

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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Are vaginal estrogens effective for preventing urinary tract infection in postmenopausal women?

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Abstract

INTRODUCTION

Urinary tract infection commonly affects postmenopausal women, probably because of the changes in vaginal flora secondary to estrogen deficiency. So, the use of vaginal estrogens could revert this process and then decrease the risk of infection. However, it is not clear whether they are really effective.

METHODS

To answer this question we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.

RESULTS AND CONCLUSIONS

We identified seven systematic reviews including four primary studies overall and all were randomized trials. We concluded it is not clear whether vaginal estrogens decrease the risk of symptomatic urinary infection because the certainty of the available evidence is very low.

Problem

Recurrent urinary tract infection is a common condition in women. The risk is higher in postmenopausal women, possibly due to changes in the vaginal flora because of the decreasing of local and systemic estrogens during menopause.

The use of vaginal estrogens has been suggested as a therapeutic strategy. The proposed mechanism is the reduction in vaginal pH, stimulating proliferation of lactobacilli, and avoiding the growth of gram negative uropathogenic bacteria. However, the real impact of this measure is not clear.

Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those

reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- It is not clear whether vaginal estrogens decrease the risk of symptomatic urinary tract infection in postmenopausal women, because certainty of the evidence is very low.
- Adverse effects of vaginal estrogens are probably frequent.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found seven systematic reviews [1],[2],[3],[4],[5],[6],[7] which include four randomized controlled trials overall [8],[9],[10],[11]. This table and the summary in general are based on the latter [8],[9],[10],[11] since the inclusion of the observational studies did not increase the certainty of the existing evidence or provide relevant additional information.
What types of patients were included*	All trials included postmenopausal women with a history of recurrent urinary tract infection. The average age reported in three trials [8],[10],[11], ranged from 58 to 68 years. One trial did not report it [9].
What types of interventions were included*	Vaginal estrogens were administered as follows: 2 mg estradiol for 36 months [8]; 25 µg/day estradiol for a week, followed by 25 µg twice a week for five months [9]; 0.5 mg/day estriol for two weeks, followed by 0.5 mg twice a week for eight months [10] and 1 ovule of estriol (1 mg) once a day for two weeks, followed by 2 ovules of estriol once a week for 6 months [11]. All trials compared against placebo or no treatment.
What types of outcomes were measured	The systematic reviews pooled results of the different trials in the following outcomes: Urinary tract infection at the end of the treatment period, probability of suffering at least one urinary infection, vaginal PH, positive lactobacilli, adverse effects.

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

Summary of Findings

The information about the effects of vaginal estrogens for the prevention of urinary tract infection is based on two randomized trials which include 201 patients [8],[10]. It was not possible to reuse data from two trials [9],[11] because they did not report any outcome of interest or none of the identified reviews could extract the data in a way it could be incorporated into a meta-analysis. Both trials reported urinary tract infection at the end of the treatment period and adverse effects (201 patients) [8],[10].

The summary of findings is the following:

- It is not clear whether vaginal estrogens decrease the risk of symptomatic urinary tract infection in postmenopausal women, because certainty of the evidence is very low.
- Adverse effects of vaginal estrogens are probably frequent. The certainty of the evidence is moderate.

Vaginal estrogens for the prevention of urinary tract infection.				
Patients	Postmenopausal women with a history of urinary tract infection.			
Intervention	Vaginal estrogens			
Comparison	Placebo			
Outcome	Absolute effect*		Relative effect (IC 95%)	Certainty of evidence (GRADE)
	WITHOUT Vaginal estrogens	WITH Vaginal estrogens		
	Difference: patients per 1000			
Symptomatic urinary tract infection	724 per 1000	304 per 1000	RR 0.42 (0.16 a 1.1)	⊕○○○ ^{1,2,3} Very Low
	Difference: 420 less per 1000 (Margin of error: 609 less to 72 more)			
Adverse effects**	51 per 1000	241 per 1000	RR 4.72 (0.67 a 33.53)	⊕⊕⊕○ ⁴ Moderate
	Difference: 190 more per 1000 (Margin of error: 17 less to 1000 more)			
<p>Margin of error:95% confidence interval (CI). RR: Risk ratio. MD: Mean difference. GRADE: Evidence grades of the GRADE Working Group (see later).</p> <p>*The risk WITHOUT vaginal estrogens is based on the risk in the control group of the trials. The risk WITH vaginal estrogens (and its margin of error) is calculated from relative effect (and its margin of error).</p> <p>** Vaginal bleeding, non-physiological discharge, vaginal irritation, burning or itching.</p> <p>¹ The certainty of the evidence was downgraded as the primary studies presented high risk of bias. ² The certainty of the evidence was downgraded one level for inconsistency because some trials showed a lower risk of symptomatic urinary tract infection meanwhile others showed an increase. ³ The certainty of the evidence was downgraded for imprecision. The decision made on both ends of the confidence interval would vary widely. ⁴ Even though the confidence interval is very wide, we only downgraded the certainty of the evidence for imprecision in one level, since it is unlikely that adverse effects do not exist. However, their magnitude is uncertain.</p>				

Follow the link to access the interactive version of this table ([Interactive Summary of Findings- iSoF](#))

About the certainty of the evidence (GRADE)*
<p>⊕⊕⊕⊕</p> <p>High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.</p>
<p>⊕⊕⊕○</p> <p>Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate</p>
<p>⊕⊕○○</p> <p>Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.</p>
<p>⊕○○○</p> <p>Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.</p>
<p>*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.</p> <p>† Substantially different = a large enough difference that it might affect a decision.</p>

Other considerations for decision-making

To whom this evidence does and does not apply

- The evidence provided in this summary applies to postmenopausal women that have presented at least one urinary tract infection episode.
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About the outcomes included in this summary

- The outcomes included in the summary of findings table are those considered critical for decision-making by the authors of this article. They generally agree with those reported in the systematic reviews identified.
-

Balance between benefits and risks, and certainty of the evidence

- It is an intervention with uncertain benefits and probably frequent adverse effects. It is not possible to make an adequate balance between risks and benefits due to the existing uncertainty about the latter.
-

Resource considerations

- The cost and availability of vaginal estrogens varies, specially for the different presentations that have been evaluated in the trials (cream or vaginal ring).
 - It is not possible to make an adequate balance between the cost and benefit of this intervention due to the uncertainty about the latter.
-

What would patients and their doctors think about this intervention

- Faced with the evidence presented in this summary, most patients and clinicians should incline against the use of vaginal estrogens for urinary tract infection prevention.
 - The fact they are not usually employed for this indication should reinforce this behavior.
-

Differences between this summary and other sources

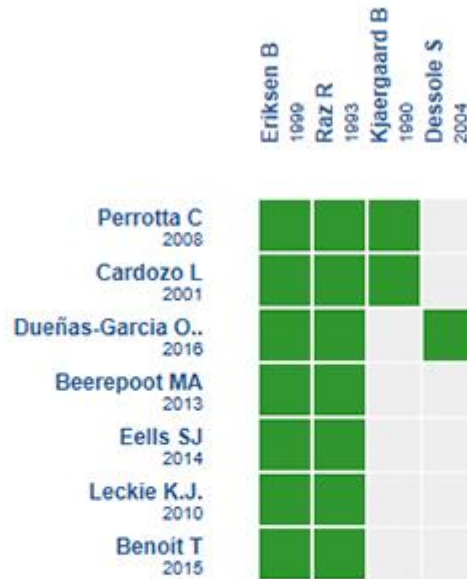
- The conclusions of this summary agree with the systematic reviews analyzed.
 - The clinical guideline NICE [12] did not include vaginal estrogens as a therapy for the prevention of recurrent urinary tract infections, whereas the clinical guideline of the European Urology Society [13] provides a favorable recommendation.
-

Could this evidence change in the future?

- The conclusions of this summary would probably change with future evidence, due to the existing uncertainty about the benefits of this intervention.
 - We identified at least one ongoing trial [14] in the International Clinical Trials Registry Platform of the World Health Organization.
 - We did not identify any high-quality systematic review including the totality of the trials identified in this summary, so a new review could contribute with relevant information.
 - We did not identify any ongoing systematic review on this topic in PROSPERO database.
-

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question.

Rows represent systematic reviews, and columns show primary studies.

The boxes in green correspond to studies included in the respective revisions.

The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version**: [Estrogens for preventing urinary tract infection in postmenopausal women](http://dx.doi.org/10.5867/medwave.2014.06.5997)

Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the

body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (<http://dx.doi.org/10.5867/medwave.2014.06.5997>)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

Potential conflicts of interest

The authors do not have relevant interests to declare.

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