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New approaches to treat women's urogenital problems

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av
Shahla Hamza Al-Saqi
MD

Huvudhandledare:
Associate Professor Aino Fianu Jonasson
Karolinska Institutet
CLINTEC/ Division of Obstetrics & Gynecology

Bihandledare:
Professor Outi Hovatta
Karolinska Institutet
CLINTEC/ Division of Obstetrics & Gynecology

Associate Professor Cecilia Götherström
Karolinska Institutet
CLINTEC/ Division of Obstetrics & Gynecology

PhD, Suvi Asikainen
Karolinska Institutet
CLINTEC/ Division of Obstetrics & Gynecology

Fakultetsopponent:
Professor Ian Milsom
Sahlgrenska Academy/ Gothenburg University
Institute of Clinical Sciences
Department of Obstetrics & Gynecology

Betygsnämnd:
Professor Angelica Lindén Hirschberg
Karolinska Institutet
Department of Women's and Children's Health
Division of Obstetrics & Gynecology

Professor Stephen Strom
Karolinska Institutet
Department of Laboratory Medicine
Division of Pathology

Associate Professor Antti Perheentupa
University of Turku, Finland
Department of Obstetrics & Gynecology

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ABSTRACT

Women's urogenital problems adversely affect their quality of life. In this thesis, I address two of such urogenital problems: namely, postmenopausal vaginal atrophy (VA) and stress urinary incontinence (SUI).

In the first two studies of this thesis, an intravaginal oxytocin gel (Vagitocin) was used for the treatment of VA in double-blinded randomized controlled trials. The hypothesis was that oxytocin could serve as an alternative to local estrogen treatments for postmenopausal VA, particularly for women, whom estrogens are contraindicated for use by any means, including by local administrations. Breast cancer survivors and other hormone-dependent cancer patients form the core of this group. Oxytocin improved both the subjective symptoms of VA (i.e., dryness, irritation, itching, dyspareunia and postcoital bleeding), including the most bothersome symptom, and the objective features of VA. We observed an increase in the percentage of superficial cells in the vaginal mucosa, an increased maturation value, a decreased vaginal pH and decreased vaginal atrophic scores, as evaluated by a histopathology. Furthermore, oxytocin had no influence on the endometrial lining of the uterus, as evaluated by both ultrasound and endometrial biopsy, and we did not observe any serious side effects. In conclusion, oxytocin induced remarkable clinical and laboratory improvements in postmenopausal VA without inducing any serious adverse effects. Thus, oxytocin (Vagitocin), as a non-estrogenic compound, may be a good alternative treatment for postmenopausal VA, particularly in women who cannot or do not wish to use estrogen-containing products.

Traditional treatments for SUI are not always effective. Therefore, we developed a clinical expansion protocol of mesenchymal stem cells (MSCs). The hypothesis is that MSCs can be injected into the defective sphincter urethrae in order to improve its function by restoring the structure and, eventually, maintaining the continence. We isolated MSCs from the minimally invasive source adipose tissue (Ad) and expanded and stored the MSCs in clinical grade culture and cryopreservation media. We showed that, after isolation and expansion, Ad-MSCs had a stable morphology and shorter population doubling time than standard bone-marrow-derived MSCs (BM-MSCs). Furthermore, Ad-MSCs sustained their surface marker characteristics along five passages and were able to differentiate into both bone and fat lineages. In the last study, we showed that Ad-MSCs could be successfully cryopreserved and thawed in a clinical grade serum- and xeno-free cryoprotectant medium. This is important because such cryopreservation allows Ad-MSCs to be held on the shelf until their planned use(s). The Ad-MSCs exhibited a stable morphology, and they preserved their surface marker characteristics and differentiation potentials into bone and fat lineages. In conclusion, we believe that autologous Ad-MSCs, when cultured and cryopreserved in the described clinical grade media, can be successfully tested for their ability to improve women's SUI in the future.