Intralesional Verapamil Injection in the Treatment of Peyronie's Disease: Initial Experience

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ABSTRACT

Background: Peyronie's disease is a wound-healing disorder occurring in a presumably genetically vulnerable individual, can cause the penis to abnormally curve, causing painful erection and problems in intercourse. Intralesional injection has proved the promising therapy and reasonable approach in selected patients. It is an alternative treatment to surgery. Verapamil works on fibroblasts, also it increases collagenase activity in scar tissues

Objectives: To report the effect of intralesional verapamil injection in the treatment of Peyronie's disease through its effects on penile pain, curvature, plaque size and erectile function status.

Methods: Twenty-nine men with Peyronie's disease received intralesional verapamil injection; every week for 6 injections; 25 completed the study. We used 10 mg of verapamil diluted to 6 ml normal saline. A multiple puncture technique were distributed throughout the plaque. Patients initially were assessed regarding penile pain, erectile function, plaque size and curvature angle before initiation of the treatment protocol, 3 months later after 6 weekly injections. All above parameters scores were re-evaluated.

Results: All 25 patients with Peyronie's disease. Mean patient age was 40.4±4.6 (30-50) year. None of our patients had history of penile trauma or sexually transmitted diseases. Penile pain resolved in 88% of the patients, while 62% reported an improvement in the ability to engage in coitus. The plaque size shows 50% reduction in patients enrolled in study measured objectively.

Conclusions: Intralesional verapamil injection of Peyronie's disease contributed to the improvement of penile pain, sexual function, and decreased plaque size. We recommend using intra-lesional verapamil injection as first line therapy instead of oral agents.

Keywords: Peyronie's disease, Penile pain, Verapamil.

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Peyronie's disease (PD) is a wound-healing disorder occurring in a presumably genetically vulnerable individual whose tunica albuginea responds improperly to a provoking event, most commonly to penile trauma, with a proliferative fibrotic reaction resulting in a profuse inelastic scar found in a flaccid penis[1]. This disordered healing process can cause the penis to abnormally curve, causing painful erection and problems in intercourse[2,3].

Intralesional verapamil acts through its effect on fibroblasts; it increases collagenase activity in scar tissues and decreases matrix deposition[4,5].

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Verapamil inhibits collagen biosynthesis by blocking DNA biosynthesis[6].

Intralesional injection is promising therapy and is the only alternative treatment to surgery recommended by the European Association of Urology (EAU) guidelines[7].

The aim of the study is to evaluate the role of intralesional verapamil injection (IVI) in the treatment of PD through its effects on penile pain, curvature, plaque size and erectile function.

Methods

Of 29 men with Peyronie's disease who were offered intralesional verapamil injection (IVI) in a prospective, 25 completed treatments from Sept. 2016 until Sept. 2018.

Patients who recently diagnosed with PD those had penile plaque, with curvature not intervening with coitus, with ability to attain erection and sexual intercourse spontaneously or on phosphodiesterase 5 inhibitors were included in this study.

Patients were excluded if they had been taken oral agents (potassium para-aminobenzoate, colchicine, tamoxifen), treated by penile shock wave therapy, or prior intralesional agents within last 3 months of commencing intralesional therapy or duration of symptoms more than 18 months.

The assessment of the patient was made by a detailed history, physical examination and sexual function using the International Index of Erectile Function (IIEF-5) include five domains (erectile function, orgasm, sexual desire, intercourse satisfactory and overall satisfaction)[8].

All patients were interviewed before commencing treatment and the schedule of injections were explained to them, three month later reevaluation were undertaken regarding the following parameters (Penile pain, curvature, plaque size, erectile status and adverse effects).

The pain was assessed by visual analogue scale of pain (VASP). "It is a pain assessment tool range from 0-10 scale for patient self-assessment, it helps patient care provider assess pain intensity"[9].

While, degree of curvature was assessed by goniometer applied to a photography of the penis in different angles taken by the patient himself during erection at home. The plaque size was measured in square cm by a ruler and/or gray scale ultrasound.

Intralesional injection technique: In this study, a dose of 10 mg of verapamil (two ampoules) each (5 mg/2 ml) diluted to 6 ml of isotonic saline. Apply antiseptic to the site of injection. A penile block with 5 ml 2% xylocaine solution was used at base of penis, needle passed below the symphysis pubis at midline then directed on either side. Verapamil was distributed throughout the plaque using a 23-gauge needle. A multiple puncture technique was performed. Once the needle has been withdrawn, we apply local pressure and apply a dressing.

Analysis of data was carried out using the Statistical Packages for Social Sciences version 25 (IBM Corporation). The significance of difference of different percentages were tested using Pearson Chi-square test (2-test) with application of Yate's correction or Fisher Exact test whenever applicable.

Results

Of 29 men with Peyronie's disease only 25 patients completed treatment schedule. Mean patient age was 40.4±4.6 (30-50) year. None of our patients had history of penile trauma or sexually transmitted diseases.

Penile pain during erection was present in all 25 patients but with different degrees from (1-10) were assessed according to Visual Analogue Scale of Pain.

Regarding penile plaque of our study group 25 patients, n:16 plaques were in dorsal midline proximal shaft, n:5 plaques at dorsal midline in mid-shaft of penis and n:4 plaques at dorsolateral penile shaft.

All 25 patients had erectile function sufficient for intercourse (spontaneously or on phosphodiesterase 5 inhibitors).

The statistical analysis of following parameters penile pain, curvature, plaque size and erectile status were detailed: Penile pain of 25 PD patients, 22 (88 %) patients their penile pain decreased significantly after intralesional verapamil injection according to VASP score dropped from 6.2 ±1.5 pretreatment to 3.6 ± 1.5 post treatment. Erectile function of studied patients was assessed by using five domains of IIEF. The score increased from 17.3 points ±3.9 pretreatment to 25.3 ±2.1 points post treatment. This improvement seen only in 17 patients (68%) enrolled in study. Plaque size (cm^2) 50% of patients their plaque size decrease from 2.9 cm^2 ±1.0 pre-injection to 2.2 cm^2 ±1.2 post-

injection but this change was not statistically significant. More than two thirds of patients n: 17 had penile plaque their size ranging from 1-4 cm² pre-injection. Curvature angle data were incomplete, only 8 patients brought a photograph of their erect penis; we found their penile curvature was decreased from 41.4° ±9.7 to 36.4° ±10.7.

Ten patients had associated medical conditions n: 4 diabetes mellitus, n: 6 patients hypertension. Eight patients were smokers and one patients had Dupuytren's contracture.

Complications: Intralesional verapamil injection technique is safe and associated with minimal morbidity as shown in table 1.

Table 1: Complications of intralesional verapamil injection.

Peyronie's disease side effects	No.	%
Ecchymosis	2	22.2
Pain	6	66.7
Nausea	1	11.1
Hypotension	-	-
Arrhythmia	-	-

——————————Discussion

Peyronie's disease natural history, diagnosis, and treatment remains a matter of a conflict. Multiple intralesional therapies have been used like verapamil, collagenase clostridium histolyticum (CCH), hyaluronic acid, and interferon α-2b[7,10].

A questionnaire for 639 urologists showed 67% of urologists used intralesional verapamil injection[11].

In this study, we used calcium antagonist (verapamil) as intralesional injection in addition to its efficacy it is available and cost effective therapy. IVI was done on weekly basis, while other studies injection were every 2 weeks, we believe that patient compliance was better than every two weeks. Results of IVI were variable. 88% reported their penile pain were improved after IVI according to visual scale of pain.

Other studies reported that penile pain reduction was noticed in 90-100% after IVI[12-14]. One study used phosphodiesterase inhibitor in addition to intralesional verapamil author stated that more pain control and better sexual capacity achieved[15]. PD has negative effect on erectile function; which is due to vascular insufficiency similar to the etiology found in the general public with ED alone[16,17].

The improvement of erectile function after IVI seen in 62% of patients enrolled in the present study which is statistically significant change (P= 0.001), our findings is similar to other study that found improvement about 66%[18]. Other intralesional (hyaluronic acid, interferon α-2b and clostridium collagenase histolyticum CCH drugs also revealed improvement in erectile capacity[10].

The plaque size reduction was seen in 50% of patients, other study stated that change of plaque size also was not significant and about 2 mm decrement in plaque size[19]. While in the present, study it was found about 4 mm probably this difference in readings related to different method of plaque measurement.

As multiple puncture technique might help in fragmenting the plaque and the role of verapamil as remodeling agents but we need to emphasize on the error of measurement of plaque that might happened in pre and post injection that could affect our results.

While the study of Sharma R et al they revealed better overall success with verapamil over placebo cases. Reduction in plaque size was 56%[18]. Our results compared with other studies outlined in table 2.

Our reported complications were minimal mainly pain at time of injection and mild bluish discoloration (ecchymosis) that resolved spontaneously.

Limitation in this study included incomplete data of penile curvature response to IVI. In addition, it was a non-comparative study.

Table 2: Comparison of this study data with other series.

Parameter	Levine LA-2000 (12)	Bennet -2007 (13)	Heidari M-2010 (14)	Sharma et al -2014 (18)	This study
No. of patients	156	94	16	67	25
Study type	Non-randomized prospective study	Non-randomized uncontrolled trial	Randomized clinical trial	Randomized single blind ,placebo controlled study	Non-randomized prospective study
Drugs	Verapamil	Verapamil	Verapamil	Verapamil	Verapamil
Dosage	10mg every 2 weeks	10 mg every 2 weeks	10 mg every 2 weeks for 6 months	10 mg every 2 weeks	10 mg every week
No. of Injections	12	6	12	6	6
Pain reduction	>95%	100%	> 90%	97%	88 %
Sexual Improvement	72%	26%	……	66%	62%
Improved Curvature (%)	60%	18%	30%	62%	…….
Plaque size reduction (%)	……	……	30%	56%	50%

In conclusion; Intralesional verapamil injection of PD contributed to improvement in penile pain, sexual function, and decreased plaque size. We recommend using intralesional verapamil injection as first line therapy instead of oral agents.

This study had been done in accordance to the ethical standards laid down in the ' 1964 Declaration of Helsinki' revised in the year 2000.

Both authors No conflict of interest

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