

THE ROLE OF STEM CELLS IN THE TREATMENT OF URINARY INCONTINENCE-SURGERY¹

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Abstract: *At present, there are many approaches in the treatment of urinary incontinence: lifestyle modification and behavioural therapy (pelvic floor muscle strengthening exercises, quitting caffeine and fizzy drinks and so on); pharmacologic (M-cholinolytics, b3-agonists, norepinephrine - serotonin reuptake inhibitors), surgical (colposuspension, sling surgeries, artificial sphincter), minimally invasive therapy (use of botulinum toxin – type A, different types of laser, volume-forming substances). The low efficacy of both behavioural and medication therapies as well as the patients' unwillingness to undergo a surgery, necessitates searching less invasive and more effective alternative treatment for urinary incontinence. In this regard, a potential approach to treat UI is the use of cell-based therapies. Currently, clinical trials are performed to determine the role of stem cells.*

Keywords: *Urinary incontinence, pubourethral tendon, stem cells*

JEL Codes: *I12, I19*

INTRODUCTION

Stress urinary incontinence is the most common type of incontinence. In this type of incontinence, the urethral and bladder neck retention and closure mechanisms are insufficient, particularly in "stress conditions" – coughing, sneezing, weight lifting.

This type of incontinence mainly affects women due to their anatomy. First, each pregnancy is a risk factor for pelvic floor weakness and injury and in the second place, the short female urethra has less capacity to retain urine.

Many authors think that the most common reasons for urinary incontinence in women are pubourethral tendon damage as a result of traumatic deliveries, repeated heavy lifting, post-operative urinary dysfunction after a surgery of the pelvic floor organs.

Female urinary incontinence is one of the present-day problems in the modern urogynecology. ICS (International Continence Society) defines urinary incontinence as – an involuntary leakage of urine of any type, which involves – stress urinary incontinence, overactive bladder symptom, neurogenic bladder dysfunction, incontinence of excessive leakage, extra urethral incontinence and mixed type of incontinence.

Currently, studies are performed to determine the role of the stem cells. At present, there are many approaches in the treatment of urinary incontinence: lifestyle modification and behavioural therapy (pelvic floor muscle strengthening exercises, quitting caffeine and fizzy drinks and so on), pharmacological (M-cholinolytics, b3-agonists, norepinephrine - serotonin reuptake inhibitors), surgical (colposuspension, sling surgeries, artificial sphincter), minimally invasive therapy (use of botulinum toxin – type A, different types of laser, volume-forming substances). The low efficiency of both behavioural and medication therapy as well as the patients' unwillingness to undergo a surgery necessitates searching less invasive and more effective alternative treatment for urinary incontinence.

In this context, a potential treatment method is the use of cell techniques. Currently, examinations are performed to determine the role of the stem cells. The three defining characteristics of the stem cells are: the ability to differentiate into different cell types, the ability to form clonal cell populations derived from a single stem cell and the ability to self-renew. Due

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to these characteristics and because there is no immune response towards their use, it might be suggested that the use of stem cells is a promising approach for the treatment of the disease.

This article aims at presenting the literary review and thematic scientific articles for the use of stem cells in treating urinary incontinence.

Urinary retention in women is mainly caused by the anatomical and functional bladder structure, vesicoureteral segment, the mucosa and the urethral submucosal layer, the urethral sphincter, muscles and pelvic junctions. The process of urination is controlled by the internal sphincter (smooth muscle, involuntary) and the external sphincter (striated muscles, voluntary). Malfunction of one or set of elements leads to female UI.

EXPOSITION

Collagen, polytetrafluoroethylene, silicone particles, autologous fatty tissue, autologous chondrocytes, dextranomer/ hyaluronic acid copolymer and others in their capacity of bulking agents have been used for a long time for the treatment of UI. Over the past years, with the improvement of cell techniques, different types of cultivated stem cells have been injected.

Stem cells are divided into embryonic and non-embryonic ones; totipotent, pluripotent, multipotent, unipotent according to their ability to differentiate. According to their source of origin, stem cells from umbilical cord blood, bone marrow stem cells, adipose-tissue derived stem cells and so on. The use of embryonic stem cells is associated with ethical aspects that limit their use.

Dozens of clinical trials, based on the role of stem cells in the treatment of UI have been performed. Most of the trials refer to stress urinary incontinence. They differ according to the stem cell-injection method, volume of the injected substance, periods of observation and ways of evaluating the efficiency of the procedure and the outcome. Transurethral approach of injecting stem cells is more frequently used in the region of striated sphincter and submucosal layer of the urethra.

The largest study, related to the treatment of female stress urinary incontinence is M. Mitterberger study, which involved 123 women with transurethral injection of autologous stem cells (fibroblasts and myoblasts) in the urethral submucosa and rhabdosphincter. One year after injecting the cells, 94 (79%) patients reported complete urine retention, 16 (13%) – significant improvement and 9 (8%) – slight improvement, contractility and electromyography activity of the striated sphincter in patients with myoblasts injection.

In M.K. Shirvan study, peripheral venous blood was used as a source of stem cells. All 9 patients reported improvement after a 6-month follow-up.

Most studies have had short - term follow-up (till the 1,5 year), except J.N. Cornu and colleagues study, who have analyzed results in the course of 6 years after the endourethral injection of autologous bone marrow stem cells; 3 out of 11 patients reported positive effect (18). Stangel-Wojcikiewicz has followed his patients after the 4th year – improvement in the quality of life has been reported by 12 out of 16 patients.

All the treatment complications may be divided into 3 groups: related to substance collection (early hematoma); intraoperative (pain, hematoma on the place of injection) and postoperative (perineal pain, urinary tract infection – urethritis, cystitis, hematuria, itching in the vulvovaginal area, worsening of urinary incontinence, occurrence of urge incontinence). These complications are rare.

In order to prevent trauma of the surrounding tissues, injections are given under the control of transurethral ultrasound examination, which allows the culture of stem cells to be injected right into the area of the rhabdosphincter and the submucosal layer of the urethra.

CONCLUSION

These clinical trials show significant role of the stem cells in the treatment of UI as an alternative method of the already existing ones. The techniques described have their own efficacy and do not cause significant complications. The cell techniques demonstrate their potential in the

treatment of stress urinary incontinence and might be used more effectively in the treatment of mixed types of incontinence with sufficient long-term results.

Currently, the questions in regards with choosing the source of stem cells and their method of injection are left open. In stress urinary incontinence the use of bone marrow stem cells and adipose-tissue derived stem cells and transurethral method for injecting substance of the submucosal layer and the area of rhabdosphincter is appropriate.

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