INPLASY PROTOCOL

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None declared.

A systematic review and meta-analysis of intravaginal oxytocin gel for improving postmenopausal vaginal atrophy

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Review question / Objective: **(P) Population: Postmenopausal women with vaginal atrophy; (I) Intervention measures: oxytocin gel; (C) Control group: control group with only placebo gel; (O) Result: The treatment effect of postmenopausal women with vaginal atrophy. (S) Research type: Randomized controlled trials.**
Condition being studied: **The dominant symptoms in the postmenopausal stage are urogenital system symptoms, previously described as vulvovaginal atrophy or atrophic vaginitis. As estrogen levels decrease in menopausal women, blood flow to the vagina and vulva also decreases, making these tissues thinner, drier, and less elastic, leading to impaired vaginal lubrication, burning, dryness, and atrophy. And an increase in pH value, which can affect sexual function and lead to difficulty in sexual intercourse. At present, estrogen is the gold standard for treatment, and low-dose vaginal hormone therapy is the foundation of treatment. However, some side effects may occur when estrogen is applied. At the same time, some studies have found that local application of oxytocin gel can alleviate vaginal atrophy and promote the proliferation of epithelial cells in the vagina. Therefore, oxytocin may serve as an alternative treatment for estrogen.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 June 2023 and was last updated on 01 June 2023 (registration number INPLASY202360006).

INTRODUCTION

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Condition being studied: The dominant symptoms in the postmenopausal stage are urogenital system symptoms, previously described as vulvovaginal atrophy or atrophic vaginitis. As estrogen levels decrease in menopausal women, blood flow to the vagina and vulva also decreases, making these tissues thinner, drier, and less elastic, leading to impaired vaginal lubrication, burning, dryness, and atrophy. And an increase in pH value, which can affect sexual function and lead to difficulty in sexual intercourse. At present, estrogen is the gold standard for treatment, and low-dose vaginal hormone therapy is the foundation of treatment. However, some side effects may occur when estrogen is applied. At the same time, some studies have found that local application of oxytocin gel can alleviate vaginal atrophy and promote the proliferation of epithelial cells in the vagina. Therefore, oxytocin may serve as an alternative treatment for estrogen.

METHODS

Search strategy: The researchers in this article searched five electronic databases (Pubmed, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, and CNKI) from their creation until March 2023. The search strategy is built around the PICOS tool: (P) population: postmenopausal women with vaginal atrophy; (I) Intervention measures: oxytocin gel; (C) Control group: control group with only placebo gel; (O) Result: The treatment effect of postmenopausal women with vaginal atrophy. (S) Research type: Randomized controlled trials. The detailed search strategy is as follows (using Pubmed as an example)
#1 Postmenopause [MeSH Major Topic]
#2 ((((((((Postmenopause[MeSH Major Topic]) OR (Postmenopausal Period[Title/Abstract])) OR (Period, Postmenopausal[Title/Abstract])) OR (Post-Menopause[Title/Abstract])) OR (Post Menopause[Title/Abstract])) OR (Post-Menopauses[Title/Abstract])) OR (Post-menopausal Period[Title/Abstract])) OR (Period, Post-menopausal[Title/Abstract])) OR (Post menopausal Period[Title/Abstract])
#3 #1 OR #2
#4 atrophic vaginitis[MeSH Major Topic]
#5 ((((atrophic vaginitis[MeSH Major Topic]) OR (Atrophic Vaginitides[Title/Abstract])) OR (Vaginitides, Atrophic[Title/Abstract])) OR (Vaginitis, Atrophic[Title/Abstract])) OR (Vaginal atrophy[Title/Abstract])
#6 #4 OR #5
#7 Oxytocin[MeSH Major Topic]
#8 (((Oxytocin[MeSH Major Topic]) OR (Ocytocin[MeSH Major Topic])) OR (Syntocinon[MeSH Major Topic])) OR (Pitocin[MeSH Major Topic])
#9 #7 OR #8
#10 #3 AND #6 AND #7.

Participant or population: Postmenopausal women with vaginal atrophy.

Intervention: Local application of oxytocin gel in the vagina.

Comparator: Local application of placebo gel in vagina.

Study designs to be included: Randomized and non randomized trials, cohort study, cross-sectional study, case control study.

Eligibility criteria: Selection criteria(1) The experimental group using oxytocin gel as intervention measures (2) the control group using placebo gel (3) the clinical randomized controlled trial (4) the outcome indicators, including at least one of the following: vaginal PH value, blood estradiol concentration, endometrial thickness, pathological biopsy, vaginal cytology, self-evaluation of vaginal atrophy symptoms, and sexual function.Exclusion criteria(1) Studies with incomplete or unreported data (2) Non randomized controlled trials [including quasi randomized controlled trials, animal studies, protocols, meeting summaries, case reports or letters].

Information sources: PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, Google.

Main outcome(s): Effect evaluation indicators: Vaginal pH value, vaginal

cytology examination, blood estradiol concentration, endometrial thickness, pathological biopsy, self-evaluation of vaginal atrophy symptoms, and sexual function.

Quality assessment / Risk of bias analysis: The RCT was independently evaluated by two evaluators according to the bias risk assessment criteria in the Cochrane system evaluator manual version 5.1. Any inconsistencies were resolved through the intervention of a third evaluator and a consensus was reached through discussion. Evaluate the following aspects: ① generation of random allocation schemes, ② concealment of allocation schemes, ③ implementation of blind methods, ④ completeness of result data, ⑤ non-selective reporting of results, ⑥ other sources of bias; Low risk "indicates low bias risk," High risk "indicates high bias risk, and" Unclear risk "indicates that the literature does not provide sufficient or uncertain information for bias assessment.

Strategy of data synthesis: The meta-analysis was conducted using RevMan 5.1 software provided by the Cochrane Collaboration Network. First, by $\chi 2$ test and I2 test evaluate the heterogeneity between similar studies. If $P \geq 0.1$ and $I2 \leq 50\%$, it indicates that the possibility of heterogeneity between studies is low, and a fixed effects model is used; If P50%, it indicates heterogeneity between studies, and a random effects model is used. The counting data uses relative risk (RR) as the analysis statistic, and for continuous data, if the measurement tools are the same, weighted mean difference (MD) is used for analysis; If different measurement tools are used for the same variable, standardized mean difference (SMD) is used for analysis. All analyses were calculated with a 95% confidence interval (CI). If the clinical trial provides insufficient data, only descriptive analysis will be conducted.

Subgroup analysis: If sufficient data is found, subgroup analysis will be conducted based on the following variables: (1) oxytocin dose, (2) study design (IOP), and other variables, provided that the relevant data is fully present in the included study. In addition, if there is a sufficient number of trials, sensitivity analysis will be conducted on the main outcome to determine if the analysis is limited to high-quality (low bias risk) trials, and the estimated effects will be different.

Sensitivity analysis: Analyze the sources of heterogeneity and conduct subgroup analysis based on possible heterogeneity factors (such as using the same statistics as meta-analysis for only one study in the subgroup). If necessary, use sensitivity analysis to analyze the stability of the test results. If the heterogeneity is too large to determine its source, abandon meta-analysis and change to descriptive analysis.

Country(ies) involved: China.

Keywords: oxytocin, postmenopause, vaginal atrophy, meta-analysis, system evaluation.

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