This article will be credited by TMA within the scope of CME/CPD.

Efficacy of hyoscine in pain management during hysteroscopy: a systematic review and meta-analysis

Greg J. Marchand[1], Wesam Kurdi[2], Katelyn Sainz[1], Hiba Maarouf[3], Kelly Ware[1,4], Ahmed Taher Masoud[1,5], Alexa King[1], Stacy Ruther[1], Giovanna Brazil[1], Kaitlynne Cieminski[1], Nicolas Calteux[1], Hollie Ulibarri[1], Julia Parise[1], Amanda Arroyo[1], Diana Chen[6], Maria Pierson[6], Rasa Rafie[7], Mohammad Abrar Shareef[8]

[1]Department of Minimally Invasive Surgery, Marchand Institute for Minimally Invasive Surgery, Mesa, AZ, United States of America
[2]Department of Obstetrics and Gynecology, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia
[3]REProVita Fertility Center, Recklinghausen, Germany
[4]International University of Health Sciences School of Medicine, Basseterre, Saint Kitts and Nevis
[5]Fayoum University Faculty of Medicine, Fayoum, Egypt
[6]Midwestern University College of Osteopathic Medicine, Glendale, AZ, United States of America
[7]Rocky Vista University College of Osteopathic Medicine, Parker, CO, United States of America
[8]Department of Internal Medicine, Sebasticook Valley Hospital, Pittsfield, ME, United States of America

Abstract

We conducted a systematic review and meta-analysis of relevant clinical trials from full-text, scientific journal archives to assess the efficacy of hyoscine for the management of pain during in-office hysteroscopy (OH) procedures. Cochrane CENTRAL, ClinicalTrials.Gov, MEDLINE, PubMed, SCOPUS and the Web of Science were searched for all clinical trials that matched our search criteria. A full assessment of bias was made using the Cochrane Group tool-set. The following outcomes were included: visual analogue scale (VAS) score for postoperative pain, postoperative need for analgesia, and procedure time. In the case of homogeneous data, the analysis was performed using a fixed effects system, and the random effects system was used with heterogeneous data. Inclusion criteria included only randomized clinical trials, and interventions that included patients receiving hyoscine-N-Butyl Bromide during OH, regardless of dose or mode of administration, and compared this with placebo. Three clinical trials were included. The actual mean difference (MD) of the VAS pain score showed no significant difference between hyoscine or placebo [MD: -0.28 (-1.08, 0.52), (p=0.49)]. For postoperative analgesia, the overall MD showed no significant difference between hyoscine or placebo [MD: 0.43 (0.16, 1.14), (p=0.09)]. For procedure time, the combined effect estimate failed to show any significant difference between hyoscine and placebo [MD: -0.66 (-2.77, 1.44) (p=0.54)]. Contrary to previously published data, our meta-analysis using the latest available RCTs fails to show hyoscine as being effective in reducing pain or the need for other forms of anesthesia in OH. (J Turk Ger Gynecol Assoc 2022; 23: 51-7)

Keywords: Office hysteroscopy, hyoscine; office surgery, ERAS protocol, ERAS hysteroscopy

Received: 02 April, 2021 **Accepted:** 21 September, 2021

Introduction

Hysteroscopy is considered the most accurate tool in the diagnosis of disorders of the endometrial cavity (1,2). Office hysteroscopy (OH) carries most of the benefits of hysteroscopy performed under general anesthesia in the operating room, but has many other advantages. Thus, in the opinion of many surgeons, OH represents a cornerstone for both diagnosis and treatment of many gynecological conditions, such as submucosal polyps or leiomyoma (3). OH is also of importance in the diagnosis and management of other pathologies, such as recurrent miscarriage and infertility (4). Prior to the advent

Address for Correspondence: *Greg J. Marchand*
e.mail: gm@marchandinstitute.org ORCID: orcid.org/0000-0003-4724-9148

Journal of the Turkish-German Gynecological Association published by Galenos Publishing House.
DOI: 10.4274/jtgga.galenos.2021.2021-0057

of hysteroscopy, the management of intrauterine pathology was based largely on blind curettage of the uterus (5). Blind curettage could provide some important information, but dilatation and curettage (D&C) is limited for the recognition of focal lesions, which can result in a higher proportion of false negative results (5). D&C also requires a higher degree of anesthesia to tolerate, usually being performed under general or spinal anesthesia (5).

Conventional hysteroscopy, performed for diagnostic purposes, employs specula and may require dilation of the cervix (6). In recent years, the use of cervical dilators has been widely replaced by the introduction of smaller "mini-hysteroscopes," which limit the need for cervical dilation prior to the procedure (7). Despite these advances, intraoperative pain remains a major problem limiting the use of hysteroscopy. It can be challenging for the hysteroscopist to perform a hysteroscopy without the use of an anesthetic (8). Introducing even a small hysteroscope into the uterine cavity through the cervical canal may produce severe discomfort and pain, especially in sensitive patients (9). The use of sedation, local anesthesia, and cervical ripening agents, such as vaginal misoprostol, have all been utilized in attempts to reduce this pain (10). Hyoscine-n-butyl bromide (HBB) is a peripheral anticholinergic and does not readily cross the blood-brain barrier (11,12). Its mechanism of action is to block the nerve impulses that originate in the parasympathetic ganglia within the abdomen (13). Through blocking the muscarinic receptor, it exerts a spasmolytic action on muscle tissues of the biliary, gastrointestinal and genital organs, with smooth muscles being most affected (13,14). It has been hypothesized that the mechanism of pain reduction by HBB might be the blockage of these impulses, which may prevent uterine spasms (14).

There are few randomized controlled trials (RCTs) investigating the effectiveness of different premedications administered for control of pain during and after OH. A previous meta-analysis failed to find any evidence of the benefit of administration of opioids during OH, when administered orally (15). Another study, this time an RCT, showed that certain anti-inflammatory medications were effective in reducing pain associated with OH, but this was complicated by the addition of a second variable as the study only considered the use of smaller (5 mm) hysteroscopes (16).

Given the scarcity of good evidence, the aim was to conduct a meta-analysis to assess the effect of HBB in women undergoing OH for reducing postoperative pain assessed using the conventional visual analogue pain scale (VAS) score and also the need for postoperative analgesia. It was planned to use the latest available RCTs to produce the highest quality data possible.

Methods

This meta-analysis conformed strictly to the "Preferred Reporting Items for Systematic Reviews and Meta-analyses" (PRISMA) (17) guidelines. In addition, every stage of the study was performed in accordance with the recommendations of the "Cochrane Handbook for Systematic Reviews of Interventions" (18).

Literature search

Six databases were investigated for studies providing evidence about the topic. These were: Web of Science, SCOPUS, Cochrane CENTRAL, ClinicalTrials.Gov, MEDLINE, and PubMed, from inception until January 2021. We followed this search strategy with no restriction on time or languages; [(HBB OR Hyoscine OR Scopolamine OR Buscopan) AND hysteroscopy].

Eligibility criteria

Studies were included according to five criteria: 1) Patient population: patients receiving outpatient hysteroscopy; 2) Intervention: HBB administration regardless of the dose and the mode of administration; 3) Comparator: placebo; 4) Primary outcomes: recorded VAS score during and after OH, as well as usage of postoperative analgesia, while a secondary outcome was the total duration of the procedure (in minutes); and 5) Included study types: only RCTs. Exclusion criteria included: 1) any non-randomized controlled clinical trials; 2) studies that did not report data for the selected outcomes; 3) trials without the full text available; and 4) trials with only a single arm.

Screening process

After results were retrieved from the search, the data was entered into dedicated meta-analysis software (Endnote X8.0.1 Build 1044), where duplicates were removed automatically. The first step was to screen the title and abstract, and this was followed by screening of the entire text. Two different researchers screened each article before final inclusion. Any disagreement was resolved by consensus with a third researcher.

Extraction and analysis of data

Following the completion of screening, data was extracted from the selected studies. The selected data was classified into three categories. The first category was demographic data of the patients, including age, weight, height, body mass index (BMI), number of previous cesarean sections, and history of pelvic pain. The second data category was the indication for the performed hysteroscopy. The final data category included the postoperative VAS score, whether or not postoperative analgesia was required, and the elapsed procedure time in

minutes. In addition, data required for full assessment of risk of bias (ROB), according to Cochrane's ROB tools, was also extracted (19).

Analysis of data

Review Manager Software (version RevMan 5.4.1) was used to perform the analysis using the inverse variance method. The mean difference (MD) and standard deviations were used to express continuous data with a relative 95% confidence interval (CI). Dichotomous outcomes were expressed using percentage and total, relative to a 95% CI. Inconsistency between the studies was assessed by both the I-square test (I2), and the chi-square test to give a p-value. Any outcomes with $I^2 > 50\%$ and $p < 0.1$ were considered to be heterogeneous, while outcomes with $I^2 < 50\%$ and $p > 0.1$ were considered homogeneous, as recommended by the Cochrane Handbook (20). Data that was homogenous was analyzed using a fixed-effects model, while heterogeneous data was analyzed using a random-effects model.

Quality assessment

Quality assessment was performed in accordance with the "Grading of Recommendations, Assessment, Development, and Evaluations" (GRADE) guidelines. The analysis only included RCTs and all other observational evidence was excluded. Cochrane's ROB tool was used to assess ROB for the included RCTs (21). The characteristics assessed by this ROB tool include: 1) proper randomization; 2) proper blinding of the study participants into each group; 3) proper blinding of participants only (single-blinding), blinding of both personnel and participants (double-blinding), or the absence of any blinding; 4) bias attributed to attrition; 5) bias attributed to selection; 6) proper blinding of the outcome assessor (i.e. whether blinded or not); and 7) other biases. The total ROB for these studies was assessed and graded as good.

Results

Summary of included studies

A PRISMA flow diagram of the study literature search is shown in Figure 1. This study included an analysis of 291 patients from three studies (16,22,23). Of these 291, 144 (49.5%) received hyoscine, and 147 (50.5%) were in the placebo group. The mean age of the participant in the treatment group was 38.1±8.7 years, and that of the control group was 39.3±7.8 years. The mean BMI of patients receiving hyoscine was 26.9±6, while that of the control group was 27±5. Table 1 shows a detailed summary of the included participants from each included study. Additionally, Table 2 illustrates the indications for OH.

Results of risk of bias assessment

The ROB analysis indicated an overall low ROB according to Cochrane's tool (24). All studies were judged to be at low ROB from poor randomization. Two of the studies (16,22) reported adequate allocation concealment, and therefore they were considered a low ROB. One study (23) did not report enough data about allocation concealment thus was considered to be an unclear ROB. All of the included studies were double-blinded and so were judged to be free from participant and personnel blinding bias. Two studies (16,22) were judged to be at a low ROB from failing to blind the outcome assessment, except Souza et al. (23) which did not report sufficient details and so was considered an unclear ROB. Again, two studies (16,22) were judged to be at low risk of attrition bias, except Souza et al. (23) which was found to be at high ROB, secondary to a lack of reporting sufficient details about the described outcomes. All of the remaining domains of the Cochrane tool were at a low ROB. A summarized illustration (Figure 2) shows the bias assessment results for the three included studies.

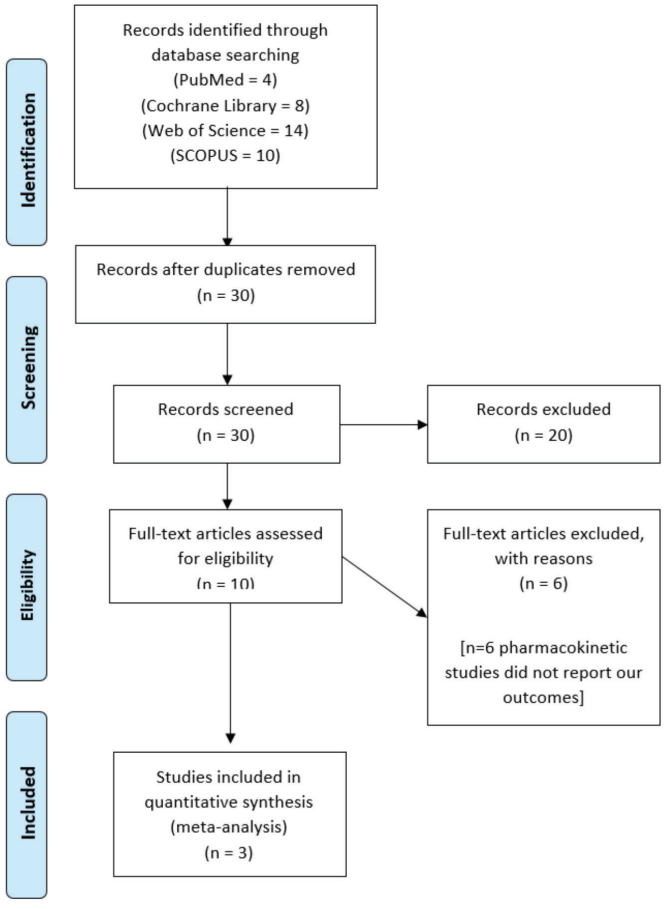

Figure 1. PRISMA flow diagram of the literature search
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

Analysis of all outcomes

1. Postoperative VAS score

All studies (291 participants) reported the postoperative VAS score for pain. Of these, 144 patients were in the hyoscine group, and 147 patients were in the control group. The overall MD of the VAS score showed that there was no significant difference between the hyoscine or placebo group [MD: -0.28 (-1.08, 0.52), (p=0.49)]. Pooled analysis was homogeneous (p=0.24); I^2=29%, as shown in Figure 3.

2. Need for postoperative analgesia

The need for postoperative analgesia was reported by all studies. The overall MD favored neither the hyoscine nor the placebo [MD: 0.43 (0.16, 1.14), (p=0.09)]. Pooled analysis was

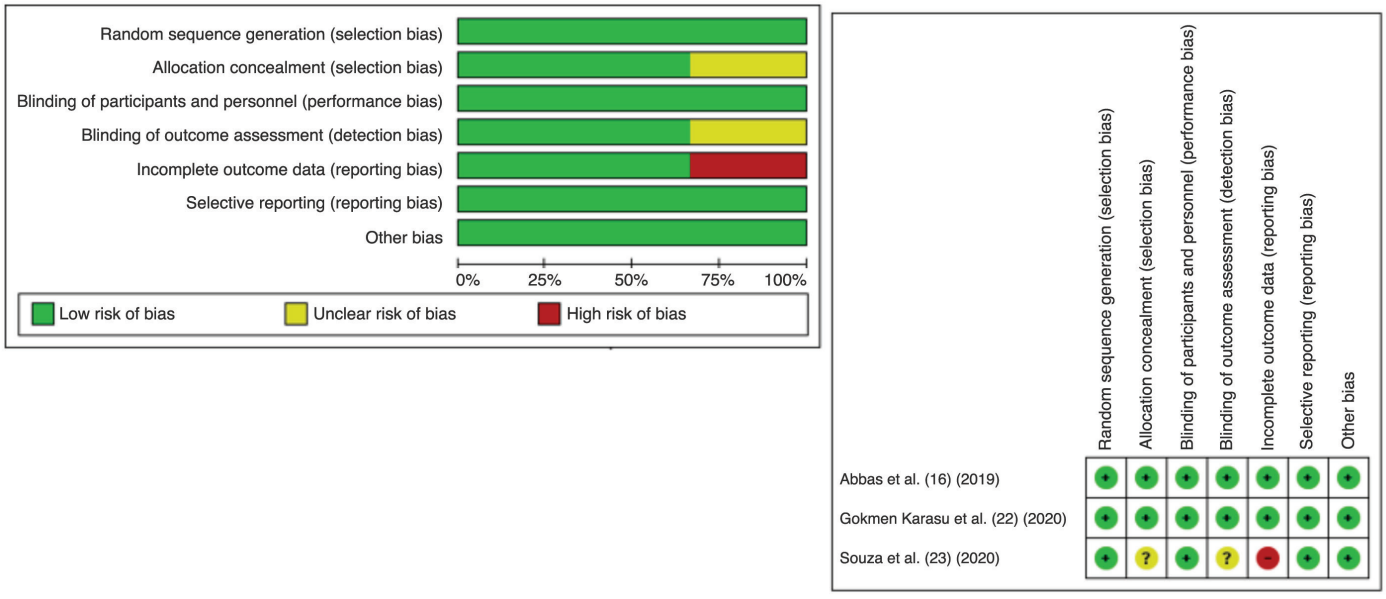

Figure 2. Summary and graph of risk of bias of the included studies

Table 1. Demographic and clinical characteristics of study participants in the groups receiving hyoscine and those receiving placebo

Study ID	Age, years (mean ± SD)		BMI kg/m² (mean ± SD)		C-section, n (%)/(mean ± SD)		Chronic pelvic pain, n (%)		Weight kg, (mean ± SD)		Height cm, (mean ± SD)	
	HBB	PL	HBB	PL	HBB	PL	HBB	PL	HBB	PL	HBB	PL
Abbas et al. (16)	29.81±6.41	30.65±6.91	24.68±2.12	23.95±2.41	9 (20.9)	10 (23.3)	6 (14)	5 (11.6)	NR	NR	NR	NR
Gokmen Karasu et al. (22)	36.2±7.1	37.1±6.3	26.1±5.7	25.9±5.7	5 (16.5)	5 (16.50)	NR	NR	69.3±13	66.1±14.1	163.4± 6.7	159.7±4.9
Souza et al. (23)	48.4±12.6	50.3±10.4	30.1±10.4	31.2±6.9	0.6±0.9	0.6±0.8	15 (6.90)	14 (6.4)	75.6±16.6	79.3±17.9	159±6	160±8

Data are reported as mean ± SD or n (%).
NR: Not reported, HBB: Hyoscine-N-butyl bromide, PL: Placebo, BMI: Body-mass index, SD: Standard deviation

Table 2. Indications of office hysteroscopy for patients in each of the three included studies, stratified by those receiving hyoscine or those receiving placebo

Study ID	Abnormal uterine bleeding		Recurrent miscarriage		Infertility	
	HBB	PL	HBB	PL	HBB	PL
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
Abbas et al. (16)	6 (14)	9 (20.9)	4 (9.3)	6 (14)	33 (76.7)	28 (65.1)
Gokmen Karasu et al. (22)	NR	NR	NR	NR	NR	NR
Souza et al. (23)	50 (23)	52 (24)	2 (0.9)	2 (0.9)	10 (4.6)	5 (2.4)

Data are reported as frequency (%).
NR: Not reported, HBB: Hyoscine-N-butyl bromide, PL: Placebo

heterogeneous (p=0.01; I^2=76%) as shown in Figure 4A. We solved the heterogeneity by the exclusion of Souza et al. (23) (p=0.69; I^2=0%). The pooled analysis after exclusion of Souza et al. (23) significantly favored the hyoscine group [MD: 0.26 (0.16, 0.43) (p<0.01)]. Figure 4B shows the recalculated results of the analysis after one study was excluded (23).

3. Procedure time

Two studies (16,22) reported the procedure time. The combined effect estimate did not show any statistically significant difference between hyoscine and placebo [MD: -0.66 (-2.77, 1.44) (p=0.54)]. Pooled analysis was heterogeneous (p=0.01; I^2=83%) as shown in Figure 5. Heterogeneity could not be solved by the exclusion of one study.

Discussion

Previously published clinical trials reported contradictory results, Abbas et al. (16) and Gokmen Karasu et al. (22) showed that hyoscine significantly reduced postoperative

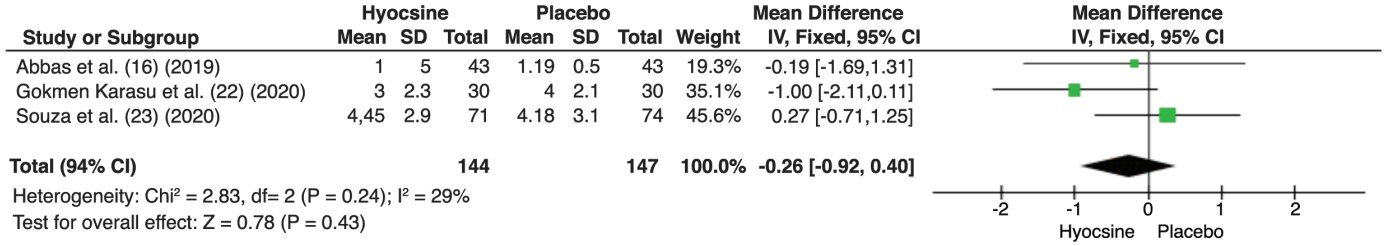

Figure 3. Forest plot for the analysis of VAS score for pain
SD: Standard deviation, CI: Confidence interval, VAS: Visual analogue scale

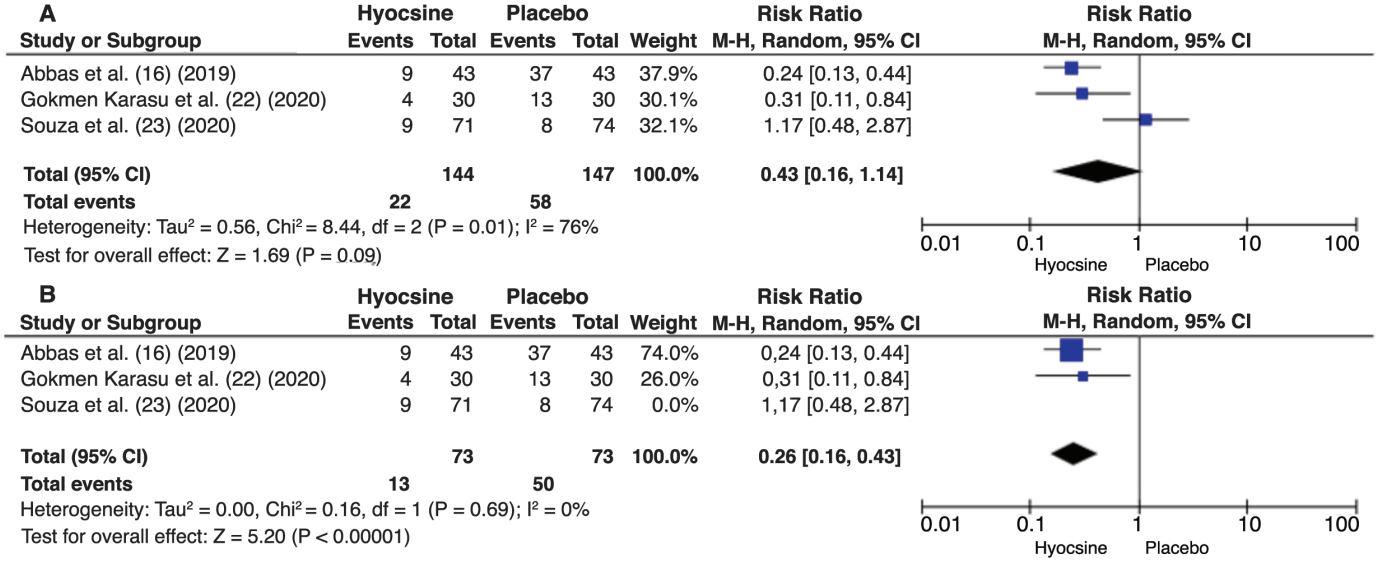

Figure 4. (a) Forest plot for the analysis of the need for postoperative analgesia, and (b) forest plot after removing Souza et al. (23) to solve for heterogeneity
CI: Confidence interval

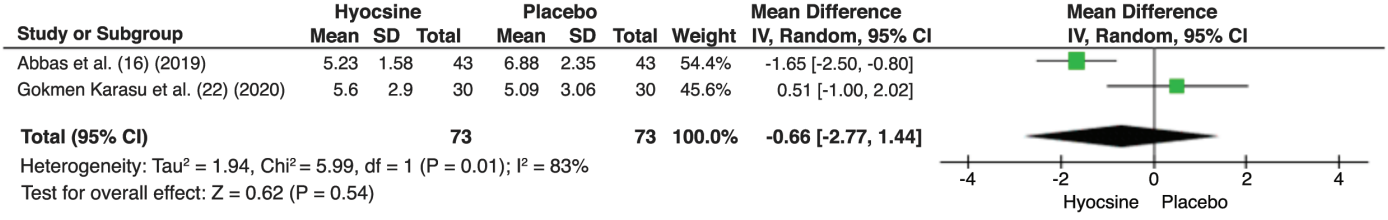

Figure 5. Forest plot for the analysis of procedure time
SD: Standard deviation, CI: Confidence interval

analgesia in patients undergoing hysteroscopy, while Souza et al. (23) reported no significant difference. This could be because Souza et al. (23) used half the dose (10 mg) compared with the studies of Abbas et al. (16) and Gokmen Karasu et al. (22), which both used 20 mg in terms of procedure time, Abbas et al. (16) found that hyoscine reduced the procedure time by 1.65 minutes while Gokmen Karasu et al. (22) showed that the procedure time was similar in both arms. As for the pain score reported during OH, these clinical trials reported no significant efficacy of hyoscine in reducing pain (16,22,23). Our meta-analysis failed to find any significant difference between hyoscine and placebo as far as procedure time, VAS pain score, and the need for postoperative analgesia, when all three studies were included.

As a common procedure carried out in many outpatient clinics, OH has a major role in diagnosing many gynecological abnormalities such as abnormal uterine bleeding, congenital anomalies of the uterus, removal of intrauterine devices and endometrial polyps, and visualization of intrauterine adhesions (1,25,26). The procedure is safe, quick, cheap, and does not usually require general or regional anesthesia (27,28). OH has few side effects reported by patients, of which pain is the most common (29,30). The prevailing explanation as to why pain might arise from the procedure is that cervical dilatation and uterine distension cause more pain to the patient than normal vaginal manipulation (31).

It has been suggested that hyoscine reduces pain by inducing cervical ripening and secreting pro-inflammatory cytokines and prostaglandins (32). It has also been tried as an analgesic for pain management after several gynecological procedures, with varying results. Jareethum et al. (11) investigated the efficacy of hyoscine in women undergoing saline infusion sonography and found no significant effect of the drug on pain reduction. Moro et al. (33) administered hyoscine to patients with infertility undergoing hysterosalpingo-contrast sonography and also found no significant effect. Although many pharmacological and non-pharmacological interventions have been used to reduce pain associated with hysteroscopy (34,35), hyoscine is still used uncommonly and with varying efficacy.

Duan et al. (36) showed that carboprost methylate suppository given vaginally before hysteroscopy is an effective method for reducing pain prior to OH. Tagliaferri et al. (37) showed that saline solution as well as carbon dioxide can be used as acceptable media for performing OH, although it was reported that carbon dioxide had more advantages in reduction of pain perception. Compared with oral diclofenac potassium, hyoscine is not as effective and may have more adverse effects. Abbas et al. (16) found that oral diclofenac potassium administration before diagnostic hysteroscopy reduced pain with subsequent easier and shorter procedure duration. A recent meta-analysis revealed that misoprostol may be an effective medication for managing pain associated with the procedure (38).

Major strengths of our analysis include the overall low ROB among the included trials and the homogeneity of data of the outcomes. Only RCTs were included to ensure high-quality evidence according to GRADE. Although all possible RCTs investigating this topic were included, the major limitation of this study was the small sample size and the low number of published clinical trials. Therefore, it is recommended that more trials to combine hyoscine with other medications or at different doses to obtain more robust data should be performed.

Conclusion

In conclusion, based on the limited evidence available from all available RCTs at this point, there is currently no evidence to support the use of hyoscine in OH.

Peer-review: *Externally peer-reviewed.*

Conflict of Interest: *No conflict of interest is declared by the authors.*

Financial Disclosure: *The authors declared that this study received no financial support.*

References

1. Sinha D, Kalathy V, Gupta JK, Clark TJ. The feasibility, success and patient satisfaction associated with outpatient hysteroscopic sterilisation. BJOG 2007; 114: 676-83.
2. Polyzos NP, Zavos A, Valachis A, Dragamestianos C, Blockeel C, Stoop D, et al. Misoprostol prior to hysteroscopy in premenopausal and post-menopausal women. A systematic review and meta-analysis. Hum Reprod Update. 2012; 18: 393-404.
3. Laganà AS, Alonso Pacheco L, Tinelli A, Haimovich S, Carugno J, Ghezzi F, et al. Management of asymptomatic submucous myomas in women of reproductive age: a consensus statement from the Global Congress on Hysteroscopy Scientific Committee. J Minim Invasive Gynecol 2019; 26: 381-3.
4. van Dongen H, De Kroon CD, Jacobi CE, Trimbos JB, Jansen FW. Diagnostic hysteroscopy in abnormal uterine bleeding: A systematic review and meta-analysis. BJOG 2007; 114: 664-75.
5. Campo R, Santangelo F, Gordts S, Di Cesare C, Van Kerrebroeck H, De Angelis MC, et al. Outpatient hysteroscopy. Facts Views Vis Obgyn 2018; 10: 115-22.
6. Lam CJ, Imudia AN. Novel uterine closure technique to prevent intrauterine adhesions. Fertil Steril 2019; 112(Suppl): E433-4.
7. Cicinelli E. Diagnostic minihysteroscopy with vaginoscopic approach: rationale and advantages. J Minim Invasive Gynecol 2005; 12: 396-400.
8. Issat T, Beta J, Nowicka MA, Maciejewski T, Jakimiuk AJ. A randomized, single blind, placebo-controlled trial for the pain reduction during the outpatient hysteroscopy after ketoprofen or intravaginal misoprostol. J Minim Invasive Gynecol 2014; 21: 921-7.
9. Floris S, Piras B, Orrù M, Silvetti E, Tusconi A, Melis F, et al. Efficacy of intravenous tramadol treatment for reducing pain during office diagnostic hysteroscopy. Fertil Steril 2007; 87: 147-51.

10. El-Mazny A, Abou-Salem N. A double-blind randomized controlled trial of vaginal misoprostol for cervical priming before outpatient hysteroscopy. Fertil Steril 2011; 96: 962-5.
11. Jareethum R, Suksompong S, Petyim S, Prechapanich J, Laokirkkiat P, Choavaratana R. Efficacy of mefenamic acid and hyoscine for pain relief during saline infusion sonohysterography in infertile women: a double blind randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2011; 155: 193-8.
12. Hadadian S, Fallahian M. Assessing the efficacy of vaginal hyoscine butyl bromide on cervical ripening prior to intrauterine procedures: A double-blinded clinical trial. Int J Reprod Biomed 2016; 14: 709-12.
13. Sirohiwal D, Dahiya K, De M. Efficacy of hyoscine-N-butyl bromide (Buscopan) suppositories as a cervical spasmolytic agent in labour. Aust New Zeal J Obstet Gynaecol 2005; 45: 128-9.
14. Yakoot M, Salem A, Yousef S, Helmy S. Clinical efficacy of Spasmofen® suppository in the emergency treatment of renal colic: A randomized, double-blind, double-dummy comparative trial. Drug Des Devel Ther 2014; 8: 405-10.
15. Ahmad G, Attarbashi S, O'Flynn H, Watson AJ. Pain relief in office gynaecology: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2011; 155: 3-13.
16. Abbas AM, Elzargha AM, Ahmed AGM, Mohamed II, Altraigey A, Abdelbadee AY. Oral diclofenac potassium versus hyoscine-n-butyl bromide in reducing pain perception during office hysteroscopy: A randomized double-blind placebo-controlled trial. J Minim Invasive Gynecol 2019; 26: 709-16.
17. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009; 6: e1000097.
18. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions: cochrane book series. In: Higgins JPT, Green S, (eds). Chichester, UK: John Wiley & Sons; 2008, pp. 1-649.
19. Higgins JPT, Julian PT. Cochrane Handbook for systematic reviews of interventions version 5.1.0. In: Higgins JPT, Green S, (Eds). [updated March 2011]. The Cochrane Collaboration; 2011.
20. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003; 327: 557-60.
21. Higgins JP, Altman DG. Assessing Risk of Bias in Included Studies. In: Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series. 2008.
22. Gokmen Karasu AF, Aydin S, Ates S, Takmaz T, Comba C. Administration of rectal cytotec versus rectal buscopan before hysteroscopy. Minim Invasive Ther Allied Technol 2022; 31: 94-8.
23. Souza CAB, Genro VK, Tarrasconi DV, Oppermann MLR, Cunha Filho JSL. Diclofenac versus a combination of hyoscine and diclofenac for outpatient hysteroscopy: A placebo controlled randomized clinical trial. Eur J Obstet Gynecol Reprod Biol 2020; 247: 1-5.
24. Higgins J, Altman D. Assessing risk of bias. In: Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series. 2008.
25. National Institute for Health and Care Excellence. Heavy menstrual bleeding: assessment and management. Nice Guidel; 2018.
26. Robinson LL, Cooper NA, Clark TJ. The role of ambulatory hysteroscopy in reproduction. J Fam Plann Reprod Health Care 2013; 39: 127-35.
27. Saridogan E, Tilden D, Sykes D, Davis N, Subramanian D. Cost-analysis comparison of outpatient see-and-treat hysteroscopy service with other hysteroscopy service models. J Minim Invasive Gynecol. 2010; 17: 518-25.
28. Graham A, Datta S. Outpatient hysteroscopy. Obstet Gynecol Reprod Med 2016; 26: 7-11.
29. Critchley HO, Warner P, Lee AJ, Brechin S, Guise J, Graham B. Evaluation of abnormal uterine bleeding: Comparison of three outpatient procedures within cohorts defined by age and menopausal status. Health Technol Assess 2004; 8: iii-iv, 1-139.
30. Jivraj S, Dass M, Panikkar J, Brown V. Outpatient hysteroscopy: an observational study of patient acceptability. Medicina (Kaunas) 2004; 40: 1207-10.
31. Elkins N, Hunt J, Scott KM. Neurogenic pelvic pain. Phys Med Rehabil Clin N Am 2017; 28: 551-69.
32. Timmons B, Akins M, Mahendroo M. Cervical remodeling during pregnancy and parturition. Trends Endocrinol Metab 2010; 21: 353-61.
33. Moro F, Selvaggi L, Sagnella F, Morciano A, Martinez D, Gangale MF, et al. Could antispasmodic drugs reduce pain during hysterosalpingo-contrast sonography (HyCoSy) in infertile patients? A randomized double-blind clinical trial. Ultrasound Obstet Gynecol 2012; 39: 260-5.
34. Amer-Cuenca JJ, Marín-Buck A, Vitale SG, La Rosa VL, Caruso S, Cianci A, et al. Non-pharmacological pain control in outpatient hysteroscopies. Minim Invasive Ther Allied Technol 2020; 29: 10-9.
35. O'Flynn H, Murphy LL, Ahmad G, Watson AJ. Pain relief in outpatient hysteroscopy: A survey of current UK clinical practice. Eur J Obstet Gynecol Reprod Biol 2011; 154: 9-15.
36. Duan H, Hao M, Wang SM, Meng YJ, Wang Y, Yuan R, et al. Clinical multicenter study of carboprost methylate suppository for cervical ripening prior to diagnostic hysteroscopy. Zhonghua Fu Chan Ke Za Zhi 2018; 53: 602-7.
37. Tagliaferri V, Ricciardi L, Ricciardi R, Pinto LR, Lanzone A, Scambia G, et al. Carbon dioxide in office diagnostic hysteroscopy: An open question. A multicenter randomized trial on 1982 procedures. Eur J Obstet Gynecol Reprod Biol 2019; 235: 97-101.
38. Al-Fozan H, Firwana B, Al Kadri H, Hassan S, Tulandi T. Preoperative ripening of the cervix before operative hysteroscopy. Cochrane Database Syst Rev 2015; CD005998.