Comparing Periurethral Injection of Autologous Muscle-Derived Stem Cell and Fibroblasts with Mid-Urethral Sling Surgery in the Treatment of Female Stress Urinary Incontinence: A Randomized Clinical Trial

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Abstract

Objective: In this study, we analyzed the therapeutic effect of periurethral injection of autologous muscle-derived stem cell versus mid-urethral sling surgery at a 1-year follow-up.

Method: This randomized controlled clinical trial was conducted on 30 women with stress urinary incontinence (SUI) who had not responded to conservative treatments, after registering the participants and obtaining informed consent. Patients were divided into two groups of 15 each treated with periurethral injection of muscle-derived stem cells (MDSCs) and mid-urethral sling surgery, respectively. Follow-ups were done at 1, 3, 6, and 12 months after the treatment using the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-USIF) and Incontinence Quality of Life Questionnaire (I-QOL) questionnaires, clinical examination, cough test, and 1-hour pad test. The results were analyzed within the groups and then compared between the two groups. Moreover, both groups were compared in terms of postoperative complications.

Results: At the 1-year follow-up, in the stem cell group, 10 patients (66.6%) experienced improvements after the periurethral injection of stem cells; half of these patients (33.3%) reported a full recovery. In the mid-urethral sling group, 13 patients (93.3%) experienced improvement, and 12 patients (80%) reported a full recovery. The analysis of ICIQ-USIF and I-QOL questionnaires indicated that the responses in both groups were significant, but the response in the stem cell group was significantly lower compared with the standard surgery group. No considerable complications were observed in the two groups.

Conclusion: Although the periurethral injection of MDSCs considerably improves the symptoms with minimum complications in women with SUI, its therapeutic response is significantly lower compared with mid-urethral sling surgery.

Keywords: Stress urinary incontinence; Muscle-derived stem cells (MDSCs); Periurethral injection; Mid-urethral sling surgery; Quality of Life

Introduction

Stress urinary incontinence (SUI), referring to the involuntary leakage of urine in the presence of an increase in intra-abdominal pressure, is a prevalent condition among women. It occurs as a result of urethral sphincter deficiency or pelvic floor muscle and fascial supporting tissue weakness.[1-3]

Initial treatments for urinary incontinence are conservative treatments, including pelvic floor physiotherapy, biofeedback, electrical stimulation, and in some cases, pharmacotherapy. If there is no response to these methods, surgical methods become the main treatment methodology for urinary incontinence.[4-5]

The aim of any type of surgery in urinary incontinence is to achieve a balance between urinary continence and the ability to urinate while considering the durability of the surgical method and ensuring it does not cause any severe complications, such as voiding dysfunction or urinary urgency. For more than a century, sling surgeries have been used to treat urinary incontinence. Since then, sling surgery has undergone a lot of improvement. The classic sling was an invasive surgical procedure with risks of postoperative complications and morbidity.[6, 7]

After classic sling, the integral theory was proposed[8], This theory is based on the claim that the most significant factor of preserving urinary continence is the proper functioning of the pubourethral ligament, suburethral vaginal hammock, and pubococcygeus muscle. Damage resulting from surgery, childbirth, aging, and hormonal deprivation to any of these components could lead to impaired mid-urethral function, and, subsequently, urinary incontinence. Therefore, mid-urethral sling surgeries using a mesh became popular.

Currently, the 2-year success rate for bulking agents, urethral suspension, and the urethral sling is 30%, 73%, and 82%-96%, respectively.[9, 10] Complications of mid-urethral sling include vaginal mesh extrusions, mesh perforation at bladder and urethra, urinary retention, pelvic and groin pain, and dyspareunia.[8, 10]

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The increase in the cases of urinary incontinence among the elderly in developed countries has triggered a search for less-invasive yet more effective treatments\[^{11}\]. Moreover, since the relationship between urethral hypermobility and incontinence symptoms and severity is insignificant, there is a shift from anatomic correction to repairing the urethral closure mechanism\[^{12}\].

None of the standard treatments that are currently being used to treat urinary incontinence aim at repairing the damaged tissue; however, regenerative medicine aims at restoring the normal function by directly affecting the damaged or dysfunctional tissue\[^{13-16}\].

Over the past few decades, using stem cells has shown promising outcomes in urologic diseases such as lower urinary tract dysfunction, bladder and urethral trauma, and renal diseases\[^{17, 18}\]. It seems that stem cells repair the tissue through multipotent differentiation and self-renewal\[^{18, 19}\]. In addition, stem cells can apply their therapeutic effect by discharging bioactive factors having anti-apoptotic, anti-scarring, neovascularization, and immunomodulatory effects\[^{20}\].

The present study aimed at assessing the results of perirethral injection of autologous muscle-derived and fibroblast stem cells in the treatment of SUI in women and comparing it with the control group that underwent mid-urethral sling surgery via a retropubic approach (tension-free vaginal tape [TVT] procedure).

**Methods**

This study was a prospective randomized clinical trial conducted during 2017–2019 after acquiring the necessary permits and approval of the ethics committee of Kerman University of Medical Sciences (ethics code: IR.kmu.rec.1395.349).

The study population consisted of 40- to 65-year-old women with SUI referred to the female urology clinic of Kerman University of Medical Sciences who had not responded to conservative treatments and pelvic floor exercises and were candidates for interventional treatments.

The inclusion criteria included having SUI confirmed using the positive cough stress test and urodynamic study, having a stress score greater than the urgency score based on the questionnaire, and having a desire to undergo surgical treatments of SUI. The exclusion criteria included having a history of previous synthetic, biologic, or fascial sub-urethral sling or any other surgery on the genitourinary tract, planning to become pregnant, having genitourinary malignancy, genitourinary fistula, or urethral diverticulum, having significant pelvic organ prolapse, having active urinary infection, having a significant post-void residual (volume of more than 150 cc), showing detrusor overactivity or low compliance bladder on multichannel urodynamic study, having uncontrolled diabetes, and having contraindications for surgery.

Patients who met the inclusion criteria were informed of the method of conducting the project, its benefits, and drawbacks. Afterward, a written consent was obtained from those who were willing to participate, and then they were included in the study. Subsequently, patients’ demographic information, including age, parity, hormonal status, and general history, was recorded. Then, the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-USIF) and Incontinence Quality of Life Questionnaire (I-QOL) questionnaires were completed for the patients. After performing a standard pelvic examination and cough test in lithotomy and standing positions, voiding diary and 1-hour pad test were completed for the patients, and paraclinical measures, such as the urine culture test, post-void residual urine test, and urodynamic test, and, if needed, pelvic ultrasound and/or cystoscopy, were undertaken. Next, using a random digit (number) table, patients were divided into the cell therapy and control groups and individuals in each group were perfectly matched in terms of influential variables such as age, BMI, parity and severity of SUI. Patients in the control group received the standard treatment using mid-urethral sling (TVT) and those in the cell therapy group were treated with periurethral injection of muscle-derived stem cells (MDSCs). All surgeries were performed in the same surgery center by the same female urologist.

**Cell therapy procedure**

Under local anesthesia, open biopsy was performed and a 0.5 × 0.5 cm sample, including skin, subcutaneous tissue, and muscle, of the quadriceps femoris muscle was taken and transferred to the Cell Therapy and Regenerative Medicine Center of Kerman University of Medical Sciences in cold boxes.

**Muscle stem cell culture procedure**

In the clean room of the Pathology and Stem Cells Research Center, after separating the skin from the muscle, the sample of the muscle was placed in a plate containing collagenase enzyme and then put in DMEM containing 15% FBS and finally placed in an incubator with 95% humidity and 5% CO\(_2\) at 37°C. The medium was renewed 3 days later and after that on every 2 days. In order to change the medium, the flask was emptied, its floor was washed with PBS, and 5 ml of the new medium containing 10% FBS was added to it. When the floor of the flask was covered with cultured cells (myoblast and fibroblast) and after reaching cell confluence of about 70–80% in the primary culture, cell passaging was done. First, the culture medium in each flask was emptied and cells were washed with 3 ml of PBS. Approximately 2 ml of trypsin-EDTA was added to each 25 cm\(^2\) flask. Afterward, the flasks were placed in the incubator for 3 minutes to improve the performance of trypsin-EDTA. After the isolation of cells, the effect of trypsin was nullified by adding 2 ml of a culture medium containing 10% FBS to each flask. In this stage, the cells were transferred to a 15-ml Falcon tube, and after centrifugation at 1200 rpm at 20°C for 5 minutes, the medium in the tube was discarded and cell suspension was produced by adding 1 ml of the culture medium containing 10% FBS to the sediment at the bottom of the tube and pipetting. Eventually, the resulting suspension (based on the cell density) was transferred to two to three new 25 cm\(^2\) flasks. Then, 4 ml of the culture medium containing 10% FBS was added to each flask, and then the flasks were placed in the incubator. Medium renewal was done once every three days until 70–80% cell density was achieved. This process was repeated two to three times until approximately 30 million cells were produced. Around 7–8 weeks after the culture, the cells were harvested, and after performing microbial tests to make sure that there was no contamination in the samples, the cells with the following characteristics were transferred to the operating room to be transplanted.

**Characteristics**

A. Muscle stem cells derived from skeletal muscle and fibroblast derived from the patient’s skin cultured for 6–8 weeks.

B. Cell carrier: physiological serum containing 20% of the patient’s serum.

C. Amount (number of cells): On average, each sample contained 30 million muscle stem cells and almost the same number of fibroblasts separately.
**Injection procedure**

In the operating room, under spinal anesthesia, the injection was administered by cystourethroscopy at four points in the mid-urethra using endoscopic needles. Injections were administered at two depths, the deeper one into the sphincter and the more superficial one into the submucosa.

**Mid-urethral sling procedure**

Patients in the control group underwent the standard mid-urethral sling procedure with the retropubic approach (TVT) using a synthetic mesh (Boston Scientific Company).

**Patient evaluation and follow-up**

Patients were evaluated at 1 and 2 weeks after the surgery to check for complications. Moreover, at 1, 3, 6, and 12 months after the injection, they were evaluated to check for complications and assess the improvement.

Subjective response was evaluated using medical history, and by completing the ICIQ-USIF and I-QOL questionnaires, and objective response was evaluated by performing a clinical examination, cough test in lithotomy and standing positions, and 1-h pad test. Complete response was attributed to negative cough test results in different positions and a pad test reflecting less than 2 g improvement, which was attributed to a decrease of 50% in the pad test weight and a negative cough test in lithotomy positions. Negative response was attributed to a positive cough test in different positions and a decrease of less than 50% in the pad test weight. Then, the results of the treatments in the two groups were compared.

**Data calculation and analysis**

The present research was a randomized controlled clinical trial in which the safety and efficacy of MDSCs and cultured fibroblasts in decreasing the symptoms of urinary incontinence in patients with SUI was analyzed, and the results were compared with the control group. In this study, biopsy was not performed on the control group; therefore, the control group was open-label.

A total of 30 patients were studied; 15 patients were randomly selected for the control group and 15 for the cell therapy group. In this study, the evaluator and analyzer of the samples were not aware of the type of groups.

Mean and standard deviation (continuous variables) along with frequency and percentage (discreet variables) were used for descriptive analysis. For comparison of the severity of cough between the two groups (cough levels: None, improvement, cure) in the follow-up, marginal model with generalized estimation equation (GEE) was used. GEE is an estimation procedure that is used for the comparison of repeated measures outcomes. This method did not need normality assumption for outcome variable. In this research, our outcome was ordinal and normality assumption was not established. There for marginal model with GEE estimation was substitute with repeated measurement analysis.

If time and group had significant interaction, then comparisons of groups were done in different levels of time.

Since scores are continues, to compare the questionnaire scores between the groups, repeated measurements analysis was conducted. Sphericity assumption was checked with Mauchly’s test. If Sphericity was not established, the result of Greenhouse-Geisser was investigated. If interaction was conducted between time and groups, the comparison of the questionnaire scores were conducted at different times. The significance level was set at 5

**Results**

**Comparison of age and parity**

The mean age of the participants in the cell therapy and control groups was 48.9 ± 2.76 and 45.7 ± 1.99 years, respectively. Moreover, the mean of parity in the cell therapy and control groups was 4.4 ± 0.76 and 3.4 ± 0.24, respectively. No significant difference was observed between the two groups in terms of these variables.

**Comparison of cough stress test and pad test**

In both groups, all patients tested positive in the cough stress test before intervention. After 12 months, complete response, improvement, and failure were observed in, respectively, 12 (80%), 2 (13.3%), and 1 (6.7%) patient of the control group. In the cell therapy group, complete response, improvement, and failure were observed in, respectively, 5.5, and 5 (33.3%) patients. There was no significant difference between the two groups at 1 and 3 months, while the outcomes were better in the control group at 6- and 12-month follow-ups, and the difference was significant (Table 1).

**Comparison of the results of ICIQ-USIF before and after intervention in the control and cell therapy groups**

The mean score of ICIQ-USIF before the intervention in the cell therapy group was significantly lower than the score at 1 month after the intervention (P < 0.001). However, in the subsequent months, no significant difference could be observed in this group (Table 2, Figure 1).

The mean score of ICIQ-USIF before the intervention in the control group was significantly lower than the score at 1 month after the intervention (P < 0.001). However, in the subsequent months, no significant difference could be observed in this group (Table 3, Figure 2).

The results presented in Table 4 show that there was no significant difference between ICIQ-USIF scores of the two groups before intervention. However, at 1, 3, 6, and 12 months after the intervention, significant differences were observed between the two groups, and the control group had a better mean score. (Figure 3)

In the cell therapy group, the mean score of the I-QOL questionnaire was significantly higher than that at 1 month after intervention (P < 0.001). However, no significant difference in I-QOL questionnaire score was observed in the subsequent months in this group. (Table 5, Figure 4)

The mean score of the I-QOL questionnaire was significantly higher than that at 1 month after intervention in the control group (P < 0.001). However, no significant difference in the I-QOL questionnaire score was observed in the subsequent months in this group. (Table 6, Figure 5)

The results presented in Table 7 suggest that I-QOL questionnaires scores were not significantly different between the two groups before intervention. However, at 1, 3, 6, and 12 months after the intervention, significant differences were observed between the two groups, and the control group had a better mean score. (Figure 6)
**Table 1. Comparison of groups at different times**

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>None</th>
<th>Imp</th>
<th>Cure</th>
<th>None</th>
<th>None</th>
<th>Imp</th>
<th>Cure</th>
<th>None</th>
<th>None</th>
<th>Imp</th>
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<td>5</td>
<td>6</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<td>2</td>
<td>12</td>
<td>5</td>
<td>12</td>
<td>5</td>
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<tr>
<td>P-value</td>
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<td>0.041</td>
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</tbody>
</table>

None: no change; Imp: improvement

**Table 2. Comparison of ICIQ-USF questionnaire scores of the stem cell group at different times**

<table>
<thead>
<tr>
<th>Before vs. 1 month</th>
<th>Mean square</th>
<th>F(Greenhouse-Geisser)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1382.4</td>
<td>43.628</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3. Comparison of ICIQ-USF questionnaire scores of the stem cell group at different times.**

<table>
<thead>
<tr>
<th>Before vs. 1 month</th>
<th>Mean square</th>
<th>F(Greenhouse-Geisser)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3435.27</td>
<td>463.63</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Table 4. Comparison of ICIQ-USF questionnaire scores between the two groups at different times.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Before</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stem cells</td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
</tr>
<tr>
<td>18.07 ± 2.61</td>
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<tr>
<td>8.47 ± 3.91</td>
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<tr>
<td>8.21 ± 5.16</td>
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<tr>
<td>8.87 ± 6.67</td>
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<tr>
<td>9.73 ± 6.56</td>
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<td></td>
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<tr>
<td>Standard</td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
</tr>
<tr>
<td>17.41 ± 2.23</td>
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<td></td>
<td></td>
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<tr>
<td>2.27 ± 3.63</td>
<td></td>
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<tr>
<td>1.81 ± 3.09</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1.53 ± 2.56</td>
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<tr>
<td>1.8 ± 2.48</td>
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<tr>
<td>P-value</td>
<td>0.458</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 5. Comparison of QoL questionnaire scores of the stem cell group at different times.**

<table>
<thead>
<tr>
<th>Before vs. 1 month</th>
<th>Mean square</th>
<th>F(Greenhouse-Geisser)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>20981.4</td>
<td>37.015</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Table 6. Comparison of QoL questionnaire scores of the control group at different times.**

<table>
<thead>
<tr>
<th>Before vs. 1 month</th>
<th>Mean square</th>
<th>F(Greenhouse-Geisser)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>39219.27</td>
<td>104.193</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Table 7. Comparison of QoL questionnaire scores between the two groups at different times.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Follow-up times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stem cells</td>
<td>Mean SD</td>
</tr>
<tr>
<td>79.47 ± 17.75</td>
<td>42.07 ± 14.16</td>
</tr>
<tr>
<td>41.47 ± 18.57</td>
<td>43.73 ± 20.56</td>
</tr>
<tr>
<td>46.6 ± 21.89</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>Mean SD</td>
</tr>
<tr>
<td>80.47 ± 17.35</td>
<td>29.33 ± 10.44</td>
</tr>
<tr>
<td>27.53 ± 7.86</td>
<td>26.87 ± 7.38</td>
</tr>
<tr>
<td>27.81 ± 7.17</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.877</td>
</tr>
</tbody>
</table>
Fig 1. The trend of International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UISF) scores in the stem cell group.

Fig 2. The trend of International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UISF) scores in the control group.

Fig 3. Comparison of International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UISF) scores between the two groups at different times.

Fig 4. The trend of Incontinence Quality of Life (I-QOL) Questionnaire mean scores in the stem cell group.

Fig 5. The trend of Incontinence Quality of Life (I-QOL) Questionnaire mean scores in the control group.

Fig 6. Comparison of Incontinence Quality of Life (I-QOL) Questionnaire scores between the two groups at different times.
**Exclusion criteria:** history of previous synthetic, biologic, or facial sub-urethral sling or any other surgery on the genitourinary tract, planning to become pregnant, having genitourinary malignancy, genitourinary fistula, or urethral diverticulum, having significant pelvic organ prolapse, having active urinary infection, having a significant post-void residual (volume of more than 150 cc), showing detrusor over activity or low compliance bladder on multichannel urodynamic study, having uncontrolled diabetes, and having contraindications for surgery.

**CONSORT Diagram**
Discussion

Preservation of urinary continence in women depends on a complex interaction between urethral and bladder neck support, intrinsic urethral properties, the urethral sphincter mechanism, and pelvic floor muscle functioning.

From a pathophysiologic point of view, tissue, nerve, or vessel damage or dysfunction aggravates with the existence of contextual morbidities such as age, obesity, and diabetes, causing urinary incontinence in women[21].

Although there are multiple mechanisms of injury in urinary incontinence, surgeries such as sling provide support for weakened pelvic floor muscles indirectly, and cell therapy for SUI is a new threshold in regenerative medicine.

Stem cells form a unique group of cells with three characteristics: self-renewal, differentiation into a number of different cells, and clonogenicity. These characteristics lead to the use of stem cells in function regeneration in different tissues. Currently, the adult stem cells (ASCs) are the best type of all that have been assessed for urologic use[14,15,16].

Mesenchymal stem cells (MSCs) are a unique subgroup of ASCs that are classically taken from bone marrow stroma; however, they can be found in other tissues with good vascularity such as muscle fat and can be differentiated into several cells and tissues[22].

MDSCs and fat-derived stem cells can be obtained using sampling with less-invasive methods and in large amounts using local anesthesia[15]. Autologous stem cells can be injected into the urethra to regenerate urethral defects (sphincter, neuromuscular synapse, and blood perfusion) and retain urinary incontinence[23].

In this study, conducted over a period of 1 year, we analyzed the efficacy and safety of transurethral injection of MDCs in female patients with SUI who had not responded to conservative treatments.

In a pilot study conducted in the USA, Carr et al. reported their 1-year analysis of injection of 18-22 × 10^6 AMDCs derived from the quadriceps femoris muscle; five out of eight patients experienced clinical improvement[24]. In their next study, they analyzed different ranges of injection dose in 38 women[25]. A higher percentage of patients experienced a decrease of equal to or more than 50% in pad weight (88.9% in high-dose group vs. 61.5% in the low-dose group) and daily leakage (77.8% vs. 53.3%) at 12-month follow-up in the group that had received a higher dose of cells compared with the group that had received the lower dose.

In the present study, we used 30 million MDCs for periurethral injection and the same number of fibroblasts, which belong to the high-dose range.

Mitterberger et al. reported the simultaneous injection of autologous fibroblast cells into the urethral submucosa and autologous myoblast cells into the rhabdosphincter under ultrasound guidance in 123 females with SUI. One year after injections, 79% were cured, 13% experienced considerable improvement, and 7% experienced minor improvement[26].

In the present study, we used a simultaneous injection of autologous myoblast and fibroblast cells into paraurethral tissue using an endoscopic approach.

Stangle et al. reported the 2-year results of their study of injecting MDCs harvested from deltoid into transurethral sphincter in 16 women with SUI. After 2 years, 50% of patients experienced cure and 25% experienced improvement. The authors stated that even with the injection of a small number of cells (0.6–25 × 10^6), they observed improvements[27].

In a systematic review performed by Marta et al., 16 articles on the effect of cell therapy on SUI were analyzed. According to the results, out of 616 male and female patients, 37.2% experienced complete improvement and 29.7% partial improvement[28].

In Iran, Sharifi Aghdas et al. assessed the results of the injection of AMDCs to treat SUI in a single-arm clinical trial at 2-year follow-up. They concluded that 59% of the 20 participants had a complete response in 2 years, and 12% had reported a partial improvement[29].

In the present study, although the analysis of the ICIQ-UISF and I-QOL questionnaires before and after cell therapy revealed a significant difference in treatment status and the difference remained until the end of the 1-year period, only a third of patients had an objectively complete response in 1 year. This shows that the effect of cell therapy decreases over time and there is a need for further injections to keep the response stable.

No randomized controlled experiment on the use of AMDCs for urethral sphincter repair has been published yet, but its primary results have been presented. The authors concluded that AMDCs could lead to stable decreases in incontinence episodes[30].

To the extent of our knowledge, no comparison has been made between the results of cell therapy and the standard treatment (mid-urethral sling) of SUI. The results of the present study demonstrated that periurethral injection of MDSCs and fibroblast can lead to an acceptable therapeutic response in patients; however, compared with the control group, the subjective response of cell therapy was significantly lower than that of the standard treatment. Moreover, this difference became even more significant over time. In terms of objective response, although there was no significant difference between the two groups in the first and third month, the response to cell therapy decreased significantly over time. In addition, no intraoperative and postoperative complications were observed in the two groups.

Nonetheless, the present study had some limitations, including the low number of participants, which was due to the high costs of using stem cells for treatment. Another limitation was the duration of the follow-up, which is not considered long enough. Moreover, another limitation was not using a subsequent injection of stem cells for the patients who had lower responses to the treatment; there was a possibility that subsequent injections could improve the results of cell therapy. Furthermore, the two groups were not compared in terms of the economic burden they imposed on the health system because the treatment was provided free of charge. Finally, it is recommended that such studies as this be conducted in larger sample sizes with more injections and longer follow-ups.

Conclusion

Periurethral injection of MDSCs leads to desirable subjective and objective results in patients with SUI. The effects of this treatment did not change significantly at 1-year follow-up. Moreover, it is a safe, convenient treatment methodology without complications; however, compared with the standard treatment, it has less efficacy. This indicates that more assessments are needed in order to establish cell therapy as a potential treatment for SUI.
References


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