

**COMPARATIVE STUDY OF ORAL AND INTRALESIONAL VERAPAMIL IN PEYRONIE'S DISEASE**Saju P. R<sup>1</sup>, Vaibhav Vikas<sup>2</sup>, Praveen Gop<sup>3</sup>, Rustum Singh Kaurav<sup>4</sup><sup>1</sup>Additional Professor, Department of Urology, Trivandrum Medical College, Trivandrum.<sup>2</sup>Senior Resident, Department of Urology, Trivandrum Medical College, Trivandrum.<sup>3</sup>Senior Resident, Department of Urology, Trivandrum Medical College, Trivandrum.<sup>4</sup>Senior Resident, Department of Urology, Trivandrum Medical College, Trivandrum.**ABSTRACT****BACKGROUND**

Treatment of Peyronie's disease is a dilemma for the treating urologist. Part of this problem is due to an incomplete understanding of the aetiopathophysiology of the disease. Multiple nonsurgical treatment are available for Peyronie's Disease (PD) including calcium channel blocker verapamil, both oral and intraplaque injectable. The use of verapamil is based on its capacity to alter fibroblast function and promote collagen degradation. As a result, calcium channel antagonists may have the capacity to slow, prevent or even reverse plaque formation. There are many studies suggesting benefits of intraplaque verapamil injection. In our study, we aim to compare the outcomes of oral versus intraplaque verapamil injection in terms of pain reduction, decrease in curvature and improved sexual function.

**MATERIALS AND METHODS**

In this randomised study, 20 patients were randomly divided into 2 groups of 10 patients each (Group I patients were treated with oral verapamil and group II patients were treated with intraplaque verapamil injection). Results from both the groups were compared and interpreted in terms of change in plaque size, curvature, erectile function and pain. Size of plaque was assessed with the help of color Doppler in pre and post-treatment period. All the 20 patients were followed for 3 years after completion of treatment. None of the 20 patients lost to follow up.

**RESULTS**

30% of group I patients (oral verapamil) showed decreased plaque volume. Softening of plaque was noted in only 60% of the patients. Subjective erectile dysfunction improved in only 40% of the patients. In group, II patients who received intraplaque verapamil injection, 70% showed decreased plaque volume with improvement in penile curvature. There was softening of the plaque in all the patients in group II. Subjective erectile dysfunction improved in 60% of the patients. No local or systemic toxicity was noted except mild ecchymosis in 2 patients of group II.

**CONCLUSION**

This study concludes that intraplaque verapamil injection is more effective and reasonable option than oral verapamil in nonsurgical patients of Peyronie's disease. Maximum benefits are seen up to 3 months of treatment.

**KEYWORDS**

Verapamil, Plaque, Peyronie's Disease, Intraplaque Injection.

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**BACKGROUND**

Peyronie's Disease (PD) is a disfiguring and psychologically devastating localised connective tissue disorder of the penis. It may cause formation of plaque, penile deformity, pain, erectile dysfunction, penile shortening, indentation, hourglass deformity of penis and emotional stress. Treating a patient of PD still poses a dilemma and frustrating situation for the practicing urologist till date. Since, it is a localised

disease, a focal therapy appears to be most appropriate. Additionally, the patients are not easily convincible to undergo penile surgery.

Many therapeutic approaches have been mentioned in the medical literature since de La Peyronie's description of induratio penis plastica. Surgical as well as nonsurgical options are available. Nonsurgical therapy involves extracorporeal shockwave therapy, radiotherapy, iontophoresis, oral agents such as vitamin E, colchicine, tamoxifen, Potaba and intraplaque injection of compounds including collagenase, steroids, Orgotein, interferon alpha 2B and verapamil. In our study, we have compared the efficacy of oral versus intraplaque verapamil injection.

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### Aims and Objectives

To compare the efficacy of oral verapamil versus intraplaque verapamil injection in patients of Peyronie's disease.

### MATERIALS AND METHODS

In this study, 20 patients were randomly divided into two groups (10 in each group). None of the 20 patients lost to follow up. Patients in group I received oral verapamil and group II patients received intraplaque verapamil injection. Results from both the groups were compared in terms of change in plaque size, pain, penile curvature and sexual life.

The patients were evaluated by detailed history (including enquiry about sexual and erectile dysfunction) and physical examination. Plaque length was measured by calipers and color Doppler was done to confirm the size and volume of plaque. All the patients were followed for a period of 3 years.

#### Inclusion Criteria

1. Age range 25 to 75 years.
2. Clinical evidence of Peyronie's disease (plaque/pain/curvature)
3. Duration of symptoms for at least 1 year.

#### Exclusion Criteria

1. Any history of previous treatment for Peyronie's disease.
2. Patient on calcium channel blocker therapy for some other reasons.

**Technique-** Group I patients were advised to take oral verapamil 40 mg daily for 6 months.

Group II penile blockage was given with 2% lidocaine. The verapamil was injected into the plaque with an insulin syringe. Punctures were done in plaque at appropriate places to distribute the drug uniformly throughout the plaque. Instillation was done by fanning technique. The verapamil was injected as 20 mg in 2 mL (1 mg/0.1 cc) weekly for 6 weeks- cycle was repeated after 6 months. The injection site was compressed for 10 minutes to prevent haematoma formation. Blood pressure and heart rate were continuously monitored throughout the procedure. No systemic or local toxicity was noted except for mild ecchymosis in 2 patients. The needle was inserted into the dorsolateral or lateral side depending up on the location of plaque to prevent nerve injury.

### RESULTS

Objective and subjective data were collected after completion of the study. Objective assessment was done by physical examination and measurement of plaque volume by colour Doppler ultrasound 3 monthly. Subjective data included questionnaire 3 monthly. Follow up as above was done for 3 years and none of the patients lost to follow up. The groups were compared using the unpaired Student's t-test at a significance of  $P < 0.05$ .

30% (3/10) of group I patients (oral verapamil) showed decreased plaque volume by mean of 15%. Softening of

plaque was noted in only 60% (6/10) of the patients. Subjective erectile dysfunction improved in only 40% (4/10) of the patients.

In group II patients who received intraplaque verapamil injection, 70% (7/10) patients showed decreased plaque volume by 43% with improvement in penile curvature. There was softening of the plaque in all the patients in group II. Subjective erectile dysfunction improved in 60% (6/10) of the patients. No local or systemic toxicity was noted except mild ecchymosis in 2 patients of group II.

### DISCUSSION

PD was first described in 1743 by the French physician Francois Gigot de la Peyronie. It has a prevalence of 8.9%.<sup>1</sup> Age group to be affected is between 45 and 60 years, however, men as young as 15 years have been reported.<sup>2</sup> Pathology involved behind PD is still unclear, but studies show that it is a wound-healing disorder occurring in a genetically susceptible individual whose tunica albuginea responds inappropriately to an inciting event, most commonly trauma (silent microfracture) leading to a proliferative fibrotic reaction resulting in formation of plaque and persistent scar.<sup>3,4</sup> PD plaque does not resolve due to absent or malfunctioning metalloproteinase and/or elevated levels of tissue inhibitors of metalloproteinase (TIMPs).<sup>4</sup> Resultant fibrous scar causes multiple deformities of the penis including curvature, narrowing, indentation, hinging, loss of penile length, pain, psychological distress and sexual dysfunction.<sup>5,6</sup> Spontaneous improvement occurs in 3% to 13% of patients, but up to 30% to 48% patients may worsen if left untreated.<sup>7</sup> 40% to 50% patients have ED at the time of presentation.<sup>8-11</sup> At this point of time, nonsurgical approach does not seem to benefit the patient, but treatment does appear to be able to stabilise scar progression and possibly reduce deformity and improve function.<sup>12</sup> So, nonsurgical treatment should be considered in the active phase (progressive deformity with painful erections) of the disease (less than 12 months from onset). Surgery is the gold standard treatment once the disease process is stable. Informed consent for any PD treatment must be taken as these patients are both physically and psychologically devastated. Urologist's aim is to make the penis functionally straight without compromising rigidity.

There is paucity of studies investigating the clinical benefits of oral therapy for PD, but the published placebo-controlled trials show that there is no evidence of benefit with the use of oral vitamin E, Potaba, colchicine, tamoxifen, carnitine or omega-3 fatty acids.<sup>12,13</sup> Injection therapy has also been used for many years starting with intralesional steroid injection. Intralesional verapamil shows decreased Peyronie's disease-derived fibroblast proliferation and decreased extracellular matrix production in vitro.<sup>14-16</sup> Levine et al<sup>17</sup> reported in the Journal of Urology in 1994 study involving 14 patients who were injected with intralesional verapamil biweekly for 6 months. Of these, 91% had resolution of pain, 42% had decrease in curvature and 58% had subjective improvement in erectile dysfunction, while 100% noticed an increase in penile girth. Levine et al<sup>18</sup> in

1997 conducted a nonrandomised prospective study in 1997 involving 46 men. Of the 38 men who completed the study, pain resolved in 97% of the patients (who initially presented with pain) after a mean of 2.5 injections. 76% of patients had a subjective decrease in curvature, 9.5% noted a worsening, while 14.5% reported curvature stability. 72% patients had an improvement in functional erection and the ability to engage in coitus. 54% patients reported decrease in curvature, an increase in 11% and stability in 34%. Levine et al<sup>19</sup> in 2002 conducted prospective nonrandomised study of 156 patients with a mean disease duration of 17.7 months and found that of the 121 of 140 patients who completed therapy (10 mg of intralesional verapamil biweekly over 24 weeks), and were re-evaluated with a second duplex ultrasound, penile curvature decreased in 73 (60%, mean reduction of 30°, range 5-90°), increased in 10 (8%, mean increase of 26°, range 5-45°) and remained unchanged in 38 (31%). These three papers by Levine et al established the optimal dose of intralesional verapamil at 10 mg.

Nine non-controlled published trials of intralesional verapamil showed consistently that 30% to 60% of patients had measured reduction of curvature when the subject was used as his own control with a mean reduction of curvature in the responder group being between 15 to 30 degrees.<sup>13</sup> Mulhall et al<sup>20</sup> reported in 2006 that of his 246 patients, 89% of them had resolution of pain, while 12% improved, 40% remained stable and 48% had worsened curvature. In 2007, Grasso et al<sup>21</sup> followed 110 patients for 6 years and reported 68% of younger patients (<50 years old) versus 31.5% of older patients (>50 years old) experienced progression of penile curvature with more patients in the older subgroup experiencing resolution of pain (69% vs. 20%). This was contradicted by Berookhim et al<sup>22</sup> who reported 176 men with uniplanar curvature on conservative management and were followed for >12 months. 67% experienced no change in penile curvature, 12% improved with a mean of 27° change and 21% worsened (mean change of angulation of 22°). These studies suggest that although pain from Peyronie's disease is often self-limiting, the clinical course of penile curvature is less predictable and needs treatment to prevent worsening loss of sexual function.

Complications reported by use of intralesional verapamil were minor ranging from pain at the injection site, penile bruising, nausea and giddiness. The latest AUA guidelines relating to the treatment of Peyronie's disease do not forbid the off-label use of verapamil in a properly precounselled patient after taking into consideration the previous evidence of benefit and the lack of serious adverse events.

## CONCLUSION

Most of the patients are understandably hesitant to pursue surgery and are willing to undergo the repeated injections to achieve a less invasive approach to their deformities. Verapamil is appropriate for less stable disease and in softer plaques. For technique, a fanning technique is appropriate for verapamil, administered via a 21G needle for maximum hydrodistention. The best results are seen when patients comply with manipulation of the plaque via a combination of

stretching, gentle bending of the erect penis in the opposite direction of the curve and massage of the plaque.

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