The Effect of Intracavernosal Injection of Stem Cell in the Treatment of Erectile Dysfunction in Diabetic Patients: A Randomized Single-blinded Clinical Trial

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Purpose: The prevalence of erectile dysfunction in men is increasing. As well, the prevalence of diabetes, as one of the causes of sexual dysfunction, is rising in many countries. Due to the failure of common therapies in some patients with sexual dysfunction, it is necessary to develop an effective alternative treatment, such as stem cell therapy, for this problem.

Materials and Methods: In this randomized single-blinded clinical trial, 20 diabetic patients with erectile dysfunction, who were resistant to common treatments, were selected and divided into two groups of intervention and control (n=10 per group). Autologous mesenchymal stem cells (MSCs) were extracted from oral mucosa and then infused via intracavernosal injection (50-60 $\times 10^6$ cells) to the participants of the intervention group. Normal saline was injected in the control group. The patients were followed up with the International Index of Erectile Function (IIEF5) questionnaire, as well as color Doppler duplex ultrasound. Peak systolic velocity (PSV), end diastolic velocity (EDV), and resistance index (RI) were determined three and six months after the interventions.

Results: The mean IIEF5 scores in the intervention group were 7.2 ± 2.1, 9.2 ± 3.4, and 10.6 ± 4.7 before, three months, and six months after the injection, respectively, showing a significant ascending trend ($P = 0.01$). Comparing the intervention and control groups, there was a significant difference in the IIEF5 score change during six months after the injection ($P = 0.02$). Regarding the PSV and RI of penis vessels, there were no statistically significant differences between the two groups. However, these parameters showed upward and improving trends in the intervention group.

Conclusion: Intracavernosal injection of stem cells improved sexual function and PSV and RI indices of penile arteries in diabetic patients.

Keywords: diabetes; sexual dysfunction; intracavernosal stem cell injection

INTRODUCTION

Erectile dysfunction is defined as the inability to achieve sufficient erection for successful penetration.[1] Underlying causes are divided into psychological, organic, and a combination of these groups. Organic causes include neurogenic, vascular, hormonal, intracavernosal (e.g. structural), and pharmacological types.[2] Erectile dysfunction is also seen following pelvic surgeries such as radical prostatectomy or after pelvic trauma, which are mainly considered as neurogenic etiologies.[3,4] Common treatments for erectile dysfunction include oral phosphodiesterase 5 (PDE5I) inhibitors, prostaglandin suppositories (alprostadil), intracavernosal injection of vasoactive agents, vacuum erection devices, and penis implants. Psychosexual interventions have also a valuable role in the treatment process.[2,4] All patients should be counseled to adjust their lifestyle including diet modification, quitting smoking, reducing alcohol consumption, losing weight, and exercising.[2] The first line treatment of erectile dysfunction is using oral PDE5Is (such as sildenafil). These are guanidine monophosphate analogues which bind to the catalytic domain of PDE5 and inhibit its hydrolytic activity.[5]

In recent years, the popularity of stem cell therapy to treat erectile dysfunction has increased. The exact mechanisms of this method; however, are not yet clear. Until now, the stem cells derived from the bone marrow, fat, muscle, urine, neural crest, and endothelial precursors have been studied to treat sexual dysfunction.[6] Mesenchymal stem cells (MSCs) have the capacity to differentiate into a variety of cell types including muscle, cartilage, bone, and fat. [7] MSCs, through several mechanisms (e.g., paracrine effects and secreting cytokines and growth factors), can lead to immunomodulation, a reduction in inflammation, and improvement of healing process.[6,8,9] Stem cells can also produce smooth muscle, endothelium, and neurons.[6]

The potential of stem cells for treating erectile dysfunction has been investigated in multiple studies.[6,10-16] It has been shown that injecting stem cells to human and animal models is safe and effective and generates potent

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Table 1. The means of age and diabetes duration in the intervention and control groups.

Parameters	Intervention		Control		*P* value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Age (year)	63.8 (7.4)	65 (7.5)	65.6 (5.1)	67.5 (7.75)	0.56
Diabetes duration (year)	10.4 (3.5)	10.5 (6.75)	10.1 (3.1)	10 (5.75)	0.78

effects. Although a role for paracrine effects of stem cells has been proposed, the potential mechanisms by which stem cells promote their therapeutic effects are not yet well-understood.[14] Nevertheless, stem cell therapy in patients with erectile dysfunction seems a safe strategy without adverse side effects.[14,15] Considering the above-mentioned, further studies are needed to accurately assess the therapeutic potential of stem cells in patients with sexual dysfunctions.[6] This is important to know that many patients fail to respond to conventional drug therapies and need an alternative treatment. In this study, we aimed to investigate the effectiveness of intracavernosal injection of stem cells to treat erectile dysfunction in diabetic patients and improve their quality of life.

MATERIALS AND METHODS

In this randomized single-blinded clinical trial, 20 diabetic patients aged 50-70 years with erectile dysfunction, who were referred to the urology clinic of Bahonar Hospital in Kerman in 2019 were selected and divided into two groups of intervention and control (n=10 per group). These patients were non-respondents to the common treatments of erectile dysfunction, including PDE5I. They had received all available treatments based on patients' acceptance, indications, and contraindications and were resistant to all these treatments. They had been diagnosed with diabetes and erectile dysfunction without any other underlying disease

Sample Size

According to similar studies, our sample size was determined using the following formula:

$$n = \frac{2\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2 \sigma^2}{d^2}$$

Where $\alpha = 0.05$ (type 1 error), $\beta = 0.90$ (study power), $\sigma = 0.5$ (standard deviation based on the study of Yiou et al., [10] and d= 1 (effect size), which means that the study will be able to detect 1 unit of change in sexual performance with 90% power. Based on this, "n" was calculated 5 per group, which considering a possible loss of samples, n=10 per group was considered as the final sample size.

Randomization

This was a single-blinded study (main researcher physician is aware). The block randomization method was used including five blocks with each block consisting of two patients from each of the intervention and control groups (i.e., four subjects per block) to proceed with a balanced distribution of all 20 patients (10 subjects per group).

Study Protocol

Initial assessments included taking a history of prior illnesses, physical examination, blood pressure measurement, checking sexual status, and cardiac function via visiting a cardiologist. The International Erectile Dysfunction Index Questionnaire (IIEF5) was filled for all the patients. Laboratory tests included testosterone, prolactin, fasting blood sugar (FBS), LH, FSH, TSH, HbA1c, cholesterol (LDL, HDL), triglyceride, liver enzymes, and PSA. In addition, Doppler ultrasound of penis vessels was performed before the intervention. Patients with confirmed diagnoses of diabetes and sexual dysfunction, BMI of 20-25, and without any other diseases were enrolled. Those with laboratory or clinical signs of other disorders (especially diseases associated with erectile dysfunction) were excluded from the study.

The IIEF5 questionnaire consists of 5 questions (provided at the end of the article). In the intervention group, after local anesthesia, a tissue sample with a diameter of about 0.5 cm was obtained from oral mucosa so that there was no need for sutures. The samples were placed in phosphate buffer solution (PBS) containing antibiotics and amphotrypsin and immediately sent to the university stem cell storage center. In the control group, obtaining oral mucosa was only pretended by inserting a swap into the patients' mouth. The mucosal tissues were washed 3 times with PBS containing antibiotics and amphotrypsin and then cut into small pieces under sterile conditions. Afterwards, they were incubated in DMEM culture medium containing 4 mg/mL dyspase enzyme and 3 mg/mL type 1 collagenase at 4 °C for 24 hours. After that, the enzyme-containing medium was gently removed and replaced with DMEM containing 15% FBS and 1% antibiotic (penicillin/streptomycin). Incubation continued in a 5% CO_2 incubator with 95% humidity at 37 ° C for at least 10 days to allow the cells to grow. The adherent cells were then treated with trypsin, and after being detached, poured into T25 flasks and incubated under the same condition mentioned above. Finally, stem cell markers (CD 73+, CD90+, $CD10^5$+, CD34-, CD45-) were examined by flow cytometry to

Table 2. The score obtained from the International Erectile Dysfunction Index questionnaire in the intervention and control groups at 0, 3 and 6 months after the injection.

Time	Intervention		Control	
	The sum of scores (T) Mean (SD)	*P* value	The sum of scores (T) Mean (SD)	*P* value
Before injection (baseline)	7.2 (2.1)	0.01	7.2 (2.1)	0.87
3 months post-injection	9.2 (3.4)		7.2 (2.0)	
6 months post-injection	10.6 (4.7)		7.3 (2.1)	

Table 3. The mean scores of individual questions of the International Erectile Dysfunction Index questionnaire in the intervention and control groups at 0, 3 and 6 months after the injection.

Question	Intervention					Control			
	Baseline	3rd month	6th month	*P* value		Baseline	3rd month	6th month	*P* value
Q1	Mean (SD)	1.67 (0.5)	2.11 (0.92)	2.56 (1.02)	0.007	1.80 (0.63)	1.90 (0.31)	1.70 (0.48)	0.472
Q2	Mean (SD)	1.60 (0.69)	2.20 (1.2)	2.50 (1.3)	0.008	1.40 (0.51)	1.60 (0.51)	1.50 (0.52)	0.472
Q3	Mean (SD)	1.30 (0.67)	1.60 (0.84)	1.90 (1.19)	0.028	1.30 (0.48)	1.30 (0.48)	1.40 (0.51)	1
Q4	Mean (SD)	1.20 (0.42)	1.60 (0.84)	1.80 (1.03)	0.019	1.2 (0.42)	1.2 (0.42)	1.2 (0.42)	1
Q5	Mean (SD)	1.50 (0.52)	1.80 (0.63)	2 (1.20)	0.042	1.50 (0.52)	1.40 (0.51)	1.50 (0.52)	0.819

verify the purity, and if the purity was more than 95%, the cells were harvested for injection as a suspension. After obtaining adequate number of stem cells (50-60 × 10^6), they were frozen and sent to the urology operating room where, after thawing and diluting with 0.9% normal saline (up to 2 mL), they were injected to the patients of the intervention group (1 mL into each corpus cavernosum). The bottom of penis was clamped with a band before the injection and then opened 3 minutes after the injection. In the control group, normal saline was injected into the corpus cavernosum. The patients were followed up by filling the IIEF5 questionnaire, performing color Doppler duplex ultrasound to obtain PSV, EDV and RI parameters, as well as determining FBS and HbA1c at three and six months after the injection. In addition, morning erections were daily recorded by the patients. The patients were encouraged to have intercourse at least three times a week and use PDE5I (Tadalafil 10 mg) during the sexual relationship. The complications of the injection (pain, swelling, ecchymosis, etc.) were checked and recorded at each visit. They were fully explained about the stem cell therapy and their disease, and for ethical considerations, their written informed consent was obtained. This study was approved by the Ethics Committee of Kerman University of Medical Sciences (IR.KMU.AH.REC.1398.115).

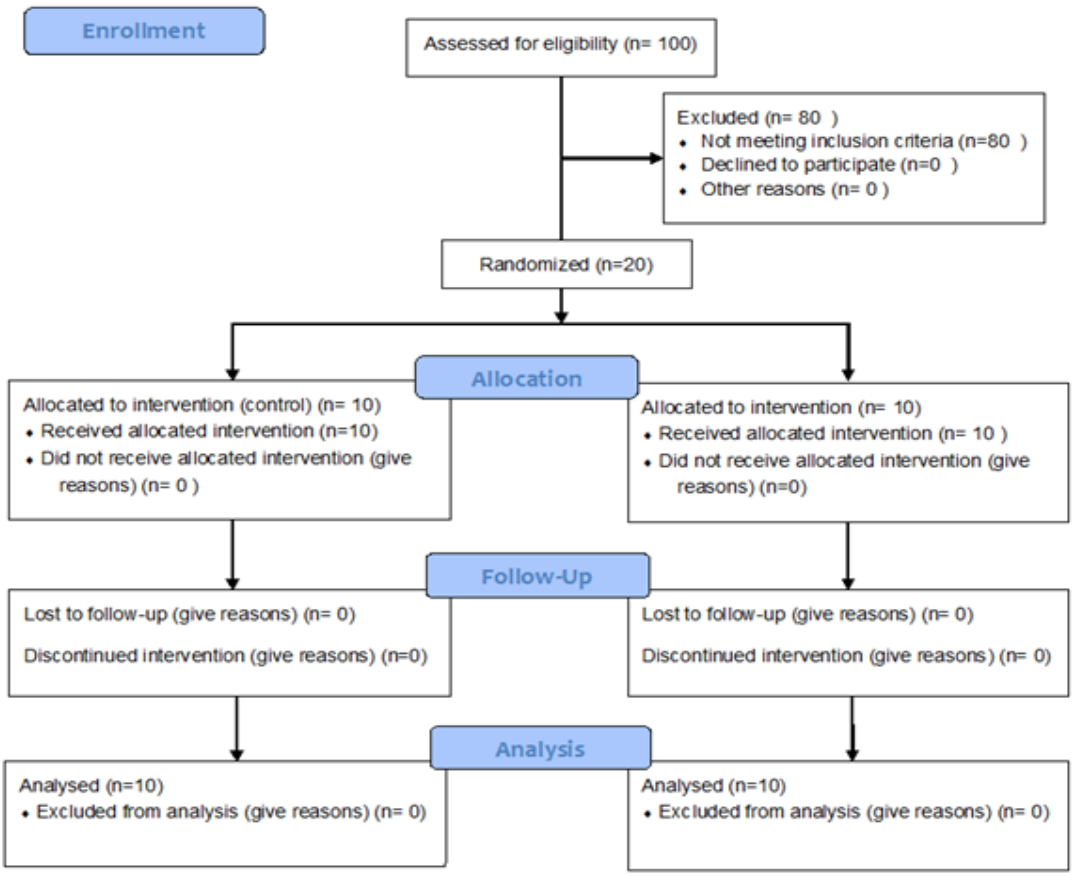

Figure 1. CONSORT diagram of the study.

Table 4: The trend of mean PSV index in the intervention and control groups at 0, 3, and 6 after the injection.

Time	Intervention PSV		*P* value	Control PSV		*P* value
	Mean (SD)	Median (IQR)		Mean (SD)	Median (IQR)	
Before injection (baseline)	8.26 (4.12)	7.7 (7.92)	0.67	8.21 (4.10)	7.5 (8.32)	0.11
3 months post-injection	9.14 (2.56)	8.7 (4.45)		8.29 (3.91)	7.5 (7.72)	
6 months post-injection	10.22 (2.09)	9.7 (3.55)		8.20 (3.87)	8.25 (7.47)	

This study was approved under the registration code of IRCT20190517043609N1 in Iranian Registry for clinical trials. The study protocols are available at this database.

Statistical Analysis

Finally, the data was analyzed by SPSS (version 22) statistical software. For describing the data, mean, standard deviation, frequency, and percentage were used. Age, diabetes duration, FBS, and HbA1c were compared between the groups using Mann-Whitney *U* test. The mean scores of the questionnaire, PSV, EDV, and RI were compared pre- and post-intervention using the Friedman test.

RESULTS

In this study, 20 diabetic patients with erectile dysfunction were selected and divided into two groups of intervention and control, 10 patients per group (**Figure 1**). The patients were recruited from 22 September 2019 to 19 February 2020. For all the participants, diabetes was under control after the intervention and during the six-month follow-up. The mean ages of the patients in the intervention and control groups were 63.8 ± 7.4 and 65.6 ± 5.1 years, respectively. The mean values of FBS at the baseline and six months after the intervention were 118 ± 9.5 and 117 ± 9.3 in the intervention group and 116 ± 9.3 and 118 ± 9.4 in the control group, respectively. The mean values of HbA1c at the baseline and six months after the intervention were 6.8 ± 2.1 and 6.7 ± 2 in the intervention group and 6.7 ± 2.05 and 6.8 ± 2.15 in the control group, respectively. The mean durations of diabetes were 10.4 ± 3.5 and 10.1 ± 3.1 years in the intervention and control groups, respectively. According to the Mann-Whitney U test, the means of age and diabetes duration were not significantly different between the intervention and control groups ($P > 0.05$, **Table 1**).

According to the Friedman test, the means of total IIEF5 score in the intervention group were 7.2 ± 2.1 (before the injection, baseline), 9.2 ± 3.4 (the third month after the injection), and 10.6 ± 7.4 (the sixth month after the injection), which showed a statistically significant improving trend (P = 0.01). In the control group, the means of total IIEF5 scores at baseline, three months, and six months after the injection were 7.2 ± 2.1, 7.2 ± 2, and 7.3 ± 2.1, respectively, showing an insignificant almost constant trend ($P = 0.87$). Comparing the two intervention and control groups according to the Mann-Whitney U test, the total IIEF5 score was significantly different at sixth month after the injection ($P = 0.02$, **Table 2**).

Based on the results of the Friedman test obtained in the intervention group, the mean scores related to each question (Q1, Q2, Q3, Q4, Q5) of the questionnaire showed a statistically significant ascending trend in all the questions from the baseline towards the end of the follow-up period. In the control group, the trend was significant in none of the questions (**Table 3**). Regarding the question related to acquiring sufficient erection for penetration after sexual arousal (Q2), out of 10 patients in the intervention group, two patients in half of the occasions and two patients in more than half of the occasions were able to achieve that at three months post-injection. At six months after the intervention, 4 patients were able to acquire adequate erections to penetrate in more than half of the occasions.

Based on the results of the Friedman test, in color Doppler ultrasound of penis vessels, the means of PSV index in the intervention group were 8.26 ± 4.12, 9.14 ± 2.56, and 10.22 ± 2.09 at the time of injection (zero month), three, and six months after the injection, respectively. This showed an ascending, but statistically insignificant trend (p-value = 0.67). The means of PSV in the control group were 8.21 ± 4.1, 8.29 ± 3.91, and 8.20 ± 3.87 at baseline, the third, and sixth month after the injection, respectively, indicating an almost constant and statistically insignificant trend ($P = 0.11$). There was no statistically significant difference between the two groups comparing PSV index, as evidenced by the Friedman test ($P = 0.25$, **Table 4**).

The means of EDV index in the intervention group were 1.8 ± 0.86, 2.13 ± 0.92, and 1.93 ± 0.85 at the time of injection (zero month), the third, and the sixth month after the injection, respectively. This trend was not statistically significant (p-value = 0.36). The mean EDV values in the control group were obtained 1.95 ± 0.83, 2.02 ± 0.81, and 1.99 ± 0.81 before, three months, and six months after the injection, respectively. This trend was also not statistically significant ($P = 0.49$). There was no statistically significant difference between the two groups regarding EDV index ($P = 1$, **Table 5**).

The mean values of RI in the intervention group were 0.77 ± 0.04 (baseline), 0.76 ± 0.09 (the third month post-injection), and 0.81 ± 0.06 (the sixth month post-injection) showing a slight upward and improving but statistically non-significant trend ($P = 0.15$). In the

Table 5. The trend of mean EDV index in the intervention and control groups at 0, 3, and 6 after the injection.

Time	Intervention EDV		*P* value	Control EDV		*P* value
	Mean (SD)	Median (IQR)		Mean (SD)	Median (IQR)	
Before injection (baseline)	1.80 (0.86)	1.8 (1.62)	0.36	1.95 (0.83)	2 (1.68)	0.49
3 months post-injection	2.13 (0.92)	2.4 (1.92)		2.02 (0.81)	2 (1.25)	
6 months post-injection	1.93 (0.85)	2.1 (1.60)		1.99 (0.81)	1.9 (1.45)	

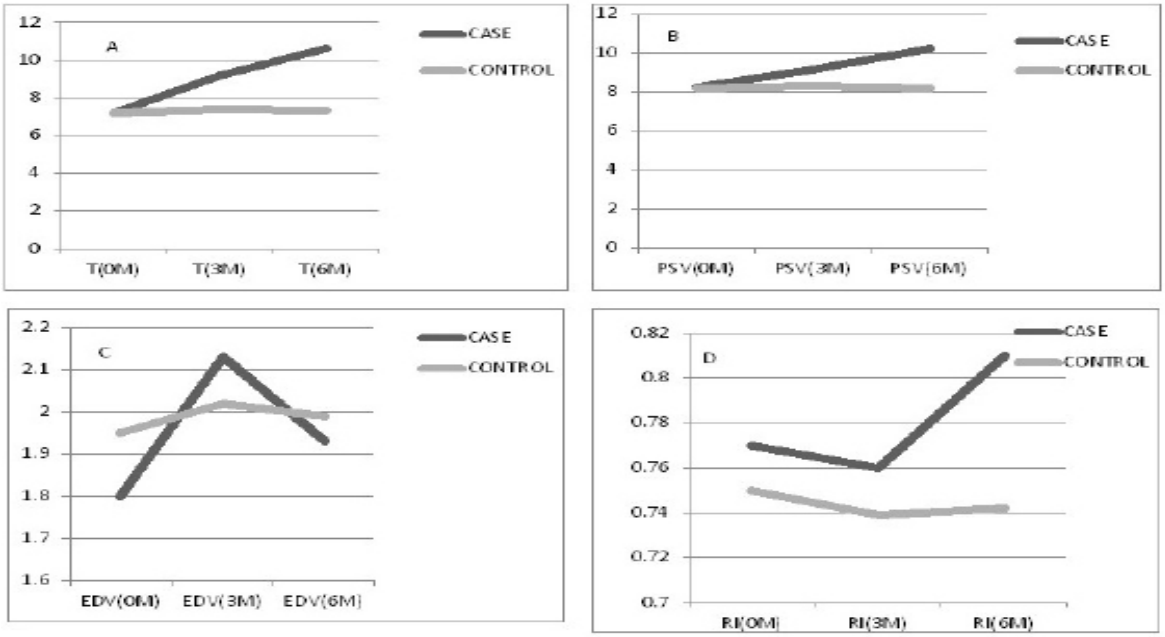

Figure 2. The trends of the International Erectile Dysfunction Index **(A)**, PSV **(B)**, EDV **(C)**, and RI index **(D)** in the intervention and control groups at 0, 3 and 6 months after the injection.

control group, mean RI values were recorded as 0.75 ± 0.03, 0.73 ± 0.05, and 0.74 ± 0.04 before the injection, and three and six months after the injection, respectively. Likewise, this descending trend was not statistically significant (*p*-value = 0.49). No statistically significant difference was noted between the two groups comparing the RI index ($P = 0.057$, **Table 6**).

Morning erection was reported by one patient from the intervention group at three-month and by another patient from the same group at six-month post-injection. No patients in the control group reported morning erection during the six months follow-up. None of the patients in neither the control nor the intervention group reported injection-related complications (bleeding, hematoma, ecchymosis, abscess, etc.) after six months follow-up. The trends of the IIEF5 score, PSV, EDV, and RI index in the intervention and control groups at 0, 3 and 6 months after the injection have been shown in **Figure 2**.

DISCUSSION

The interest in treating erectile dysfunction with stem cell injection is increasing.[6] The resistance of many patients to conventional therapies further highlights the need to develop new alternative treatments. Intracavernosal stem cell injection, the method studied here, can role as an effective option in this field and effectively improve these patients' quality of life. In a study by Peak et al. in 2016, they evaluated the effectiveness of multiple stem cell types in treating erectile dysfunction and showed that injected stem cells had paracrine effects on penis tissue and could differentiate to a variety of cells including smooth muscle cells, vascular endothelial cells, and neurons, suggesting prominent effects and excellent safety for this therapeutic method.[6,14] The recent study supports the positive effects of stem cell injection in the treatment of erectile dysfunction in diabetic patients, as observed in the present study.

In this study, we showed that intracavernosal injection of autologous mesenchymal stem cells (50-60 × 10^6) improved sexual function in most diabetic patients. There were also improvements in PSV and RI indices in color Doppler ultrasound of penis vessels in these patients. Regarding the total IIEF5 score, a statistically significant difference was noted between the intervention and control groups at sixth-month post-injection. Considering adequate erection for penetration after sexual arousal (the second question of the questionnaire), out of 10 patients in the intervention group, two patients in half of the cases and two other patients in more than half of the cases achieved sufficient erections to enter at three months after the injection. After a six-month follow-up, four patients who received stem cell injection acquired enough erection for penetration in more than half of the cases. In a similar study, Bahk et al. in 2010 investigated the effects of the intracavernosal injection of 15 × 10^6 cord blood mesenchymal stem cell

Table 6. The trend of mean RI index in the intervention and control groups at 0, 3, and 6 after the injection.

Time	Intervention RI Mean (SD)	Median (IQR)	*P* value	Control RI Mean (SD)	Median (IQR)	*P* value
Before injection (baseline)	0.77 (0.04)	0.79 (0.09)	0.15	0.75 (0.03)	0.74 (0.06)	0.49
3 months post-injection	0.76 (0.09)	0.76 (0.09)		0.73 (0.05)	0.75 (0.08)	
6 months post-injection	0.81 (0.06)	0.80 (0.14)		0.74 (0.04)	0.75 (0.08)	

in combination with oral PDE5I in seven diabetic patients with erectile dysfunction and revealed that after six months, two patients achieved successful erection for penetration. Finally, they concluded that stem cell injection had beneficial effects on the treatment of erectile dysfunction in diabetes and recommended further studies on larger statistical populations.[13] The results of the recent study were similar to ours; however, the rate of erection achievement was higher in our report (40% vs. 28%), which can be due to the higher dose of stem cells used in our study (50-60 × 10^6 vs. 15 × 10^6). In addition, the types of the stem cells used in these two studies were different (autologous mesenchymal vs. cord blood mesenchymal stem cells). Overall, both studies indicated the beneficial effects of stem cell injection in the treatment of erectile dysfunction in diabetic patients. In another study in 2018, Al Demour et al. infused 30 × 10^6 bone marrow-derived mesenchymal stem cells (BM-MSCs)
via intracavernosal injection to four diabetic patients at two 30-day apart occasions and reported significant improvements based on the IIEF-15 score within 12 months of the injection.[15] So, the results of the recent study, like ours, supported the beneficial effects of this therapeutic method in diabetic patients. In another study by Levy et al. in 2016, the effect of intracavernosal injection of placental stem cells in combination with oral PDE5I in the treatment of erectile dysfunction was assessed in eight patients. The findings showed that two patients within two months and three patients within three months nailed sufficient erections for sexual contact. Similar to our study, the trends of IIEF5 scores were not statistically significant at six-week, three-month, and six-month compared to the injection time.[17] The positive effects of stem cells in this condition can be related to their paracrine effects on the penis, which can promote the differentiation of smooth muscle cells, endothelial cells, as well as neurons, improving erectile dysfunction in patients with diabetes; nevertheless, the exact mechanisms are yet to be divulged.

In this study, out of 10 patients in the intervention group and based on total IIEF5 score, 6 patients reported improvements in sexual function and erection within six-month follow-up. In a similar study by Yiou et al.(2016), they injected stem cells (either 20 × 10^6 or 200 × 10^6 BM-MSCs) to 12 patients who developed erectile dysfunction following radical prostatectomy. In combination with oral PDE5I, nine out of 12 patients declared significant improvements in erectile function,[10] which was slightly greater than the ratio obtained in our study, which may be related to the differences in the infused doses and the nature of the stem cells used in our study compared with the recent report. In another study by Haar et al. in 2016, adipose-derived stem cells (ADSCs) were injected into 17 men who developed erectile dysfunction following radical prosatectomy and failed to respond to routine treatments. Overall, erectile function improved in eight of 17 patients, which enabled them to have sex (an improvement rate of 47%),[11] which was lower in comparison with our study (improvement of 60%). Nevertheless, the results of the recent study were similar to our study, showing the positive effects of stem cell injection in improving erectile dysfunction in about half of the patients.

In this study, of the 10 patients in the intervention group, one patient at three-month and another patient at six-month follow-up (two patients in total) reported morning erection. In a similar study by Bahk et al. ,[13] morning erection was reported in two of seven patients. In general, the results of these two studies indicated an improvement in the sexual function of patients following stem cell injection.

In our study, color Doppler ultrasound of penis vessels retrieved the mean PSV values of 8.26, 9.14, and 10.22 at baseline (before the injection), and the third and sixth month after the injection, respectively, in the intervention group. Although showing an upward and improving trend, but this was not statistically significant. Our finding was similar to that of Levy et al.[17] who also reported a remarkable improvement in PSV; nevertheless, the trend was statistically significant only at six-month follow-up. Overall, stem cell injection seems to have a significant impact on PSV index on color Doppler ultrasound of penis, which can be a predictor of improved sexual function in patients. This can be related to the ability of stem cells to differentiate to endothelial cells , ultimately leading to improved erectile function in diabetic patients via boosting the angiogenic network of the penis.[6]

Considering the EDV index in color Doppler ultrasound of penis, the mean values of EDV in the intervention group were 1.8 (baseline, zero time), 2.13 (the third month after the injection), and 1.93 (the sixth month after the injection). The trend was also not statistically significant. These results were similar to the study of Levy et al.[17] who noted insignificant and undesirable changes in EDV.

We noticed no side effects of intracavernosal stem cell injection during a six-month follow-up period. In this regard, our observation was similar to those of Levy et al.[17] and Yiou et al.[10]. In contrast, Haar et al.[11] in their study on 17 patients reported redness and swelling at the injection site in two patients, as well as penis hematoma, and scrotum, each in one patient. Al Demour et al. also noticed no considerable adverse effects on the function of the gastrointestinal, respiratory, cardiovascular, and nervous systems after two years of follow up.[15] According to a review study in 2021,[14] a drawback of nearly all studies in this area was the lack of a control group in assessing the safety and efficiency of the procedure, which in our study, this drawback was addressed by incorporating a control group.

Overall, intracavernosal stem cell injection appears to be a safe method with a low rate of complications. Another advantage of this therapeutic strategy is its positive effects on erectile dysfunction even after one injection. The therapeutic effects are generally long-term and more effective than other methods, obviating the need for using various drugs. Although the potential mechanisms of stem cells' actions are unclear,[12,14] it seems that the proliferation of MSCs can lead to immunomodulation and alleviation of inflammation via exerting paracrine effects on the production of cytokines and growth factors. In addition, stem cells can directly differentiate into smooth muscle and endothelial cells, as well as neurons.[6] This method also has lower costs compared with other methods such as implementing prosthesis. Finally, we observed no side effects in this study, indicating the excellent safety of this method. However, the efficiency of the method can be affected by the dose and nature of infused cells, the frequency of infusion, the underlying erectile dysfunction, and dura-

tion of follow up, which all should be considered when interpreting outcomes. Due to our relatively low sample size, caution must be taken when generalizing our finding to other patient with erectile dysfunction.
The limitations of this study included low sample size, one occasion of infusing cells, and the reluctance of some patients to receive the injection due to unpleasant feelings.

CONCLUSIONS

Due to the resistance of many patients with sexual dysfunction, especially in the case of concomitant diabetes, to conventional drug therapies, it is necessary to discover new alternative treatments for these patients. Based on our findings, it can be concluded that intracavernosal stem cell injection improves sexual function, as well as PSV and RI ultrasound parameters in most diabetic patients. For obtaining more accurate conclusions, it is recommended to conduct studies on larger populations.

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CONFLICT OF INTERESTS

None to declare.

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