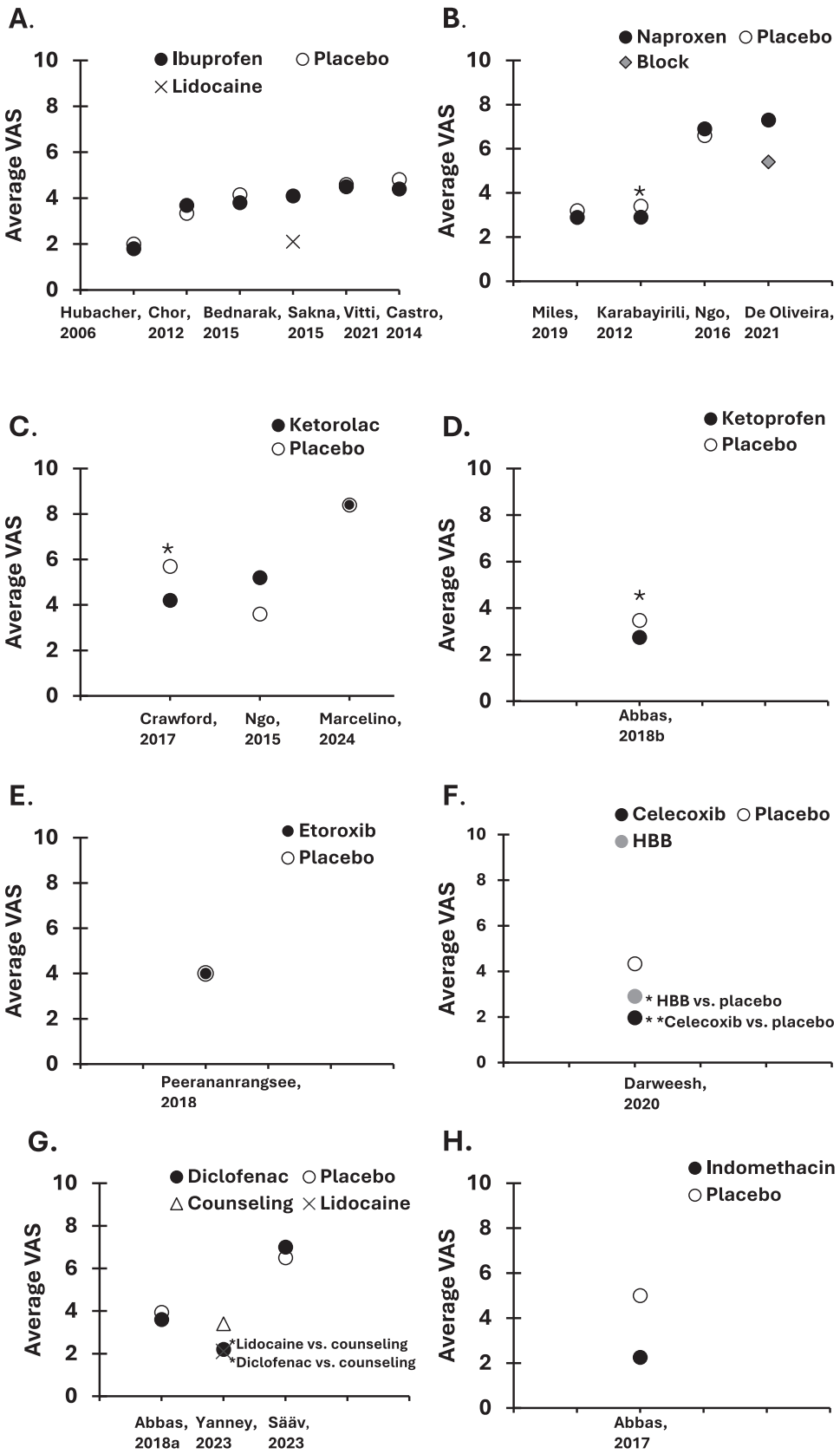

Fig. 2. Comparison of average Visual Analog Scale (VAS) pain scores between prophylactic pharmacologic comparators, counseling and placebo during IUD insertion. Each panel represents a different NSAID studied: A) Ibuprofen, B) Naproxen, C) Ketorolac, D) Ketoprofen, E) Etoroxib, F) Celecoxib, G) Diclofenac and H) Indomethacin. The x-axis indicates the specific study and year of publication. Lower VAS scores indicate less reported pain. Note that in panels C and E, average VAS scores versus placebo were the same, as indicated by the overlapping data points of different sizes. * $p < 0.05$ compared to placebo.

innervating the female cervix. An inhibition of tissue inflammation (via NSAID usage) may lead to a decrease in perceived pain but does not inhibit pain neurons directly. During IUD insertion, clinical guidelines require the tissue to be healthy and without inflammation. Therefore, a decrease in acute pain from prophylactic NSAID use is not expected when compared with a placebo.

Primary dysmenorrhea is a common gynecologic issue characterized by painful cramps in the abdomen in relation to the menstrual cycle. The pathophysiology behind the pelvic pain experienced is an increase in prostaglandin production by uterine smooth muscle [20]. NSAIDs are a well-tolerated and highly accepted treatment option for primary dysmenorrhea [25]. The efficacious results seen are due to the decreased production of prostaglandins, decreasing overall inflammation and decreasing uterine pressure. In contrast, IUD insertion is performed on non-inflamed tissue, as discussed above.

Another example of the clinical use of NSAIDs is for surgical pain management [39]. Post-operatively, NSAIDs are often used as a part of a pain control cocktail, with some patients choosing to use NSAIDs alone to relieve discomfort [18]. The positive results produced by NSAIDs in this setting can be postulated to be related to the significant inflammation created by damaged tissue and surgical manipulation. This stands in stark contrast to IUD insertion, where healthy cervical tissue is the target of the medication. Only half of the studies in our systematic review that found NSAIDs to be effective at overall pain relief during IUD insertion reported significant pain relief during tenaculum placement. One found a statistically significant difference in VAS scores during tenaculum placement but reported a lack of clinical significance (Abbas *et al.,* 2018). Therefore, it can be inferred that the inflammation caused by the tenaculum placement was not substantial enough for the anti-inflammatory properties of NSAIDs to be efficacious at this point in the procedure.

Our review expands the clinical question to explore pain relief during and after IUD placement. Pain control 5–30 min after IUD insertion was measured as a secondary outcome in eleven studies. Interestingly, five found clinical and/or statistical significance in women's VAS scores post-procedurally when compared to placebo. This observed effect may be attributed to NSAIDs role as an anti-inflammatory agent. Manipulation and insertion of a foreign body into the cervix creates inflammation in previously healthy tissue. NSAIDs are able to play a role as an anti-inflammatory agent here in line with our hypothesis. Therefore, while NSAIDs do not decrease discomfort during the procedure, they may be efficacious post-procedurally.

NSAIDs play a role in pain-management in both inpatient and outpatient settings. However, this role is largely an indirect one through their anti-inflammatory properties and not through the modulation of pain. Furthermore, NSAIDs are not without side effects, including GI upset, renal complications, and an increased risk of bleeding. Like any medication, they should be thoughtfully utilized by the practitioner with the goal of providing clinically significant relief. As the evidence stands, it is the authors' opinion that NSAIDs may help reduce post-procedural inflammatory pain but are not effective for managing pain during IUD insertion.

Study limitations

Our review is not without its limitations. The heterogeneity of NSAID types and dosages across the included studies made direct comparisons challenging. Additionally, while all studies used validated pain scales, the specific scales and timing of measurements varied, with some studies using a 100-point VAS system and others using a 10-point system. There is also the impact of publication bias, where studies showing no effect may be less likely to be published, potentially skewing our results.

Current recommendations and practices

Despite NSAIDs being readily available over the counter and perceived as a low-risk method of pain control, their effectiveness in this context appears limited. In August 2024, the CDC released updated recommendations for contraceptive use. The official recommendation encouraged counseling patients on pain associated with the procedure and against routine use of misoprostol, a prostaglandin that can be used to soften the cervix (Curtis *et al.*, 2024). Lidocaine was mentioned as an agent that might reduce patient's pain, but the data are conflicting. While the recognition of the need to address the IUD-pain management gap is promising, healthcare professionals' acceptance of these recommendations varies. The absence of a gold standard leaves pain prevention measures dependent on practitioner training and preferences [13].

The importance of patient perception of pain

A common rebuttal regarding the intensity of pain during the procedure is that it is often less severe than patients anticipate. However, a secondary analysis of the Contraceptive CHOICE project showed that over 1,000 women predicted a VAS score of 5.0, and the average level of pain experienced was 5.0 [16]. Therefore, while the perception of pain is individualized, the data indicates that the average woman undergoing the procedure will experience a level of pain like that reported by patient's post-operative laparotomy or knee surgery [21].

Multiple factors influence the pain experienced during a procedure, and parity is a well-established contributor to patient pain perception. Nulliparous women and patients without a history of vaginal delivery report tend to experience greater procedural pain (Garcia et al., 2023). In contrast, multiparous women who have delivered vaginally may have increased cervical compliance and a more distensible uterine canal, potentially contributing to a lower pain perception during insertion.

Other factors that may affect pain during IUD insertion include cervical anatomy, uterine position and the phase of the menstrual cycle (Gerkowicz *et al.,* 2019). Baseline anxiety levels, and individual pain threshold may also play a role [4]. In some cases, inadequate patient preparation or insufficient explanation of the steps involved can exacerbate discomfort by heightening anxiety and perceived pain.

Need for Improvement

The lack of efficacious alternatives and clear guidelines lead healthcare providers to rely on NSAIDs as a default option to address the pain management gap during IUD insertion. However, our results challenge this practice and highlight a gap between current practice and evidence-based medicine. Future research should be targeted towards finding new solutions, not only increasing the number of options available for women but improving the effectiveness. With women taking to social media sharing their stories and signing petitions for better pain control for IUD insertions [36], it is long overdue that they are provided with better options.

Credit authorship contribution statement

Isabella Martingano: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Emma Lakey:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **David Raskin:** Writing – review & editing, Writing – original draft, Conceptualization. **Kevin Rowland:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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