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REVIEW ARTICLE

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Is pyridoxine effective and safe for post-partum lactation inhibition? A systematic review

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Summary

What is known and objective: It has been suggested that pyridoxine has an antilactogenic effect. Studies of the efficacy of pyridoxine in suppressing lactation have reported conflicting results. The aim of this review was to evaluate the effectiveness and safety of high-dose pyridoxine in post-partum lactation inhibition.

Methods: This systematic review included published trials that compared the efficacy and/or safety of pyridoxine to placebo or to other pharmacological agents for the inhibition of post-partum lactation. We searched PubMed, Embase, ScienceDirect, CINAHL, AMED, the Cochrane library and the clinical trials registry to identify relevant literature. No limit was imposed on the year of publication of the studies, and the review included studies published until 15 January 2016. Two reviewers independently extracted data and assessed the risk of bias.

Results and discussion: Seven studies were included, with a total of 1155 women, of which 471 women received pyridoxine. Three studies were randomized controlled trials, whereas the remaining four studies were non-randomized controlled trials. All of the included studies were relatively small (n=18-482). The studies compared pyridoxine with placebo, bromocriptine and/or stilboestrol. Pyridoxine was given orally, with a total daily dose of 450-600 mg for 5-7 days. Two trials (n=349 participants) indicated that pyridoxine was effective in inhibiting lactation in approximately 95% of the enrolled patients. All other studies failed to demonstrate pyridoxine efficacy through either clinical assessment or prolactin level measurements. Pyridoxine safety was assessed by two trials in which no serious untoward side effects were reported. Overall, the risk of bias for most of the studies was low to moderate.

What is new and conclusion: Current evidence supporting the effectiveness of high-dose pyridoxine in the inhibition of post-partum lactation is inconsistent and insufficient. Larger randomized trials are needed to confirm the efficacy of pyridoxine in post-partum lactation inhibition.

KEYWORDS
breastfeeding, lactation inhibition, lactation suppression, pyridoxine, vitamin B6

1 | WHAT IS KNOWN AND OBJECTIVE

Although the benefits of breastfeeding for mothers and infants are well documented,[1-3] under some conditions, lactation suppression might be indicated for the best interest of the lactating mother and/or the infant. Some of the medical conditions that contraindicate breastfeeding include infants with the metabolic disorder classic galactosemia, mothers who are positive for human T-cell lymphotrophic virus type I or II, and untreated brucellosis, among others.[1,2,4] Furthermore, the lactating mother's use of some types of medications might necessitate avoiding breastfeeding, such as mothers undergoing chemotherapy.[1,2] Lactation inhibition might also be needed following an infant death or miscarriage.[5,6]

When the decision to suppress lactation or not breastfeed an infant is made, the prevention of breast engorgement is essential to avoid associated complications, such as breast pain and mastitis.[5-7] Up to one-third of women who do not breastfeed and use non-pharmacological approaches, such as brassieres, binders, or ice packs, or analgesics to treat symptoms associated with lactation suppression may experience severe breast pain.[8] Several pharmacological agents for lactation inhibition have been studied. Oestrogen preparations given either alone or in combination with androgens have been shown to be effective in 40%-100% of women; however, due to their high rates of rebound lactation and the associated increased risk of thrombosis and pulmonary embolism, the use of these preparations is discouraged.[9] The dopamine agonists (bromocriptine and cabergoline) have also been reported to be effective in inhibiting puerperal lactation.[9,10] However, the use of dopamine agonists is not recommended in the presence of hypertensive disorders of pregnancy, including pre-eclampsia, eclampsia, pregnancy-induced hypertension and post-partum hypertension, or in women with a history of puerperal psychosis.[11,12] Similarly, variable results were reported with other agents, such as clomiphene, prostaglandin E, serotonin antagonists and pyridoxine.[9]

Pyridoxine (ie vitamin B6) has been shown to have an antilactogenic effect.[13] The exact mechanism by which pyridoxine inhibits lactation is not well understood. However, pyridoxine is known to act as a co-enzyme that promotes the conversion of dopa to dopamine. The increase in dopamine formation in hypothalamic neurons and their major dendrites is thought to result in prolactin inhibition and consequent lactation inhibition.[14] Studies of the efficacy of pyridoxine in lactation suppression have reported conflicting results.[14,15]

No systematic review explicitly investigated the efficacy and safety of pyridoxine for post-partum lactation suppression. The objective of this systematic review was to evaluate the effectiveness and safety of pyridoxine in the inhibition of post-partum lactation.

2 | METHODS

2.1 | Selection criteria

All types of published trials that compared the efficacy and/or safety of pyridoxine to placebo or to other pharmacological agents for the inhibition of post-partum lactation were included in this review. However, reviews, letters, conference papers and abstracts were excluded. Studies that evaluated pyridoxine efficacy in women who had already established lactation and trials published in languages other than English were also excluded from the review.

2.2 | Outcome measures

Studies that described any of the following efficacy and/or safety outcomes were evaluated: suppression of lactation, as indicated by clinical assessment, breast pain, engorgement and/or milk secretion (or as described by the trial), prolactin level and adverse events related to pyridoxine. The words "inhibition" and "suppression" of lactation were used interchangeably in this review to refer to the inhibition or suppression of lactation during the early period before lactation is established.

2.3 | Search strategy

We searched PubMed, Embase, ScienceDirect, CINAHL, AMED, the Cochrane library and the clinical trials registry to identify relevant literature. The key search terms that were used to identify relevant studies were "pyridoxine," "vitamin B6," "lactation," "breastfeeding," "breast milk," "inhibition," "suppression," "prevention" and "stop." The search terms were used in various combinations along with truncations (*) and relevant Boolean operators, depending on the database. Furthermore, manual searches of the references of the identified articles were performed to identify additional articles that were not retrieved through the electronic searches. The search was limited to studies that included human subjects and were published in English. No limit was imposed on the year of publication of the studies, and the review included studies published as recently as 15 January 2016.

2.4 | Data extraction and management

RefWorks, which is a web-based reference management software program, was used to manage the retrieved references.[16] The primary reviewer (DS) conducted the initial search of the databases. This was followed by screening of the titles and abstracts of the retrieved articles by another reviewer (SS). The screening was validated by a second reviewer (AA) to ensure the comprehensiveness and relevance of the search. Full-text articles of studies that were judged to be potentially eligible during the title/abstract screening were retrieved. Finally, two authors (DS, SS) independently reviewed the full-text articles to ensure their suitability for inclusion. Any disagreements in the process were resolved through consensus. For the included studies, data were extracted independently by two of the authors (DS, SS). Any disagreements were resolved through discussion and adjudication by a third reviewer (AA) whenever necessary. A standardized data extraction tool was developed utilizing PRISMA items.[17] The extracted data were presented under the following headings: reference (author, year), objective, study design, population, intervention, comparator, outcome measures and key results. All extracted data were validated for accuracy through double entry by two authors.

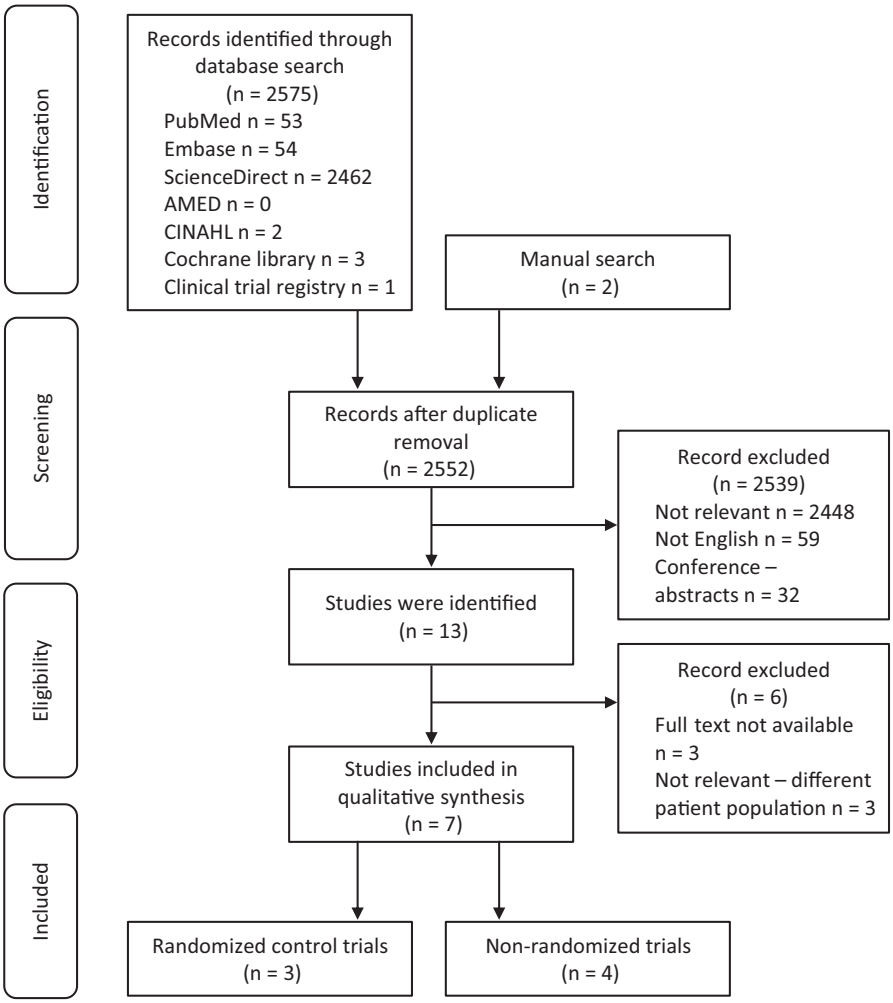

FIGURE 1 Search strategy diagram

2.5 | Quality assessment

All included studies were assessed independently by two authors to determine the risk of bias. Discrepancies were resolved through consensus. Randomized trials were assessed using the criteria outlined in the Cochrane risk of bias tool for Randomized Control Trials (RCTs).[18] Risk assessment classifies each criterion of bias assessment into low risk, high risk or unclear risk within the study and across the studies. Non-randomized interventional studies were assessed using the criteria of the Risk Of Bias In Non-randomized Studies—of Interventions (ROBINS-I) tool.[19] Risk assessment classifies each criterion of bias assessment into five categories: low risk, moderate risk, serious risk, critical risk and no information. For reasons of practicality, the five categories were merged into three categories (low-to-moderate risk, serious-to-critical risk and unclear risk), which were used for bias assessment within and across studies.

3 | RESULTS

3.1 | Characteristics of the included studies

Of the 2552 search results that were retrieved, seven studies[13-15,20-23] were considered to be eligible for inclusion in the review (Figure 1). These studies included a total of 1155 participants, of which 471 women received pyridoxine. Three studies were randomized controlled trials (Table 1),[14,15,20] whereas the remaining four studies were non-randomized controlled trials (Table 2)[13, 21-23]. The specific study designs of the non-randomized studies were not clearly defined in the articles. None of the included studies presented evidence of power analysis (ie sample size calculations); the largest study included a total of 482 participants, and four of the studies included less than 100 participants. Six studies were published in the 1970s,[13-15,21-23] and only one study was published in the 1980s[20] (Table 1 and Table 2).

3.2 | Participants

Generally, the studies recruited post-partum women who did not breastfeed or had contraindications for breastfeeding. The participants' obstetric characteristics (eg parity and gestational week at delivery) were not described in any of the studies, and exclusion criteria were not specified in many of the studies.

3.3 | Interventions

The studies compared pyridoxine with placebo, bromocriptine and/or stilboestrol. Pyridoxine was compared with placebo in four

TABLE 1 Characteristics of the included randomized studies [ordered by date of publication]

Marcus RG, 1975		
Objective	To assess the efficacy of pyridoxine in the inhibition of lactation	
Design/methodology	Randomized controlled double-blind trial	
Population	Women on the first day of puerperium N=95	
Intervention	Pyridoxine 200 mg 3 times per day for 7 d N=52	
Control	Placebo N=43	
Outcome measures	Breast discomfort, breast consistency, untoward side effects	
Results	• No significant differences in discomfort and breast consistency between the groups • Pyridoxine inhibited lactation in 96% of patients compared with 76.5% of control patients ($p<0.02$) • No untoward side effects were reported in the treatment group	
Others	Forty patients in the control group and 44 patients in the treatment group had their breasts bound with crepe bandages	
Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Sequence generation	Unclear risk	Method of sequence generation not stated. "The patients were randomly selected"
Allocation concealment	Unclear risk	No information about allocation concealment was provided
Blinding	Low risk	It was mentioned that the trial was "double blind" and "carried out with two identical tablets." It is unlikely that the blinding could have been broken, so the risk of bias for both efficacy and safety parameters was low
Incomplete outcome data	Low risk	"Two of the records were spoilt and 95 patients were therefore studied"
Selective outcome reporting	Low risk	Results of all prespecified outcomes were reported
Other sources of bias	Low risk	The study appears to be free of other sources of bias
Macdonald HN et al., 1976		
Objective	To assess pyridoxine effectiveness in the suppression of puerperal lactation	
Design/Methodology	Randomized controlled double-blind trial	
Population	Puerperal women wishing to bottle feed within the first 24 h of delivery N=175	
Intervention	Pyridoxine 200 mg 3 times per day for 6 d N=93	
Control	Placebo (Lactose) N=82	
Outcome measures	Breast discomfort, leakage of milk, breast engorgement	
Results	• No significant differences were demonstrated between the pyridoxine and placebo groups, whether assessed based on subjective discomfort, objective engorgement or the persistence of lactation	
Others	–	
Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Sequence generation	Unclear risk	Method of sequence allocation was not mentioned. Tablets were issued "in random order"
Allocation concealment	Low risk	The hospital pharmacy dispensed numbered packs containing identical tablets of either lactose or pyridoxine, and retained the identifying code until completion of the study
Blinding	Low risk	The trial was double-blind and carried out with two identical tablets. It is unlikely that the blinding could have been broken, so the risk of bias was low

(Continues)

TABLE 1 (Continued)

Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Incomplete outcome data	High risk	Of 191 randomized patients, 175 patients completed inpatient treatment (8.4% were excluded). Fourteen patients withdrew, as they discharged themselves early from the hospital (nine in the pyridoxine group, five in the placebo group), one patient decided to breastfeed and one patient was withdrawn for skin rash. Of 191 randomized patients, 131 patients completed outpatient questionnaires (31.4% were excluded); 77% of the 82 patients on placebo replied in comparison with 73% of the 93 patients on pyridoxine
Selective outcome reporting	Low risk	Results of all prespecified outcomes were reported
Other sources of bias	Low risk	The study appears to be free of other sources of bias
Boes EG, 1980		
Objective	To compare the efficacy of pyridoxine with that of bromocriptine in lactation inhibition	
Design/Methodology	Randomized controlled double-blind trial	
Population	Non-breastfeeding mothers requiring suppression of lactation during the post-partum period N=97	
Intervention	Pyridoxine 200 mg 3 times per day for 6 d, with 1 placebo tablet 3 times per day from day 7-14 (for blinding purposes) N=48	
Control	Bromocriptine 2.5 mg 2 times per day for 14 d, with 1 placebo tablet daily for 14 d (for blinding purposes) N=49	
Outcome measures	Milk secretion, mammary congestion, side effects	
Results	• Successful suppression of lactation appeared to be achieved in 29 of the 48 patients in the pyridoxine group and in all 49 patients receiving bromocriptine ($P<0.001$) • No major side effects were recorded. One patient in the pyridoxine group stopped the medication due to nausea on the eleventh day, after she had been using the inactive tablets for 5 d	
Others	Ergometrine 1 tablet 3 times per day for 3 d was prescribed routinely during the puerperal period	
Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Sequence generation	Unclear risk	Method of sequence allocation was not mentioned. Patients were randomly assigned to the groups
Allocation concealment	Unclear risk	No sufficient information about allocation concealment. It was mentioned that the tablets were packed in identical bubble packs, and the ward nurse checked that the tablets were taken in the right order. However, this information was not sufficient to judge whether patients or investigators could foresee assignment
Blinding	Unclear risk	Insufficient information to permit judgement concerning whether the ward nurse and doctor were blinded regarding efficacy and safety parameters
Incomplete outcome data	Low risk	Of the 100 patients admitted to the trial, data were available for 97 patients. Two patients, one from each group, left the hospital within 24 h of starting treatment, and 1 patient form did not reach the statistician (3% excluded after randomization)
Selective outcome reporting	Low risk	Results of all prespecified outcomes were reported
Other sources of bias	Low risk	The study appears to be free of other sources of bias

studies and with other pharmacological agents (bromocriptine or stilboestrol) in four studies. One trial compared women who received pyridoxine to suppress lactation to normally lactating women. Pyridoxine was administered orally in all of the studies, and the total daily dose ranged between 450 and 600 mg for 5-7 days. The treatment was commenced shortly after delivery in all of the enrolled women.

3.4 | Outcome measures

The method of outcome assessment varied among the studies. Two studies assessed the effect of high-dose pyridoxine use on prolactin levels,[21,23] whereas pyridoxine efficacy was evaluated clinically in six of the studies.[13-15,20-22] However, different parameters were used to describe clinical efficacy, including breast discomfort, breast

TABLE 2 Characteristics of the included non-randomized intervention studies [ordered by date of publication]

Foukas M, 1973		
Objective	To evaluate the efficacy of pyridoxine in the suppression of lactation in puerperal patients	
Design/Methodology	Placebo-controlled, double-blind trial	
Population	Puerperal patients in their second or third day after delivery. Women with deficiency or failure of lactation were excluded. N=254	
Intervention	Pyridoxine 200 mg 3 times per day for 6 d N=75 (blinded) Pyridoxine 200 mg 3 times per day for 6 d N=25 (not blinded)	
Control	Placebo 1 tablet 3 times per day for 6 ds N=86 Stilboestrol 5 mg 3 times per day for 6 d N=68	
Outcome measures	The time of cessation of lactation	
Results	• Ninety-five per cent of the women treated with pyridoxine had their lactation successfully suppressed within 1 wk, compared to 83 per cent for stilboestrol and 17 per cent for the placebo	
Others	After the second course of pyridoxine, lactation ceased completely in the remaining five patients	
Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Confounding	Unclear risk	No information concerning whether confounding might be present
Selection of participants into the study	Unclear risk	No information is reported about the selection of participants into the study
Classification of interventions	Low-to-moderate risk	Interventions were well defined. Three identical tablets were used and contained a placebo, 5 mg of stilboestrol, or 200 mg of pyridoxine. A course of treatment consisted of one tablet three times per day for 6 d, beginning on the second or third day after delivery
Departures from intended interventions	Low-to-moderate risk	Participants adhered to the assigned interventions. After analysing the results of the assigned interventions, a second course of pyridoxine was provided to five patients who failed to suppress lactation
Missing data	Low-to-moderate risk	Of 375 questionnaires issued, seventy questionnaires were not completed, and 51 questionnaires were inadequately filled in. The 254 patients for whom full information was available were divided into four groups, and all of these patients were included in the analysis
Measurement of outcomes	Serious-to-critical risk	Twenty-five patients were un-blinded to pyridoxine. These patients all (100%) ceased lactation within 1 wk, compared to 93% in the blinded group. A possibility of influencing outcome measures due to lack of blinding was present
Selection of the reported result	Low-to-moderate risk	The outcome measurements and analyses are consistent with an a priori plan
Canales ES et al., 1976		
Objective	To investigate the influence of pyridoxine administration on prolactin release and milk production	
Design/Methodology	Not well stated; described as a control trial	
Population	Puerperal women on the first day after delivery with contraindications for breastfeeding due to medical reasons N=34	
Intervention	Pyridoxine 150 mg 3 times per day for 7 d N=14	
Control	Bromocriptine 7.5 mg daily for 7 d N=20	
Outcome measures	Serum prolactin, milk production	
Results	• All 14 women who received pyridoxine experienced painful breast engorgement • Pyridoxine had no effect on serum prolactin levels	
Others	–	

(Continues)

TABLE 2 (Continued)

Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Confounding	Unclear risk	No information concerning whether confounding might be present
Selection of participants into the study	Unclear risk	No information was reported about the selection of participants into the study
Classification of interventions	Low-to-moderate risk	The study mentioned the types of interventions that were provided for each group
Departures from intended interventions	Low-to-moderate risk	No bias due to deviation from the intended intervention
Missing data	Low-to-moderate risk	The results of all included patients were presented. Fourteen puerperal women received 150 mg of pyridoxine three times per day for 7 d, beginning on the first day after delivery. The control group of 20 puerperal women received 7.5 mg of bromocriptine each day throughout the study period
Measurement of outcomes	Low-to-moderate risk	The outcome measure was expected to be minimally influenced by knowledge of the intervention. Serum prolactin was measured via radioimmunoassay for both groups
Selection of the reported result	Serious-to-critical risk	There was evidence or strong suspicion of selective reporting of results. A third group of lactating women was presented in the figure but not mentioned in the methodology section

Felming S, 1977	
Objective	To compare the effectiveness of pyridoxine, stilboestrol and placebo in the inhibition of puerperal lactation
Design/Methodology	Not well stated; double-blind trial
Population	Women who had vaginal delivery with a negative history of thromboembolism and wished to suppress lactation N=482
Intervention	Pyridoxine 200 mg 3 times per day for 5 d N=155
Control	Stilboestrol 5 mg 3 times per day for 5 d N=165 Sucrose 1 tablet 3 times per day for 5 d N=162
Outcome measures	Breast tenderness, breast engorgement, lactation Rebound engorgement, lactation or increased lochia 6 wk post-partum
Results	• Stilboestrol was significantly more effective in inhibiting the onset of lactation than pyridoxine or the placebo ($P<0.01$) • Pyridoxine was only marginally more effective than placebo • Regarding the incidence of rebound phenomena, results were not statistically significant ($P>0.3$) • No patients reported increased lochia
Others	Women were issued written advice concerning fluid restriction and the wearing of a firm brassiere. One patient reported calf tenderness on day 3 post-partum. The code was broken. The subject was found to be receiving pyridoxine, and a deep vein thrombosis was excluded

Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Confounding	Serious-to-critical risk	Women were issued written advice that fluid restriction and the wearing of a firm brassiere would assist in preventing the onset of lactation. The differences in applying these instructions between the different groups were not measured, which can confound the results
Selection of participants into the study	Unclear risk	No information was reported about the selection of participants into the study
Classification of interventions	Low-to-moderate risk	Intervention status was well defined
Departures from intended interventions	Low-to-moderate risk	No bias due to deviation from the intended intervention is expected. Women who received additional medications known to influence lactation (N= 14) or decided to breastfeed were excluded to avoid deviation from the intended intervention

(Continues)

TABLE 2 (Continued)

Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Missing data	Serious-to-critical risk	Of the 600 patients commencing the trial, 24 patients subsequently decided to breast-feed, 14 patients received additional medications known to enhance lactation, and 11 patients discontinued the trial for other reasons. For 69 patients, the records were incomplete, often because of the patient's early discharge from the hospital. Thus, 482 patients comprise the subject matter of this report (19.7% were excluded)
Measurement of outcomes	Low-to-moderate risk	The methods of outcome assessment were comparable across intervention groups
Selection of the reported result	Low-to-moderate risk	The outcome measurements and analyses are consistent with an a priori plan
De Waal JM et al., 1978		
Objective	To determine the effect of pyridoxine administration on serum prolactin levels in post-partum women	
Design/Methodology	Not stated	
Population	Post-partum women who did not want to breastfeed N= 18	
Intervention	A single dose of pyridoxine 200 mg immediately post-partum Then, pyridoxine 200 mg 3 times per day for 7 d N= 9	
Control	Normally lactating women N= 9	
Outcome measures	Serum prolactin levels	
Results	• Mean (±SD) serum prolactin levels on day 5 relative to day 1 were 53% (±29%) in the pyridoxine group and 68% (±39%) in the control group. The difference was not statistically significant • None of the pyridoxine-treated patients was lactation suppressed	
Others	Serum prolactin was measured for a third group who had drug-induced hyperprolactinemia, but analysis was carried out separately	
Risk of bias		
Criterion	**Authors' judgement**	**Support for judgement**
Confounding	Unclear risk	No information concerning whether confounding might be present
Selection of participants into the study	Unclear risk	No information was reported about the selection of participants into the study
Classification of interventions	Low-to-moderate risk	Intervention status was well defined and based solely on information collected at the time of intervention
Departures from intended interventions	Low-to-moderate risk	No bias due to deviation from the intended intervention was mentioned
Missing data	Low-to-moderate risk	Data were reasonably complete
Measurement of outcomes	Serious-to-critical risk	None of the pyridoxine-treated patients was lactation suppressed. No information about how this outcome was measured was provided, and it is unknown if this outcome is a reflection of prolactin level measurements only
Selection of the reported result	Low-to-moderate risk	All the intended and planned outcomes were presented in the results

consistency, breast engorgement and cessation of lactation. Safety was evaluated in only two of the studies.

Two of the included studies reported that the use of high-dose pyridoxine (ie 200 mg three times per day for 6 days) resulted in the suppression of lactation in approximately 95% of the enrolled subjects.[13,14] In these two studies, 193 patients received pyridoxine, which accounted for 41% of the total number of patients who received pyridoxine in all of the included studies. Efficacy was assessed clinically in both of these studies. However, all other studies failed to demonstrate pyridoxine efficacy through either clinical assessment or prolactin level measurements.[15,20-23] No untoward side effects were reported in either of the two studies that assessed the safety of the use of high-dose pyridoxine.[14,20]

3.5 | Quality assessment and risk of bias

The details for the risk of bias assessment for each study are presented in Table 1 and Table 2. Overall, the risk of bias for most studies was low or low-to-moderate (Figure 2 and Figure 3).

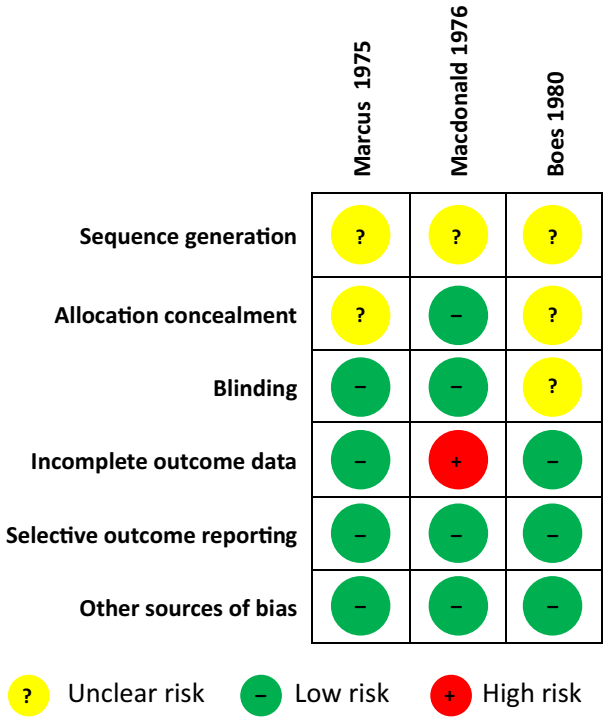

FIGURE 2 Risk of bias summary: review authors' judgments for risk of bias for randomized controlled trials [Colour figure can be viewed at wileyonlinelibrary.com]

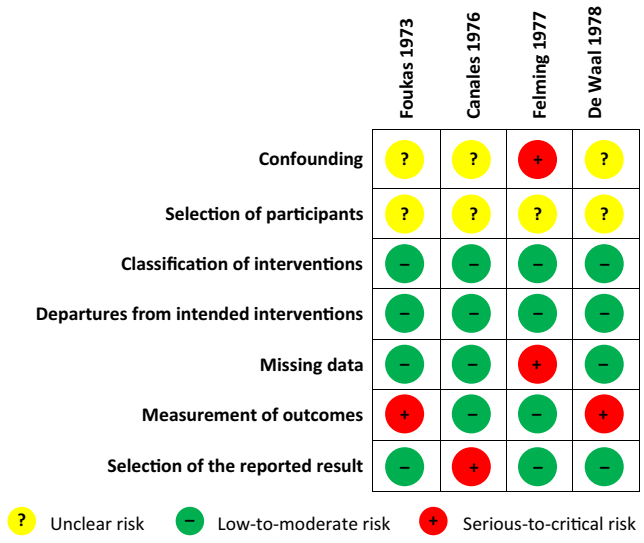

FIGURE 3 Risk of bias summary: review authors' judgments for risk of bias for non-randomized trials [Colour figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

Despite the availability of dopamine agonists (eg cabergoline and bromocriptine) for use in post-partum lactation inhibition, many maternal medical conditions necessitate avoiding the use of these agents due to safety concerns. These concerns highlight the need for alternative effective and safe agents. A small number of studies suggested that pyridoxine has an antilactogenic effect; however, data related to the clinical effectiveness and safety of pyridoxine are limited. This review evaluated the effectiveness and safety of pyridoxine in post-partum lactation inhibition.

Foukas was the first to report the effectiveness of high-dose pyridoxine in post-partum lactation suppression.[13] Thereafter, Marcus reaffirmed that finding.[14] In both studies, effectiveness was assessed clinically. However, all other studies failed to produce similar results through clinical assessment [15,20-22] or prolactin level measurements.[21,23] Similar conflicting results were reported with pyridoxine use for treating galactorrhoea-amenorrhoea syndromes. Initially, near the time at which Foukas and Marcus published their findings, McIntosh suggested a role for pyridoxine in the management of women with hyperprolactinemia and galactorrhoea-amenorrhoea.[24] Later, pyridoxine was demonstrated to lack effectiveness for reducing prolactin levels in these patients.[25-27] These conflicting results make it difficult to confirm the effectiveness of pyridoxine for clinical use in post-partum lactation inhibition.

In our review, pyridoxine safety was not a concern, as no untoward side effects were reported. However, the assessment of pyridoxine safety was limited to only two of the included studies.[14,20]

The studies included in the current review used varying methods to assess lactation inhibition, including clinical evaluations and/or laboratory investigations. Furthermore, the criteria used for clinical evaluations of pyridoxine efficacy were also defined in different ways in different studies. These criteria included leakage of milk, breast engorgement and the time of lactation cessation. Overall, the total number of patients who received pyridoxine was not very large (n=471 patients), and sample size calculations were not presented in any of the included studies. Furthermore, the specific study designs were not clearly defined in the non-randomized studies,[13,21-23] and all of the studies included in the current review had been published for more than 35 years ago.[13-15,20-23] Based on these observations, the strength of the current evidence is not sufficient to recommend the routine use of pyridoxine for post-partum lactation inhibition in clinical practice.

This review was limited to literature published in the English language, and studies published in other languages were excluded, although such studies may contain valuable information for this review. The quality of the included studies is another limitation of this review. The study design was not well stated in many of the studies. We used Cochrane risk of bias assessment tools to evaluate how this weakness impacted the study quality, but the risk of bias appeared to be low to moderate.

5 | WHAT IS NEW AND CONCLUSION

The available evidence is conflicting and insufficient to confirm the effectiveness of high-dose pyridoxine in post-partum lactation inhibition. Limited data suggest that high-dose pyridoxine is safe in women who aim to inhibit lactation. However, larger and well-designed randomized controlled trials are needed to reaffirm the effectiveness and safety of pyridoxine in post-partum lactation inhibition before recommending the use of this regimen in routine clinical practice.

CONFLICT OF INTERESTS

The authors declare no conflict of interests in this work.

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