Hyaluronic acid in the treatment of premature ejaculation by glans augmentation

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ABSTRACT

Background: Premature ejaculation (PE) is a sexual debilitating condition affecting a large number of men worldwide, influencing the patients' affective and emotional life. Hyaluronic acid (HA) is a natural and safe compound that has been widely used not only in the aesthetic medicine clinic but also for the treatment of osteoarthritis.

Objective: To show the effectiveness of a HA-based procedure for treatment of PE.

Patients and Methods: A total of 20 male patients were treated with HA injections in the deep dermis of their glans penis to increase the volume and the circumference of their penis to prevent male PE and improve the patients' and their partners' sexual satisfaction.

Results: At 6-month follow-up, intravaginal latency time was still significantly higher when compared with baseline values. The maximal glandular circumference was significantly increased at 6-month follow-up. At baseline, patients' self-rated satisfaction with sexual intercourse was 1.5±0.07, and partners' self-rated satisfaction with sexual intercourse was 1.48±0.06. At 6-month follow-up, patients' self-rated satisfaction with sexual intercourse was 6.2±0.08, and partners' self-rated satisfaction with sexual intercourse was 5.5±0.07. The procedure is well tolerated without adverse reactions.

Conclusion: HA injection is a promising treatment for PE.

Key Words: Glans augmentation, hyaluronic acid, premature ejaculation.

INTRODUCTION

Premature ejaculation (PE) is one of the most common sexual problems. The prevalence of PE has been estimated between 2 and 23%[1]. Mathers et al.[2] stated that among men older than 18 years, PE incidence is ~30–45% compared with 20–30% reported by most of the other studies. This shows that PE is a very prevalent sexual disorder.

A proofed integrated description for PE was released by the International Society of Sexual Medicine including the following observations:

1. Nearly in every intercourse, ejaculation is too early, occurring after 1 min or less after vaginal penetration, either from the first sexual attempt (primary PE) or a recent obvious decrease in intravaginal latency time (IELT) (secondary PE).

2. Nearly in every intercourse, there is a loss of control on ejaculation.

3. PE causes unfavorable personal sequelae, such as distress, upset, disappointment, or even avoidance of sexual relation[3].

PE was announced by the ‘Diagnostic and Statistical Manual of Mental Disorders, fifth ed.,’ as a part of a number of sexual dysfunction troubles which are highly distinguished by considerable failure in giving a sexual response or feeling pleasure in sex[4].

The treatment options available for PE included topical agents, creams, sprays, and systemic therapy[1]. The pharmacological treatment of PE includes using local anesthetic agents, antidepressants, and type 5 phosphodiesterase inhibitors; currently, dapoxetine is the only short-acting selective serotonin reuptake inhibitor that is licensed for PE treatment[5].

Filler materials have been used widely for augmentation of soft tissue in aesthetic surgery, but only recently in the field of glans penis augmentation, an important application
that allows achieving a volume sufficient to prevent PE has been found[6].

It has been shown that HA possesses many properties suggesting its value in multiple medical applications, particularly in ophthalmology, orthopedics, and soft-tissue augmentation with proven efficacy and safety, in the past decade[7].

Positive results in a 5-year long-term study have been reported by Kwak et al.[8]. In that study, they injected hyaluronic acid (HA) gel in 38 men. Compared with the 6-month follow-up, it was shown that IELT decreased at 5 years. However, it was still higher when compared with the pretreatment period. High satisfaction for the procedure, consisting of 76 and 63%, respectively, has been reported by the patients and their partners.

Furthermore, the effect of HA in 60 men who were affected by PE was evaluated by Abdallah et al.[6], showing that IELT increased 1 month after the injection of the compound in their penis.

We investigated the effectiveness of injection of HA in the glans penis deep dermis to expand the volume and the circumference of the penis, thus preventing male PE and improving the sexual satisfaction of the patients and their partners.

PATIENTS AND METHODS

This clinical study was conducted on 20 male cases presented with PE at outpatient clinics of Banha and Zagazig University Hospitals during the period from April to December 2017. Consent was taken from all patients before the study. Ethical approval for this study was provided by the Institutional Review Board for Faculty of Medicine, Zagazig University, and Banha University.

Inclusion criteria

The study included patients with PE, aged between 28 and 45 years, who were married with stable, monogamous, and heterosexual relationship for at least 12 months. Lifelong PE was diagnosed on the basis of the International Society of Sexual Medicine definitions, including the evaluation of IELT by stopwatch. Pre-assessment IELT was measured for a 4-week baseline period during which all participants were asked to have sexual intercourse at least four times. Penile skin vibratory sensitivity thresholds were assessed by means of a biothesiometer (Sensiometer A200; Laxons Technology Co. Ltd, Beijing, China), a tool that delivers vibratory stimuli and simultaneously quantitatively measures peripheral sensory thresholds at different genital sites and index finger.

Exclusion criteria

A history of medication that can affect ejaculation 6 months before the beginning of the study; a drug abuse history of within 2 years before enrollment for the procedure; a history of or current major psychiatric disorder, such as schizophrenia, mood and anxiety disorders, and other psychotic disorders, alcoholism, erectile dysfunction, and decrease interest of patients or their partners in sexual intercourse; and patients complaining of sexual problem (impotence) were the exclusion criteria.

METHODS

An informed consent was taken from the participants before history taking and sample collection. Informed consent represents one of the most fundamental rights of patient autonomy in medical decision making. All studied persons were subjected to the history taking, with respect to age, sex, marital status, occupation, education, residence, smoking habit, social history, and sexual history (from both partners).

Surgical procedure

Each patient underwent the procedure in a comfortable sitting position. The glans penis circumference was divided into three circles (from the base of the glans at a 1-cm distance from each other). Each circle was then divided into quarter circles. After application of the topical anesthetic cream Emla (lidocaine 25 mg, prilocaine 25 mg; AstraZeneca, Mississauga, Ontario, Canada) for 30 min, a single injection of 3 ml of HA gel (Hyalift 3.5% micronized HA; Aesthetic Dermal, Girona, Spain) using the multiple puncture technique described by AbdAllah et al.[6] was performed in the deep dermis into each quarter circle with a 27-G needle for a total of 12 points performed; only 0.25 ml was injected at each point.

The satisfaction of the patients and the partners was rated on the basis of Q5 How often was sexual intercourse satisfactory for you? and Q6 How often was sexual intercourse satisfactory for your partner?, where (a) almost never, (b) rarely (c) sometimes (d) often, and (e) most of the time, from the Arabic Index Premature Ejaculation by Arafa et al.[9] on a scale 1–5 (1=dissatisfied and 5=satisfied). IELTs of all patients were recorded before 1 month prior to the start of therapy and 1, 3, and 6 months after the injection. Postinjection adverse reactions were also reported. Moreover, evaluations of glans circumference were done. Following the procedure, no further aesthetic treatment was received, and no other psychotherapy medication was allowed during the study period. Computer software package SPSS 15.0 (IBM Corp., Armonk, New York, USA) was used in the analysis.
RESULTS

(Table 1) shows demographic data of the patients. The IELT increased significantly from 88.3±3.14 to 192.5±7.6 s 6 months after the procedure (P<0.001). Maximal glandular circumference increased from 90.5±0.7 mm before treatment to 105.6±0.8 mm at 6 months (P<0.001; Tables 2). At baseline, self-assessed satisfaction with sexual intercourse of the patients was 1.5±0.07. Self-assessed satisfaction with sexual intercourse of the partners was 1.48±0.06 (Table 3).

Table 1: Characteristics of the participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=20</th>
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<tr>
<td>Age (years) Mean±SD</td>
<td>32.5±5.9</td>
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<tr>
<td>Range</td>
<td>28–45</td>
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<tr>
<td>Duration (years) Mean±SD</td>
<td>5.3±2.1</td>
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<td>Range</td>
<td>3–9</td>
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Table 2: Intravaginal latency time and glandular circumference before and after treatment

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<tr>
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<th>n=20 (mean±SD)</th>
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<tr>
<td>Intravaginal latency time</td>
<td></td>
<td></td>
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<tr>
<td>Before</td>
<td>88.3±3.14</td>
<td>&lt;0.001  (HS)</td>
</tr>
<tr>
<td>After</td>
<td>192.5±7.6</td>
<td></td>
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<tr>
<td>Glandular circumference</td>
<td></td>
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<tr>
<td>Before</td>
<td>90.5±0.7</td>
<td>&lt;0.001  (HS)</td>
</tr>
<tr>
<td>After</td>
<td>105.6±0.8</td>
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There was a highly statistically significant (HS) difference in patients regarding intravaginal latency time and glandular circumference before and after treatment.

Table 3: Satisfaction in patients and their partner’s after treatment

<table>
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<th>Before (mean±SD)</th>
<th>After (mean±SD)</th>
<th>P</th>
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<tbody>
<tr>
<td>Self-rated satisfaction with sexual intercourse</td>
<td>1.5±0.07</td>
<td>6.2±0.08</td>
<td>&lt;0.001 (HS)</td>
</tr>
<tr>
<td>Partner’s self-rated satisfaction</td>
<td>1.48±0.06</td>
<td>5.5±0.07</td>
<td>&lt;0.001 (HS)</td>
</tr>
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At 6-month follow-up, self-assessed satisfaction with sexual intercourse of the patients was 6.2±0.08 (P<0.001). Self-assessed satisfaction with sexual intercourse of the partners was 5.5±0.07 (P<0.001; Table 3).

DISCUSSION

HA is a naturally occurring polysaccharide, present in the same chemical and molecular composition in the intercellular matrix of dermal layers of the skin of all species. Therefore, it is highly biocompatible to use animal sources in humans without having foreign body reactions[10].

Potential space existence, technical achievability, and long-term residence should be demonstrated to use injectable HA gel in glans penis augmentation, although the efficacy of HA has been proved in various fields[11].

This study demonstrates that the injection of HA can be efficiently used for PE treatment, leading to accomplishing a remarkable increase in IELT. At 6-month follow-up, IELT was still remarkably higher compared with baseline values (from 88.3±3.14 to 192.5±7.6 s after 6 months from the procedure). The maximal glandular circumference was remarkably increased at 6-month follow-up (from 90.5±0.7 mm before treatment, to 105.6±0.8 mm at 6 months).

At baseline, self-assessed satisfaction with sexual intercourse of patients was 1.5±0.07, and self-assessed satisfaction with sexual intercourse of partners was 1.48±0.06. At 6-month follow-up, self-assessed satisfaction with sexual intercourse of patients was 6.2±0.08 (P<0.001), and self-assessed satisfaction with sexual intercourse of partners was 5.5±0.07 (P<0.001).

Conforming to this study, the procedure is well tolerated without adverse reactions. We described an original approach based on HA to treat PE and confirmed the favorable outcome, which was previously reported in an experimental study in rabbits and dogs, in which HA was injected into the glans penis, thus proving its potential for glandular augmentation. In fact, after 6 months, HA can still be found in the glans penis lamina propria[12].

As a cause of PE, the hypersensitivity of the glans penis is still controversial. Human phallus skin is innervated by the dorsal nerve of the penis (DNP). Two different populations of axons compose the main trunk of DNP. The first group is that which travels along the dorsal midline and terminates in the glans, whereas the other group of fibers radiates from the main trunk over the lateral and ventral aspects of the penile shaft with branches to the corpus spongiosum and urethra. The DNP dorsal trunk divides into two to three nerve bundles 1–2 cm proximal to the corona glandis. The DNP and its branches along the shaft run just beneath the skin and fascia; the main branches within the glans are 3–6 mm from the epithelial surface. The nerve fibers extent, including in dorsal neurectomy, is important in postoperative sensory of the glans penis[13].

The sensory factors of the human glans penis were studied by Halata and Munger[14]. The human glans penis is covered by stratified squamous epithelium and a dense layer of connective tissue parallel to the dermis of typical skin. The papillary dermis is continuous with and blends into the dense connective tissue forming the tunica albuginea of the corpus spongiosum of the glans penis. Free nerve endings are present in almost every dermal papilla, and also the most numerous nerve terminals are scattered throughout the deeper dermis. Genital bulbs are
found throughout the glans but are most numerous in the corona and near the frenulum.

Taking the studies of Yang and Bradley\(^{13}\) and Halata and Munger\(^{14}\) in consideration, we can inject injectable implants into the dermis of glans penis just above the nerve terminal successfully.

The effect of glans augmentation with the use of injectable HA gel for treating PE by blocking tactile stimuli from reaching nerve receptors was evaluated by Kim and colleagues\(^{15,16}\). In 139 patients with PE, dorsal neurectomy (group I), dorsal neurectomy with glandular augmentation (group II), and glandular augmentation (group III) were performed, respectively. Two centimeters proximal to coronal sulcus, two branches of dorsal nerve were cut, preserving that of the midline. For glandular augmentation, 2 ml of HA was injected into the glans penis, subcutaneously. After each procedure at 6 months, glandular circumference changes were assessed by tapeline in groups II and III. In every group, ejaculation time, the satisfaction of patient, and satisfaction of partner were also assessed. Using HA as a safe and efficient approach for the augmentation of the glans penis and PE treatment was supported. They suggested that glandular augmentation with injectable HA gel is a safe and efficient method to reduce the sensation of the glans penis. Glans penis augmentation is an auspicious treatment for hypersensitivity of glans penis in patients of PE.

The therapeutic effect of HA gel injection in patients with PE was evaluated by Abdallah and colleagues\(^{15,16}\). A total of 60 men with self-reported PE who were referred to our outpatient andrology clinic were included in this study. Participants were randomly assigned using random sampling numbers into two distinct groups. Group A (n=30) received a single injection of 2 ml of HA gel using the previously described fan technique. Group B (n=30) received a single injection of 2 ml of the HA gel using the multiple puncture technique. Twenty-three (46.9%) patients received injection by the fan technique, whereas 26 (53.1%) patients received it through the multiple-point technique. The mean IELT increased significantly from 2.12±1.16 to 7.71±7.86 min, after 1 month of injection and then dropped to 5.32±3.52 min, but still remaining significantly higher than the baseline values. They demonstrated the usefulness of the application of HA dermal fillers in the treatment of PE.

Littara et al.\(^{17}\) showed the effectiveness of a HA-based procedure for treatment of PE. They supported that HA injection is a promising treatment for PE.

CONCLUSION

We supported the use of HA for the treatment of PE. Further studies, with a follow-up extending beyond 6 months, are necessary to determine with precision the long-term therapeutic capacity of this treatment. In aesthetic surgery, HA has been widely used, and the complications are very rare and promptly manageable by expert surgeons. Therefore, it is possible that such a procedure, based on the protocol that we are proposing, may be integrated into the aesthetic clinic and performed on a routine basis.

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES


