

Evaluation of Intralesional injection of Verapamil in treatment of Peyronie's disease

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Abstract

Objective: To evaluate the effect of intralesional injection of verapamil in Peyronie's plaque with confirmed lesion.

Methods: This randomized clinical trial was carried out between March 2005 and March 2006 on 16 patients with Peyronie's disease who were referred to the Urology Clinic of Shohadaye Ashayer Hospital in Khorram Abad, Iran. Performing a comprehensive physical exam, the genitalia of the patients were checked to confirm the diagnosis and reject other sexual disorders. Besides, parameters such as penis curving, lesion size were measured. Then, based on the 10-point visual analogue scale, sexual satisfaction of patients and their wives were recorded in a questionnaire. Patients got intralesional verapamil every 14 days and were treated for 6 months. After that, the parameters were assessed and data collected was analyzed using paired t-test. P-value <0.05 was considered statistically significant.

Results: On average, lesion size and penis curving decreased 30%. Almost 20% of patients and their wives were satisfied with the outcome of the treatment. No significant side effect was seen during the treatment.

Conclusion: Injection of calcium channel blockers are effective for treatment of the Peyronie's disease; however, more studies with more patients are needed (JPMA 60:291; 2010).

Introduction

The presenting symptoms of Peyronie's Disease (PD) include induration and curvature of the penis due to fibrosis in a layer of tunica albuginea in the penis shaft, painful erection, and erectile dysfunction (ED).^{1,2} Severe deformities of the penis, a flail penis, impaired vascular function, stress and anxiety are the factors that lead to ED³ which has a prevalence of 30% in PD.⁴ Etiology is unknown but factors such as trauma to the penis during intercourse and sudden penis curvature are said to be the major causes.^{5,6}

Most of the patients recovered by conservative treatment; however, some with severe deformity required surgical procedures.⁷ Various treatments have been used like; oral drugs as vitamin E, para-amino benzoate, tamoxifen and colchicine; and systemic or local injections such as steroids, collagenase, interferon and verapamil. Some patients require surgical intervention.^{7,8} But none of the aforementioned treatments proved absolutely satisfactory. However, local injection of verapamil has been effective in a number of investigations. Verapamil, which is a calcium antagonist, was first used as an intralesional treatment of PD in 1994. It can alter the fibroblast genesis in extra cellular matrix. Verapamil plays a role in the balance of the metabolism of extra cellular matrix by inhibition of collagen product and increasing collagenase

proteolytic activity. Calcium inhibitors modify the release of cytokines, interleukins 6 and 8 and plaque growth factor; and inhibit the inflammation process and formation of fibrotic tissue. Therefore, calcium antagonists have a potential to decrease, inhibit or invert the plaque formation and development of PD.^{7,8} The purpose of this study was to assess the effectiveness of the intralesional verapamil injection in the treatment of Peyronie's disease.

Patients and Methods

This randomized clinical trial (RCT) was carried out between March 2005 and March 2006 on 25 patients with PD who were referred to the Urology Clinic of Shohadaye Ashayer Hospital in Khorram Abad, Iran.

Patients who had the disease for at last 6 months were included. Patients with complications of Peyronie's Disease, having undergone multiple treatment and with co-morbid as diabetes mellitus, hypertension, renal failure, and heart diseases were excluded from this study. Furthermore, patients who were in the acute phase of the disease and those with diffuse fibrous plaque along the penis were also excluded. Finally, 16 patients could fulfill the inclusion criteria and were enrolled in this study.

The study subjects underwent a genitalia physical examination. The lesion size was measured by colis and the extent of the fibrous plaque was determined through

sonography by a single sonologist. For measuring the penile curvature, in case of an erection, the penis was captured on a film by the patient himself and was shown to his physician and the medical intern, before and after the treatment. Besides, the patient's and his wife's satisfaction of sexual activity was recorded based on the 10-point visual analogue scale. Then, patients received intralesional injection of verapamil 10mg/cm² every 2 weeks for a total of 6 injections and were followed for 6 months. Eventually, data were analyzed using paired t-test and p-value <0.05 was considered significant.

Results

The patients studied were in the age range of 40-69 years, mostly 50-56 years. Table-1 demonstrates the comparison of lesion size and penis curvature before and after verapamil injection in patients with PD. There were statistically meaningful association of p<0.001 and p<0.004

steroids and intralesional therapies including steroids, interferon and verapamil.

The advantage of injective drugs is that they are used weekly or every 2 weeks and are easy to administer. Systemic steroids have severe side effects including immuno suppression, osteoporosis, skin disorders, hypertension and cataract. The local injection of steroids leads to skin atrophy at the injection site in addition to aforementioned side effects which may cause difficulties in next probable surgery.¹⁰ In a study done by Gol Bard and colleagues in 1993, on 49 men with Peyronie's disease, the intralesional collagenase outweighed the placebo. Interferon has been reported to be successful in inhibiting the proliferation of fibroblasts and increasing the collagenase production,¹² but it is expensive and has side effects like transient flu-like symptoms, hypotension and gastrointestinal disorders.¹³⁻¹⁵ Calcium channel blocker

Table-1: Comparison of lesion size and penis curving before and after verapamil injection in patients with Peyronie's disease.

Variables	Number		Mean		S.D		Mean difference	P-value
	Before	after	Before	after	Before	after		
Lesion size (cm ²)	16	16	1.84	1.34	0.83	0.92	0.5	<0.001
Curving of penis (%)	16	16	17.18	12.5	16.52	13.4	4.86	<0.004

Table-2: Comparison of sexual activity satisfaction before and after verapamil injection in patients with Peyronie's disease and in their wives.

Variables	Number		Mean		S.D		Mean difference	P-value
	Before	after	Before	after	Before	after		
Satisfaction of sexual activity in patients	16	16	4.62	5.81	1.40	1.64	-1.18	<0.001
Satisfaction of sexual activity in patients' wives	16	16	4.43	5.31	1.75	2.15	-8.7	<0.001

*Patient's and his wife's satisfaction of sexual activity was recorded through a questionnaire based on the 10-point visual analogue scale.

between the lesion size and penis curvature with verapamil injection, respectively.

The comparison of sexual activity satisfaction before and after verapamil injection in patients with PD and their wives are demonstrated in Table-2. There was a significant difference between patients' and their wives' satisfaction of sexual activity before and after verapamil injection (p<0.001).

On the whole, the lesion size, penis curvature, patient's satisfaction of sexual activity and the wife's satisfaction improved to 27%, 27%, 20% and 17%, respectively, compared to before treatment.

Discussion

Most of the patients in this study were in the age range of 50-56 years which is compatible with a study done in Minnesota,⁹ where the average age of onset of PD was reported 53 years with a prevalence of 0.4%. Various protocols have been reported for treatment of PD such as oral drugs like vitamin E, systemic injective drugs as

drugs like verapamil can decline the interplaque formation and development of PD, theoretically.^{7,16,17} It has been observed that if lesion size is larger than 2cm², the lesion is like a ring around the penis and there is no desirable response to treatment.

In a study performed by Levin et al in Ohio University in 1997 on 46 patients, decrease in penis curve and improvement in sexual activity was reported as 54% and 72%, respectively.¹⁶ Considering the outcomes, our findings seem to provide more acceptable results.

In a study carried out by Levin et al on 156 patients with PD, of those who completed the treatment with intralesional verapamil, 60% had a decrease in penis curvature and 71% had an increase in sexual function.¹⁷ In a study done by Rahman et al¹⁸ in 1998 in Virginia University on 14 patients, decrease in plaque size in patients and control group was reported as 57% and 28%, respectively, and the lesion size decreased from 1.42cm² to 0.63 cm². Decrease in penis curvature was reported in 30% of patients. Improvement in sexual activity in patients and

control group was reported 43% and 0%, respectively. Our study is comparable with these findings.

In another study performed by Helstrom¹⁹ in Florida University in 2006 on 14 patients, decrease in penis curving was seen in 62% of patients, and 71% had improvement in their sexual activity. It appears that the difference between treatment outcome in our patients and other studies is due to the lesion size. Lesion size was smaller in other studies in comparison with our subjects. On the other hand, it can be as a result of a smaller number of patients enrolled in our study.

Apparently, injection of calcium channel blocker drugs seems to be effective in the treatment of PD, however, further investigation must be carried out in this regard.

Conclusion

The study concluded that injecting a calcium channel blocker agent in the fibrous plaque of Peyronie's Disease leads to the reduction of size of the plaque and improved sexual satisfaction both the patient and his spouse.

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