Urogynecology digest

Presented by Debjyoti Karmakar

Vaginal estrogen: a dual-edged sword in postoperative healing of the vaginal wall

Ripperda CM, Maldonado PA, Acevedo JF, et al. *Menopause*. 2017; doi:[10.1097/GME.0000000000000840](https://doi.org/10.1097/GME.0000000000000840)

The authors of this animal model research investigated interventions to prevent impaired wound healing or vaginal wall regeneration, as they felt that reconstructive vaginal surgery for pelvic organ prolapse has high failure rates, possibly because of impaired surgical wound healing. They tested the hypothesis that the postoperative administration of local estrogen, direct injection of mesenchymal stem cells (MSCs), or both would lead to improved wound healing of the injured vagina in a menopausal rat model. In this study, ovariectomized rats underwent surgical injury to the posterior vaginal wall and were randomized to treatment with placebo ($n = 41$), topical estrogen (conjugated equine estrogen) cream ($n = 47$), direct injection of MSCs ($n = 39$), or both ($n = 43$). Treatment groups were euthanized 1 or 3 weeks after injury.

Interestingly, MSCs did not survive after injection and had no appreciable effects on the healing of the vaginal wall.

Acute postoperative administration of vaginal estrogen altered the response of the vaginal wall to injury with decreased stiffness, decreased collagen content, and decreased expression of transcripts for matrix components in the stromal compartment. This effect in the stromal layer of the vagina was contrary to the expected positive benefits based on existing clinical research showing the beneficial effects of the preoperative administration of estrogen cream. However, vaginal

estrogen resulted in positive effects in the form of marked proliferation of the epithelial layer and increased expression of genes related to epithelial barrier function and protease inhibition. Transcripts for genes involved in chronic inflammation and adaptive immunity were also down-regulated in the estrogenized epithelium.

The research seems to have good external validity within the framework of the usual limitations of differences in the biological attributes of animals and human beings inherent to every animal study. The results of the study population seem to be representative of the source population, with no obvious source of bias. However, the key limitation is that results are only reflective of changes in the vagina and not endopelvic fascia or pelvic floor muscles, which are critical tissues for a successful prolapse repair. Thus, although the study is appropriately designed to detect the research question proposed by the authors, i.e., the effect of estradiol or stem cells after operative injury to the vaginal wall in an animal model, it fails to address the effect of these interventions on the underlying tissues, which may well be more crucial to surgical success or failure. Also, wound healing is a dynamic process of synthesis and degradation over time and short-term effects may not necessarily extrapolate to longer term tissue effects and the authors acknowledged this limitation. Nonetheless, the interestingly dichotomous and previously unreported effect of estradiol on the different components of the vaginal wall opens up an interesting area of further research, including possible human clinical trials, which may have a bearing in clinical practice.

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