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Does Prophylacitc Medication Reduce Intrauterin Device (IUD) Insertion Pain in Women of Childbearing Age?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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Abstract

Objective: The objective of this selective EBM review is to determine whether or not prophylactic medication reduces intrauterine device (IUD) insertion pain in women of childbearing age.

Study Design: Review of 3 English language trials: a randomized controlled trial, double-blinded randomized control trial, and a double-blinded randomized placebo controlled trial.

Data Sources: A randomized controlled trial, double-blinded randomized control trial, and a double-blinded randomized placebo controlled trial comparing the prophylactic medications: lidocaine and mistoprostol or placebo group. All articles were found using Medline, PubMed, and OVID.

Outcomes Measured: Reduction of pain with IUD insertion was compared between mistoprostol or lidocaine for the prophylactic treatment of IUD pain insertion via visual analog scale (VAS) by patient self-report; a 10-point pain scale was used to assess pain during IUD insertion; 100-mm visual analog scale (VAS) at several time points rating their pain during the procedure. Secondary outcomes measured included: provider "ease of placement", side effects and IUD retention after 1 month.

Results: One randomized control trial, one double-blinded randomized control trial, and one double-blinded randomized placebo controlled trial were included in this review. None of the prophylactic medications were shown to reduce intrauterine device (IUD) insertion pain in women of childbearing age.

Conclusions: The results of the three randomized controlled trials did not demonstrate that prophylactic medication using mistoprostol, endocervical lidocaine, or lidocaine paracervical block reduce pain with insertion of intrauterine devices (IUDs). Thus far all methods used to try to treat IUD insertion pain have not shown significant improvement in patient pain scores. Currently there are no recommendations for best practice to relieve pain associated with IUD insertion, but ibuprofen, mistoprostol, & lidocaine are being utilized at this time, but have not proven effective. IUD's are one of the most effective, safe, and cheapest forms of long-term birth control. IUD's are underutilized in the U.S compared to Europe, which has been credited to the discomfort experienced during IUD placement. The hope is that with improved patient satisfaction and decreased pain with IUD insertion that this form of birth control will be utilized more.

Key Words: IUD, insertion pain, childbearing age, nulliparous, functionally nulliparous, multiparous

INTRODUCTION

The intrauterine device (IUD) is a highly effective contraceptive method. In the overview from Uptodate by Gillian et al[1] Modern IUDs are made of plastic and release either copper or a progestin to enhance the contraceptive action of the device.[1] Several terms are used to describe intrauterine contraception, such as: intrauterine contraceptive (IUC), intrauterine progestin-containing device referred to often as intrauterine system (IUS) and intrauterine devices as (IUD). While the IUD offers safe and highly effective contraception, IUDs are underutilized in the United States. IUDs are considered "top tier contraception" due to their efficacy rivaling that of implants and sterilization and minimal user effort is warranted.[1] Intrauterine devices are highly effective, private, long acting, and rapidly reversible, with few side effects. Furthermore, IUDs are safe for most women, including teens and nulliparous women. IUDs also provide means of contraceptive while avoiding exogenous estrogen. Although several factors contribute to the low prevalence of IUD use in the United States, some women may avoid obtaining an IUD due to fear of pain during insertion.[2]

Although there are many forms of birth control on the market today, the efficacy and convenience offered by IUDs surpass most other forms of birth control for women in childbearing ages.[2]

The average cost for an IUD in the United States is $500.00-$1000.00.[5] It is estimated that annual medical expenses for unintended pregnancies is approximately 4.6 billion dollars in the United States.[1] According to Planned Parenthood Federation of America 6 out of every 100 American women use an IUD as form of birth control.[5] It has been estimated that 77% of women in reproductive years use contraceptive; however 49% of the pregnancies in 2006 were unintended.[1]

Gillain et al[1] provides rationale that is believed to explain the mechanism of action of IUDs which has postulated that several factors are involved.[1] IUDs function by preventing fertilization, but do not act as abortifacients (defined as interruption of an implanted pregnancy).[1] When the uterus is exposed to a foreign body, a sterile inflammatory reaction occurs, which is toxic to sperm and ova and impairs implantation.[1] The production of cytotoxic peptides and activation of enzymes lead to inhibition of sperm motility, reduced sperm capacitation and survival, and sperm phagocytosis.[1] Gillain provides supportive evidence by three different means. First, sensitive assays for HCG (human chorionic gonadotropin) in IUD users did not detect transient "chemical" pregnancies. Second, tubal flushing studies did not find sperm or fertilized ova in the fallopian tubes of IUD users, but commonly found them in noncontraceptors. Lastly, IUD users have lower rates of both intrauterine and tubal pregnancy than women not using contraception.

Gillian et al[1] introduces the 3 categories of IUDs currently available in the United States: the copper T380A (commercial name ParaGard) and two levonorgestrel-releasing IUDs (commercial names Mirena and Skyla). There are additional IUDs available worldwide.

Gillain et al[1] Lists contraindications for IUDs according to UpToDate are as follows: severe uterine distortion, active pelvic infection, known or suspected pregnancy, Wilson's disease or copper allergy, unexplained abnormal uterine bleeding, and breast cancer for levonorgestrel-releasing IUDs.

Thus far all prophylactic medications used to try to treat IUD insertion pain have not shown statistically significant improvement in patient pain scores. Currently there are no recommendations for best medication prophylaxis practice to relieve pain associated with IUD

insertion, but ibuprofen, mistoprostol, & lidocaine are being utilized at this time, but again have not been proven effective.[2]

IUD's are one of the most effective, safe, and cheapest forms of long-term birth control and are surpassed only by permanent sterilization in regards to effectiveness at preventing pregnancy.[5] IUD's are underutilized in the U.S compared to Europe, which has been credited to the discomfort experienced during IUD placement. The hope is that with improved patient satisfaction and decreased pain with IUD insertion that this form of birth control will be utilized more.[2]

OBJECTIVE

The objective of this selective EBM review is to determine whether or not prophylactic medication reduces IUD insertion pain in women of childbearing age.

METHODS

A specific criterion was utilized for the selection of the three trials used in this paper. Criteria for population included multiparous women, nulliparous women, and women of childbearing age, which is defined as women 18-45 years of age.[2,3,4] The interventions used were paracervical block with 1% lidocaine, intracervical gel with 2% lidocaine, and mistoprostol 400 mcg applied to the buccal mucosa.[2,3,4] Outcomes measured included the efficacy and tolerability of mistoprostol or lidocaine for the prophylactic treatment of IUD insertion pain as well as secondary outcomes measured including: provider "ease of placement", side effects and IUD retention after 1 month.

The study by Mody's et al[2] was a randomized controlled trial. The 50 study participants were all women seeking an IUD at the Obstetrics and Gynecology practice of the Northwestern Medical Faculty Foundation. The women were randomized into two groups, either the treatment

group receiving 10mL of a 1% lidocaine paracervical block prior to insertion of the IUD & 2mL of 1% lidocaine at tenaculum site or the control group receiving no local anesthetic medication. There was a standardized 3-min waiting period between the administration of the paracervical block and the insertion of the IUD. The no-treatment group had the insertion of the IUD without local anesthetic. The primary end point was pain with IUD insertion. Women in the study marked their pain on a 100-mm visual analogue scale (VAS) (0 mm= no pain, 100 mm= worst pain possible) at various points of the procedure: speculum insertion, tenaculum placement, paracervical block administration, IUD insertion and 5 min post procedure.[2]

The study by Edelman et al[4] was a randomized, double-blind, placebo controlled trial consisting of 40 nulliparous, reproductive-aged women desiring and IUD for contraception. Participants of the study were randomized to receive either 400 mcg of mistoprostol or placebo buccally 90 minutes prior to their appointment time. The IUD insertion was performed in standardized fashion using local anesthesia was placed at the tenaculum site (benzocaine spray or 1-2 mL of 1% lidocaine injected). Any prophylactic analgesics or additional cervical analgesia was documented. Patient's rated their pain using a 100-mm VAS (0= none, 100mm=worst imaginable pain) at several points. Any side effects experienced by patients were recorded prior to IUD insertion.[4]

The study by McNicholas et al[3] was a double- blind, randomized control trial that involved 200 women ages 18-45 years who were approached at the Contraceptive CHOICE Project, which is a perspective cohort study. Participants were randomly assigned to recieve 0.5mL of 2% lidocaine gel that was inserted via a 20G angiocatheter into the endocervical canal versus a water-based lubricant.[3] Patient's were given a 10-point visual analog scale (VAS) and then asked to indicate their current pain level and anticipated pain level with insertion. Participants in the

study were asked to rate their pain immediately following tenaculum placement and immediately following device insertion using the same 10-point VAS. All patients received ibuprofen approximately 10 minutes prior to their procedure to minimize post procedure cramping.[3]

Key words used in the literature search were: "IUD", "insertion pain", "child-bearing age", "nulliparous", "functionally nulliparous", and "multiparous". All articles were published in peer-reviewed journals and written in the English language. Literature searches were conducted via Medline, Pubmed, and OVID. Articles were selected based on their relevance and on the importance of outcomes that are important to patients (POEMs). Studies included in the search were randomized control trials, double blind, placebo-controlled studies, those that were performed/published after 1996, and women between the ages of 18-45 years. Exclusion criteria consisted of those that were performed/published before 1996, and those whose participants were outside of the age range 18-45 years. Statistics reported in these studies included standard deviations, p-values, mean, median, baseline pain scores, pain score by parity, and VAS scores.

Table 1- Demographics & Characteristics of Included Studies

STUDY	TYPE	# PTS	AGE	INCLUSION CRITERIA	EXCLUSION CRITERIA	W/D	INTERVENTIONS
Edelman[4], 2011.	Randomized, double-blind, placebo-controlled trial	40	18-45 yrs	Nulliparous women aged 18-45 years requesting an IUD for contraception were recruited. Demographics form completed prior to IUD iinsertion.	Subjects were ineligible if they had: a prior pregnancy greater than 20 wks of duration; if they were pregnant within 6 wks of study entry; had a prior attempted or successful IUD insertion; hx of cervical procedures such as: cone biopsy, loop electrosurgical excision procedure, or cryotherapy. Also ineligible if considered a category 3 or 4 precaution for an IUD according to the World Heath Organization Medical Eligibility Criteria.	5	- 400 mcg of buccal misoprostol 90 minutes prior to IUD insertion - Use of either the levonorgestrel-releasing or copper T380A IUD
McNicholas[3], 2012.	Randomized, double-blind control trial	200	18-45 yrs	Women age 18-45 yrs presenting to the Contraceptive CHOICE Project	Failed IUD insertion after randomization. Lack of interest.	1	0.5mL of 2% lidocaine gel was inserted via 20G

				were approached for participation. Ability to give written consent in English; willingness to be randomized & complete study questionnaires; no contraindication to or hx of allergic rxn to lidocaine.			angiocatheter into the endocervical canal
Mody[2], 2012.	Randomized Controlled Trial	60	Mean age = 32 yrs	Women seeking an IUD at the Obstetrics and Gynecology practice of Northwestern Medical Faculty Foundation.	Excluded if: ineligible for an IUD by accepted criteria at the institution or had contraindications to the study medication (such as a lidocaine allergy); taken pain medications within 6 hrs of the procedure or mistoprostol with 24 hrs of the procedure; copper allergy, current cervicitis,levonorgestrel allergy,lidocaine allergy, PID within 3 mos, pregnancy within 6 wks, prior IUD insertion or a prior IUD insertion attempt, uterine anomaly or distortion of the uterine cavity.	50	Women received 10 mL of a 1% lidocaine paracervical block & 2 mL of 1% lidocaine at tenaculum site.

OUTCOMES MEASURED

Outcomes measured were those of patient-oriented evidence that matters (POEMs). In the Mody study et al[2] pain during IUD insertion was self-reported via a100-mm visual analog scale (VAS) at several time points rating their pain during the procedure. The scale was graded 0 (no pain) to 100 (worst pain possible) and subjects marked their pain at five points during the procedure.[2]

In the Edelman study et al[4] patient's rated their pain using a 100-mm visual analog scale (VAS; anchors: 0= none, 100-mm= worst imaginable) at several different time points. Additionally, any side effect experienced by the patient following the study drug dosing was collected immediately prior to inserting the IUD. Providers who inserted the IUDs also rated their assessment of ease of IUD insertion with 0= easy to 100 mm= extremely difficult.[4]

In the McNicholas study et al[3] a 10-point pain scale was used to assess pain during IUD insertion. Patients were asked to indicate their pain level before IUD insertion and their

anticipated pain level with insertion. Patients were asked to then rate their pain immediately following tenaculum placement and immediately following device insertion using the same 10-point VAS pain scale.[3]

RESULTS

The randomized control trial and double-blinded randomized control trial included in this review investigate the use of lidocaine on perceived patient pain during intrauterine device (IUD) insertion.[2,3] The double-blinded randomized placebo controlled trial surveyed the effects of mistoprostol prior to intrauterine device (IUD) placement that was also included in this review.[3] None of the prophylactic medications were shown to reduce intrauterine device (IUD) insertion pain in women of childbearing age.

The study by Edelman et al[4] of 40 randomized women, 35 completed the study. All participants successfully received their IUD except for one who experienced a vasovagal reaction with tenaculum placement and then subsequently declined IUD placement.[4] Three of the subjects in the placebo group required cervical dilation, and a paracervical block was placed in two of these subjects. In this study there was no significant difference seen in the reduction of IUD insertion pain outcomes with IUD insertion [mistoprostol mean 65mm (SD 21), placebo 55mm (21), p=0.83].[4] The mistoprostol group reported more pain with speculum insertion [mistoprostol mean 17 mm (SD 22), placebo 9 mm, p=0.07], but this did not equate to a statistical difference. It was found that subjects who received mistoprostol reported more preinsertion symptoms than the placebo group. The subjects who experienced nausea (mistoprostol 29%, placebo 5%, p=0.05) and cramping (mistoprostol 47%, placebo 16%, p=0.04) were significantly higher in the mistoprostol group. The provider-reported ease of placement was also not significantly different between the two groups [mistoprostol mean 24 mm (SD 19), placebo 29 mm (21), p=0.5].[4] All

36 participants in the trial were successfully contacted at least one month after IUD placement, and all but three (mistoprostol 2, placebo 1), who declined a string check, confirmed IUD retention.[4]

Table 2. Safety of Mistoprostol as a prophylactic medication in the treatment of IUD insertion pain

Study	CER	EER	RRI *(EER-CER/CER)*	ARI (*EER-CER)*	NNH (*1/ARI)*	p-value
Edelman	0.16	0.47	1.94	0.31	4	0.04

The study by McNicholas et al[3] reported that there were no significant differences in the primary outcome of insertional pain between the placebo and lidocaine group of 200 randomized women from August through December of 2011. In this study insertional pain scores reported between parous and nulliparous women were significantly different regardless of intervention. The median pain score reported in the placebo group was 7 (range, 2-10) among nulliparous women and 5 (range, 0-9) among parous women ($p< 0.1$). The median pain score reported in the lidocaine group was 6 (range, 2-10) by nulliparous women and 4 (range, 1-10) by parous women ($p= .01$).[3] In this study it was reported that there was no difference in pain scores between nulliparous and parous women as well as differences among IUD type inserted. Adverse event data was collected in this study for 6 months after the completion of enrollment in this trial. There were 5 expulsions with an overall rate of 2.5%. One perforation and one case of pelvic inflammatory disease were reported with an overall rate of 0.5% in this study.[3]

The study by Mody et al[2] of 50 randomized women reported that there was no statistically significant difference in median pain scores with IUD insertion in the paracervical block group (24 mm) compared to the non-paracervical block group (62 mm). This study did report that there was a statistically significant decrease in pain when local anesthesia was administered to patients at 12'clock prior to tenaculum site placement ($p =.008$). The two groups in this study were similar in age, race, education, and there were rare complications.[2]

Table 3. IUD insertion pain score in women of childbearing age

Study	Intervention pain score	Comparison scores	p value	CI
Edelman et al[4]	Mistoprostol 65 mm (mean score)	Placebo gel 55 mm (mean score)	0.83	95%
McNicholas et al[3]	Lidocaine (median score) 6- Nulliparou 4- Parous	Placebo gel (median score) 7-Nulliparous 5-Parous	.01 (placebo) <.01 (Lidocaine)	95%
Mody et al[2]	Lidocaine 24 mm (median score)	No Medication 62 mm (median score)	.09	95%

DISCUSSION

This literature review investigated whether or not prophylactic medication reduces intrauterine device (IUD) insertion pain in women of childbearing age. The three studies in this paper showed inconclusive evidence to support that prophylactic medication with lidociane or mistoprostol reduces pain with IUD insertion.[2,3,4]

Limitations were present in each study that decreases their legitimacy and application to the clinical question posed in this review. The paramount limitation of this literature review is the limited number of participants in the studies, inadequate randomized control trials evaluated, and scant prophylactic medication therapies applied in the studies.

The Mody study et al[2] had several components that limited its study credibility such as: a limited sample size of 50 women, lack of placebo control group, non-blinded providers, and IUD insertion were performed by practitioners of various experience and education.

The studies by Mody and McNicholas et al[2,3] implemented the use of lidocaine for paracervical block, which is considered an approved usage for this drug and recommended to allow 5-minute intervals between injecting cervical sides when administering.[7] Lidocaine currently is without black-box warnings at this time.[7]

The Edelman study et al[4] utilized prophylactic administration of mistoprostol in intrauterine device insertion which according to Lexicomp et al[8] is used off label for cervical ripening and labor induction. The only label indications for use of misoprostol is prevention on NSAID induced gastric ulcers and medical termination of pregnancy less than or equal to 49 days. Misoprostol has a black box warning due to the abortifacient property of this medication.[8]

CONCLUSIONS

The results of the three trials appraised in this literature review did not globally demonstrate that prophylactic medication using mistoprostol, endocervical lidocaine, or lidocaine paracervical block reduce pain with insertion of intrauterine devices (IUDs). Thus far all methods used to try to treat IUD insertion pain have not shown significant improvement in patient pain scores.[2] Currently there are no recommendations for best practice to relieve pain associated with IUD insertion, but ibuprofen, mistoprostol, & lidocaine are being utilized at this time, but have not proven effective.[2] IUD's are one of the most effective, safe, and cheapest forms of long-term birth control. IUD's are underutilized in the U.S compared to Europe, which has been credited to the discomfort experienced during IUD placement.[2] With future exploration and more trials there is potential for a solution to improve patient satisfaction and decrease pain with IUD insertion, with hopes that this form of birth control will be utilized more. In the future it seems advisable to find alternative methods and or medications to achieve adequate pain relief during IUD insertion since this is deemed to be one of the greatest barriers to their use.

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