



Glans penis augmentation using hyaluronic acid for the treatment of premature ejaculation: a narrative review

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Abstract: Premature ejaculation (PE) is the most common self-reported male sexual disorder estimated to occur in approximately 5% of men in the general community. Penile hypersensitivity is thought to be an etiologic factor of lifelong PE. The role of glans penis augmentation using injectable hyaluronic acid (HA) for the treatment of PE is debatable and remains to be confirmed. The creation of a barrier at the level of the glans, by the bulking agent blocking accessibility and inhibiting the tactile stimuli to reach the dorsal nerve of the penis (branch of the pudendal nerve) receptors, is the theory behind the effectiveness of HA in the field of PE. We reviewed the literature using PubMed and searched for the following keywords: premature ejaculation, glans penis and HA, over the last 20 years. Five studies were found. These studies showed that HA injection could significantly increase IELT (2.43- to 4.46-fold), and this increase could persist for long term (up to 5 years). No serious adverse reactions were reported besides transient discoloration and swelling of the glans that recovered to normal within 2 weeks. Many techniques were discussed, their effectiveness remains to be proved. However, proper patient selection and mastering the esthetics of the technique, by adequate surgical training, is necessary in order to achieve the optimal results.

Keywords: Hyaluronic acid (HA); glans penis; premature ejaculation (PE); intravaginal ejaculation latency time (IELT); augmentation

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Introduction

Premature ejaculation (PE) is the most common self-reported male sexual disorder. The two most relevant and evidence-based definitions of PE are those of International Society for Sexual Medicine (ISSM) and American Psychiatric Association (DSM-V) (1). The prevalence of PE is inconsistently variable throughout history and sometimes even overestimated. However, an approximately 5% prevalence has been reported as most consistent with Clinical PE per Althof *et al.* in 2014 (2). Both definitions agree on the chronic aspect of this disorder and the relatively short time

interval between penetration and ejaculation (≤ 1 min), the diminutive or the absence of voluntary control of ejaculation, and the negative consequences, such as distress in nearly all vaginal penetrations (3,4). A third definition has been recently proposed by the American Urological Association Guidelines 2020, PE is defined as poor ejaculatory control, associated bother, and ejaculation within about 2 minutes of initiation of penetrative sex that has been always present for lifelong PE, and ejaculation latency that is markedly reduced from prior sexual experience for acquired PE (5). Two main subtypes of PE are distinguished based on the duration of

intravaginal ejaculation latency time (IELT), frequency of reports, and course in life. In lifelong PE, early ejaculation is present at nearly every intercourse within 30 to 60 seconds in the majority of cases (80–90%) or between 1 to 2 minutes (10–20%). Conversely, acquired PE occurs at some point in life, it is often situational and preceded by normal ejaculation experiences.

Lifelong PE may be due to 5-HT_{2C} hyposensitivity and/or 5-HT_{1A} hypersensitivity but also to peripheral penile hypersensitivity (1,6,7).

The sensory innervation of the penis is provided by the deepest divisions of the pudendal nerve which pass through the Alcock canal and continue as the dorsal nerves of the penis. These nerves richly supply the glans. They travel alongside the dorsal arteries. On the other side, small branches of the perineal nerve supply the ventrum of the penis (1).

Several forms of pharmacotherapy have been used in the treatment of PE. These include the use of topical local anesthetics, long- or rapid-acting and short half-life SSRIs (dapoxetine), tramadol, phosphodiesterase type 5 inhibitors, and α -adrenergic blockers. Psychosexual cognitive behavioral therapy and coaching has an important role as an adjunct to pharmacotherapy. Surgical neurotomy, percutaneous cryoneurolysis or neuromodulation of the dorsal penile nerve are surgical therapies described in some studies.

Among them, the role of glans penile augmentation

Table 1 Summary table

Study	n	Design	Location	Groups	Quantity of HA (mL) and needle gauge (G)	Mean age	Evaluation interval	IELT (s)	VT (mA)	GC (mm)	Patient satisfaction	Residual volume
Kim et al. 2004	139	Three arms, non-randomized, prospective study	Seoul, Korea	I: dorsal neurectomy (n=25)	N/A	43.2 [25-67]	Pre	89.2 [30-150]	4.14 [3-7]	N/A	68% (17/25)	N/A
				II: dorsal neurectomy with glandular augmentation (n=49)	2 cc of Perlanes, 27 G	41.8 [28-70]	Pre	101.5 [25-180]	4.38 [3-7]	15.41 [13-16]	80% (39/49)	N/A
				III: glandular augmentation (n=65)	& N/A cc of Restylanes, 30 G		6 months	324.2 [220-480]*	9.80 [8-12]*			
					2 cc of Perlanes, 27 G	42.1 [27-66]	Pre	96.5 [35-210]	4.54 [3-7]	16.58 [12-17]	75% (49/65)	N/A
					& N/A cc of Restylanes, 30 G		6 months	165.5 [115-235]	5.65 [4.5-6.5]	16.22 [12-22]	75% (49/65)	N/A

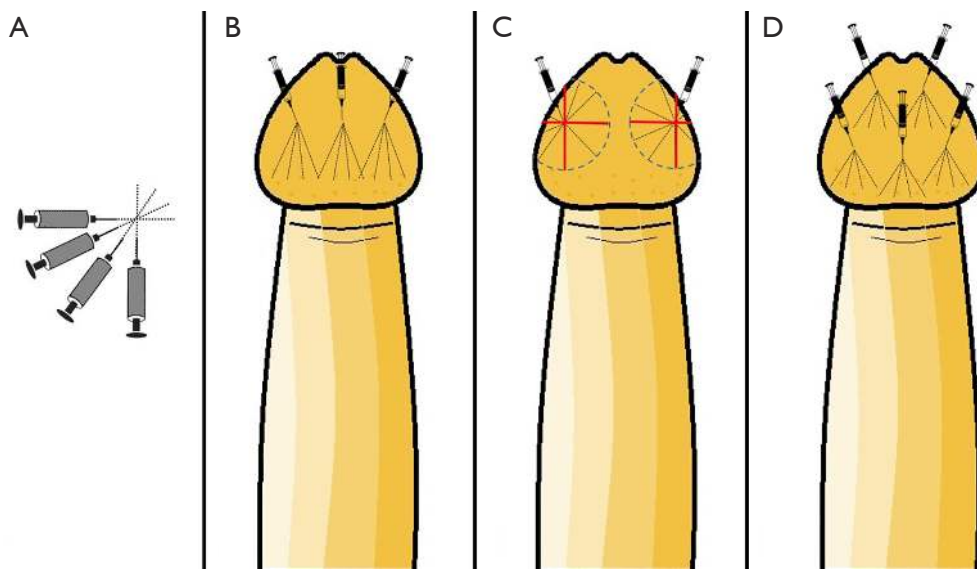


Figure 2 Injection techniques. (A) The fan technique; (B) Kim *et al.* one-third technique; (C) the three circles technique; (D) the two circular levels technique.

inhibiting the tactile stimuli to reach the nerve receptors, is the theory behind the effectiveness of HA in the field of PE (7). HA can be successfully injected into the dermis of glans penis just above the nerve terminal (9).

HA has been shown to possess many valuable medical properties. It is biocompatible, non-antigenic, non-pyrogenic, non-inflammatory, and nontoxic. It is also easy to use, stable after injection, non-migratory, long lasting but reabsorbable, and natural looking (7). HA has a characteristic of isovolemic degradation (9). The appropriate filler can restore symmetry, volume and create a smooth skin surface (10).

Techniques

Kim *et al.* performed glans penis augmentation under local anesthesia, 30 min after topical application of Emla (lidocaine and prilocaine), 2 cc of injectable HA gel, Perlanes®, was injected via 27-gauge needle. Injection needle was indwelled subcutaneously at proximal one-third from tip of glans to coronal sulcus. Thereafter, HA gel was injected by Fan technique (Figure 2A,B). After injection of Perlanes, undulation of glandular surface was

performed in a single session.

In 2019, Alahwany *et al.* modified the technique used by Abdallah *et al.* Under topical anesthesia (30 min of Emla cream), two prefilled 1 ml syringes of cross-linked HA were injected with 30 G needle (Teosyal®) using multiple puncture technique at two circular levels: one at the level of corona and the second one mid-way between the corona and urethral meatus. Six injections were performed at coronal level and four in the second level, each injection containing 0.2 mL into deep dermis (*Figure 2D*). All participants were previously circumcised.

Outcomes

The designs, the results and the conclusions of the different articles are presented within the summary table (*Table 1*). Vibratory threshold (VT) of glans penis was measured using a biothesiometer.

Interestingly, in all five studies, IELT was significantly increased at every interval evaluation. A rise of 2.92 times at 6 months was demonstrated by Kim *et al.* with 75% patient satisfaction. It was increased even more, by 4.46 times at 6 months and 4.18 times at 5 years for Kwak *et al.* with 76% overall patient satisfaction. Similarly, an increase of 3.58 times and 2.43 times at 1 month was observed, respectively, for Abdallah *et al.* and Alahwany *et al.* Littara *et al.* also

considering the small surface and space as well as the low elasticity present within the glandular area. Finally, the number and the distribution of injection sites remains to be tailored according to each glans anatomical appearance and surgeons' experience while considering the risk/benefit ratio. The main risk of multiple injections being the increased incidence of injections sites complications (ecchymosis, pain, local infection...) while the main benefit being esthetically more adequate and homogenous repartition of the filler material throughout the glandular surface.

The reason behind performing a prior circumcision in the setting of glans penis augmentation is probably purely esthetic. However, some studies had shown that distal circumcision itself may be an effective surgical treatment of lifelong PE in patients with an excessive prepuce (13,14) while others rejected this theory (15).

It is noteworthy to mention that most of these studies (except that of Kwak *et al.*) lack long term follow-up (*Table 1*).

Another limitation is patient satisfaction assessment. In fact, two studies only reported the patient satisfaction rate and this was done using a non-validated tool (*Table 1*).

Finally, it is important to note, in these studies, the small samples size, the extremely variable and different patient

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