

Effectiveness of Intralesional Verapamil versus Saline for Treatment of Peyronie's Disease- a Randomized Single Blind, Placebo Controlled Study

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Abstract

Objective: Peyronie's disease has been known to mankind for long, but still the treatment remains a dilemma. We investigated the efficacy of intralesional verapamil over saline.

Methodology: We randomized 70 patients into two groups, receiving verapamil and NS intralesionally, after assessing their symptoms, plaque characteristics, curvature in erect state and erectile function. After 6 biweekly injections, all above parameters and satisfaction score was reexamined.

Result: Out of 35 patients in verapamil group and 32 in NS group, reduced plaque size, attenuated curvature and better erection were found in 56%, 62% and 66% of patients respectively in former group. In NS group improvement in above mentioned parameters were 32%, 38% and 41% (P value=0.083, 0.085 & 0.071) however extent of improvement was less compared to former. Pain decreased in both groups considerable 97% and 91%. Overall satisfaction level was higher in verapamil group 74% to NS group of 39% (P value=0.008).

Conclusion: Intralesional verapamil is a good alternative non-surgical therapy for Peyronie's disease with overall decent success rate and minimal complications.

Keywords: Peyronie's disease, penile plaque, penile curvature, verapamil

Abbreviations: NS- Normal saline, PD- Peyronie's disease

I. Introduction

Peyronie's disease is a condition characterized by formation of fibrous plaque within tunica albuginea of corpora cavernosum. It presents as a palpable induration over shaft of penis. Estimated prevalence ranges from 0.5% to 13% [1]. One-third of these patients report having difficulty related to sexual activity, due to bending, lessened rigidity, plaque, shortening or pain [1]. Precise etiology of PD is uncertain, repeated trauma appears to be inciting cause, though most patients do not recall any event. Diagnosis is based on history and physical examination, followed by ultrasound. There is no definite treatment so far except surgery, which is indicated only in minority of patients with severe curvature precluding sexual intercourse and/or erectile dysfunction in stable disease [2]. For mild to moderate disease, variety of non-surgical approaches including medical therapy, intralesional therapy, radiation, penile traction devices and ESWT are available, however most studies are not randomized and are underpowered [3]. In our randomized controlled study we evaluated response and treatment related effects of intralesional verapamil in patients of active PD.

II. Methods

We included 70 patients of peyronie's disease in the study, between 2011 and 2014, after proper consent and ethical committee approval. Patients <18 years, >60 years and having calcified plaques were excluded. Presenting symptoms like pain, curvature, palpable nodule, difficulty in intercourse, rigidity, erectile dysfunction and duration were recorded. Physical examination included stretched penile length, plaque measurement and degree of curvature assessment following artificial erection using intracavernosal papaverine. Photograph of penile deformity during erection taken. Erectile functions were assessed using International Index of Erectile Function (IIEF) tool. Penile duplex scan was done in all subjects. Patients were randomized into two groups. One group received intralesional injection of verapamil 10 mg (5mg/2cc) diluted to 4cc volume with saline using 25G needle. Injection site were compressed for 2minutes followed by blood pressure monitoring to 30 minutes. Routine penile blocks were not given. Other group received 4cc of normal saline using similar protocols. Biweekly 6 injections were given in both groups. Reassessment was done at 3 month, which included symptom profile and phallus examination following artificial erection. Medcalc application was used for calculation. Endpoints used were change in plaque size (width, length or depth, softening), resolution of plaque related symptoms, changes in penile curvature and overall sexual satisfaction.

III. Results

Out of 70 patients included in the study, three were lost to follow up. Mean age was 44 years, range from 30-58 years. 2 patients had history of Dupuytren's contracture and 3 had positive family history. 12 patients reported onset of disease after penile trauma during sexual intercourse. The mean time between onset of the disease and diagnosis was 7 months (range: 1-11 months). Pain during erection was found in 35 patients [Table 1]. Erectile dysfunction was present in 15 patients. 5 patients reported difficulty having sexual intercourse. Mean plaque volume was 1.3 ml; range from 1.4 to 2.6 ml. Sixty one patients had single plaque, while 6 patients had two plaques. Mid-shaft was the most common site of plaque in 47 patients, while proximal and distal shaft was involved in 9 and 11 patients respectively. 60 patients had plaques on dorsal aspect and 6 had it on ventral aspect. Penile curvature was mild in 42 patients, moderate in 23 patients and severe in 2 patients; (Using Kelamin classification). Mean penile curvature and stretched penile length was 36 +/- 5 degree and 11 +/- 3 cm. Baseline characters were similar in both groups.

After randomization, 35 patients received injection verapamil (Group 1) and 32 received normal saline (Group 2). In group 1, 56% of patients had reduction in plaque size (mean reduction in length 1.2 ± 0.14 cm, width 0.44 ± 0.21 cm and volume 0.43 ± 0.17 ml), 62% had decrease in curvature (25.2 ± 3.7 degree) and 95% were relieved of pain [Table 2]. Improved quality of erection was noted in 66% of patients and overall satisfaction score was good in 74% (average in 16% and poor in 10%). In group 2, 32% of patients had plaque volume reduction (0.3 ± 0.12 ml), 38% had decreased curvature (20 ± 4.1 degree) and 91% reported pain subsidence [Table 3]. Quality of erection was improved in 41% of patients and overall satisfaction level was good in 39% of patients.

IV. Discussion

Peyronie's disease has been known for decades. Despite much research in its pathogenesis, natural history and diagnosis, treatment remains dilemma. Verapamil, with its effect on fibroblasts, has been found to decrease matrix deposition and increased collagenase activity in scar [4]. Initially Levine et al. (1994) and Rehman J et al. (1998) reported successful outcome with verapamil, though these studies were underpowered [5, 6]. Recent research on intralesional verapamil has shown variable success rate from 30% to 60% [Table 4].

Bennett et al, in his study on 94 patients in 2007, reported 18% improvement in curvature and 100% resolution of pain, however it was a non-randomized study and satisfaction level was not recorded in patients [7]. Cavallini et al worked on various dilution of verapamil in his randomized study and shown improved efficacy with increasing dilution, though not statically significant [8]. In another double blind, placebo controlled study done by Greenfield JM in 2007, on electromotive drug administration of verapamil versus saline, demonstrated modest superiority of former with increasing dilution [9]. Shirazi et al, in his randomized, single blind, placebo controlled study in 2010, did not found any improved outcome (17.5% v/s 12.8%) with verapamil over saline injection [10]. Zuchhi et al in 2010, showed promising result with combining verapamil with betamethasone, with improvement in curvature in 51% (n=56), plaque size reduction in 43% and better sexual function in 72% [11]. Heidari et al in his randomized clinical trial in 2010 reported mixed result with plaque size reduction and curvature improvement in 30% (n=16) of patients [12].

In our study, we found better overall success with verapamil over placebo cases. Reduction in plaque size was 56% with verapamil versus 32% with NS (P value=0.08), similarly decrease in curvature was 62% versus 38% (P value=0.085), [Table 4]. Pain reduction was above 90% in both groups, suggesting natural resolution over a period of time. Satisfaction level however, was definitely high in verapamil group 74% versus 39% (P value=0.008),. Reason for measurable decrease in plaque size and curvature with NS was not completely understood, though psychological affect cannot be ruled out.

V. Tables

Table 1: Baseline characteristics of study population

Parameters	Range	Mean
Age (years)	30 – 58	44
Duration of Symptoms (months)	1 – 11	7
Plaque Length (cm)	0.5 – 2.5	1.7
Plaque Width (cm)	0.4 – 2.3	1.3
Plaque Volume (ml)	1.4 – 2.6	1.33
Plaque Curvature (Degree)	22 – 56	36
Stretched Penile Length (cm)	8 – 14	11

Table 2: Difference in size of plaque and curvature after treatment in both groups

Parameter	Verapamil group (35 patients)		NS group (32 patients)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Plaque Length (cm)	2.5 ± 0.31	1.2 ± 0.14	2.4 ± 0.30	1.6 ± 0.36
laque Width (cm)	1.1 ± 0.26	0.44 ± 0.21	1.2 ± 0.22	0.8 ± 0.25
Plaque Volume (ml)	1.33 ± 0.21	0.43 ± 0.17	1.30 ± 0.23	0.91 ± 0.21
Penile Curvature (Degree)	36 ± 5	22.2 ± 3.7	34 ± 6	28 ± 4

Table 3: Subjective and objective response after treatment both groups.

Parameter	Verapamil group	NS group	P Value
Plaque Size			
• Decreased	56%	32%	0.083
• Same	44%	68%	
Penile Curvature			
• Decreased	62%	38%	0.085
• Same	38%	62%	
Quality of Erection			
• Better	66%	41%	0.071
• Same	34 %	61%	
Pain			
• Relieved	97%	91%	0.60
• Not Relieved	3%	09%	
Satisfaction Score			
• Good	74%	39%	0.008
• Avg	16%	36%	
• Poor	10%	25%	

Table 4: Comparison of our data with other series

Parameter	Rehman J-1998	Levine LA-2000	Bennet-2007	Greenfield JM-2007	Zucchi A-2010	Shirazi M-2010	Heidari M-2010	Our series-2014
No of patients	14	156	94		56	80	16	67
Study type	Randomized single blind study	Non-randomized prospective study	Non-randomized, uncontrolled trial	Randomized double blind, placebo controlled trial	---	Randomized single blind, placebo controlled study	Randomized clinical trial	Randomized single blind, placebo controlled study
Drugs	Verapamil	Verapamil	Verapamil	Verapamil	Verapamil + Betamethasone	Verapamil	Verapamil	Verapamil
Dosage	weekly for 6 months	10mg every 2 weeks	10mg every 2 weeks	10 mg verapamil**, twice weekly for 3 months	10mg/4mg every 2 weeks	---	Every 2 weeks for 6 months	10mg every 2 weeks
No. of injections	24	12	6	24	10	---	12	6
Improved curvature (%)	28%	60%	18 %	30%	26.6%	17.5%	30%	62%
Plaque size reduction (%)	57%	-----	-----	65%	43%	17.5%	30%	56%
Pain reduction (%)	-----	>95%	100%	-----	96%	30%	>90%	97%
Improvement of sexual function (%)	42.87%	71%	26%	-----	84%	5%	-----	66%
Satisfaction score (Good)	---	---	---	---	---	---	20%	74%

** - via electromotive drug administration, ----- Data not applicable or available

VI. Conclusion

Peyronie's disease is a bothersome problem, by the virtue of anxiety and stress it brings to the patient and lack of standardized treatment. In our randomized control trial, we found considerable improvement in symptoms and statistically significant benefit in overall satisfaction level in verapamil group compared to placebo. We recommend intralesional verapamil to be decent alternative to other nonsurgical treatment, with fair discussion with patient regarding variable but notable success rate.

Conflict of Interest

Author has no conflict of interest of any kind to this article.

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