DOI: 10.4081/aiua.2020.3.253

ORIGINAL PAPER

Intralesional injection of the calcium channel blocker Verapamil in Peyronie's disease: A critical review

Murad Asali [1], Muhammad Asali [2]

[1] Assuta Medical Center, Ben Gurion University of the Negev, Beer Sheva, Israel;
[2] International School of Economics, Tbilisi, Georgia; IZA, Bonn, Germany; and School of International and Public Affairs, Columbia University, New York.

Summary ***Objective: To assess the effectiveness of an intralesional injection of verapamil in men with Peyronie's disease (PD).***
Materials and Methods: The data provided in the current review are based on a thorough review of the available original articles on PD retrieved with a systematic literature search using PubMed- Medline, and the Cochrane Central Register of Controlled Trials, up to December 2019, to identify studies dealing with Peyronie's disease and its treatment. Included were only original articles, that we thoroughly evaluated. We searched for the primary and secondary terms of: "Peyronie's disease," "Penile curvature," "Erectile dysfunction," "Verapamil and Peyronie's disease," "Calcium channel blocker," and "Intralesional injection."
Results: The initial search of the databases yielded a total of 1240 studies (PubMed: 1058; Cochrane: 182), as of December 2019. Seventy studies were removed due to duplication. Further 986 studies were removed due to not being in English (except for one study by Arena F. for which we got a translation form Italian), being about animal experimentations, not being full-text, and not being clinical trials. Likewise, studies not referring at all to verapamil were excluded (148). From the remaining 36 full-text articles we focused on 13 studies which met the inclusion criteria, mainly being deemed relevant to the context of this study.
Conclusions: Calcium channel blockers have been shown in both in vitro and in vivo studies to inhibit the synthesis and secretion of extracellular matrix molecules, as well as to increase collagenase activity. Patients with localised plaque are the best candidates for intralesional injections of verapamil. The beneficial effects of intralesional verapamil are apparent within the first three months. For patients who respond to treatment, the injections should be continued for six months. Patients who fail to respond to intralesional verapamil or whose angulation is greater than 30° at presentation should be considered candidates for surgery. Injection of verapamil is clinically safe for patients with Peyronie's disease, and it appears to induce a rapid, beneficial effect in patients for the reduction of plaque size. Intralesional verapamil injection for Peyronie's disease could reduce pain, decrease penile curvature, and improve sexual function.

KEY WORDS: *Peyronie's disease, Verapamil, Calcium channel blocker, Penile curvature, Erectile dysfunction.*

Submitted 2 March 2020; Accepted 15 March 2020

INTRODUCTION

Peyronie's disease (PD) was described in the eighteenth century by de la Peyronie as an induration of the male sexual organ's tunica layers (1). The estimated rate of the disease is 3.2% to 8.9% (2, 3). Although more than 260 years have elapsed since de la Peyronie's description, the disease is not yet well understood. No perfect treatment is available, and many surgical and non-surgical approaches have been suggested and used in practice. illiams and Thomas were the first to describe the natural course of the disease, and they claimed that all of the patients they followed maintained the same plaques, unchanged over time; therefore, they suggested that these patients should be followed and that there was no need for any treatment. When their data were examined later, however, it was found that there were not sufficient follow-up studies conducted and that the follow-up varied from patient to patient (4). *Gelbard et al.* and, later, *Kadioglu et al.* claimed that PD is a progressive disease in most cases and that only in a few cases is the disease ameliorated without treatment (5, 6). In a retrospective review of men with PD, at least one risk factor for systemic vascular disease was identified in 67.5% of patients, and hypercholesterolemia and diabetes were the most common. Patients with at least one risk factor were at a significantly higher risk for severe penile deformity. Their data showed that penile deformities were disabling (greater than 30°) in 62.5% of cases. Risk factors, such as serum lipid abnormalities, diabetes, and hypertension, seemed to have a significant impact on the severity of symptoms and on outcomes (6). Despite the lack of understanding of the aetiology and pathophysiology of the disease, there has been some success with non-surgical approaches, including with vitamin E (tocopherol) (7), colchicines (8), tamoxifen (9), and POTABA (potassium para- aminobinzoate) (10); similarly, different intracavernosal injections have been suggested, including collagenase (11), steroids (12), orgotein (13), interferon alpha 2B (14), and verapamil (a calcium channel blocker) (15-18), and other non-surgical treatments have been attempted, including radiation (19) and extra-corporeal shockwave therapy (20). It should be noted that vitamin E, colchicine, and tamoxifen can provide some benefit, but there have been no large placebo-controlled trials of these agents (7-9).

MATERIALS AND METHODS

Literature search

We carried out a systematic search in *PubMed* and *Medline* and the *Cochrane Central Register of Controlled Trials*, up to December 2019, to identify studies dealing

No conflict of interest declared.

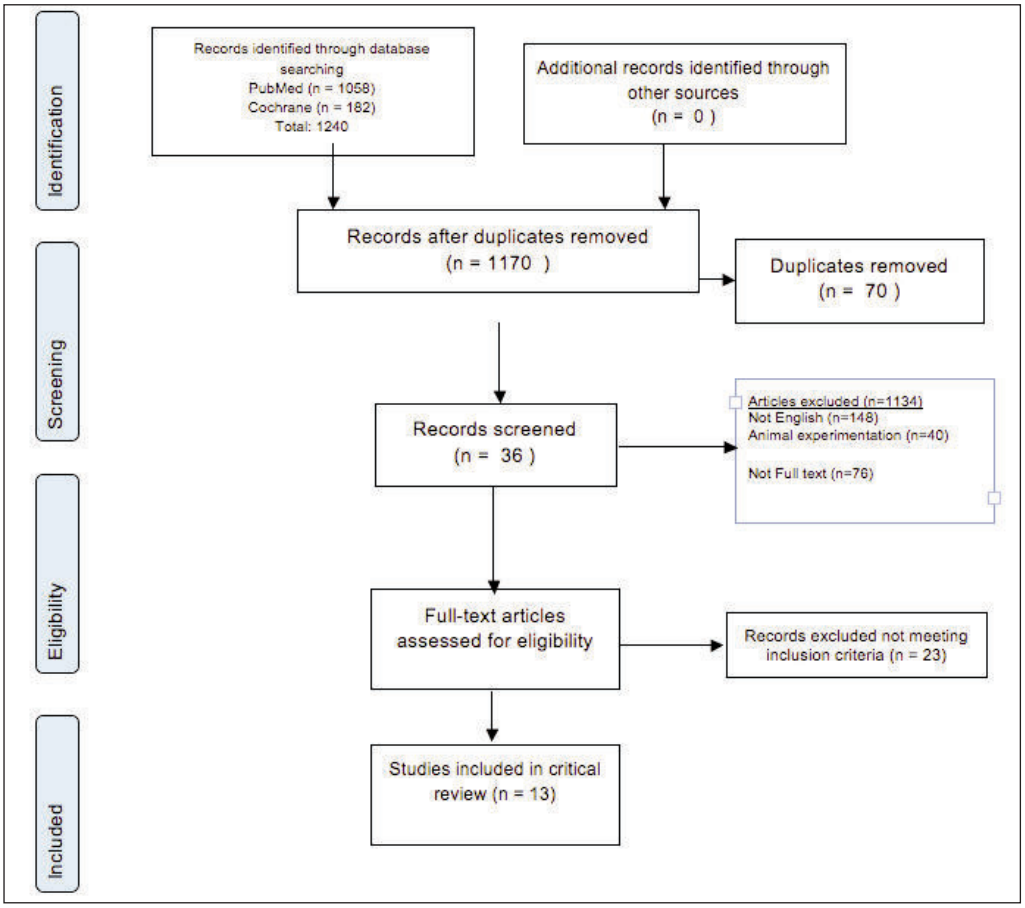

Figure 1.
PRISMA flow diagram.

with Peyronie's disease and its treatment. Included were only original articles, that we thoroughly evaluated. We searched for the primary and secondary terms of: "*Peyronie's disease*", "*Penile curvature*", "*Erectile dysfunction*", "*Verapamil and Peyronie's disease*", "*Calcium channel blocker*" and "*Intralesional injection*".

Studies selection and evaluation

Only results from original studies were included.
The search further imposed the restrictions that: the articles being in English; the studies being performed on humans; that they exist as full-text studies; including clinical trials; referring to verapamil and focused on the

Figure 2.
Risk of Bias Analysis

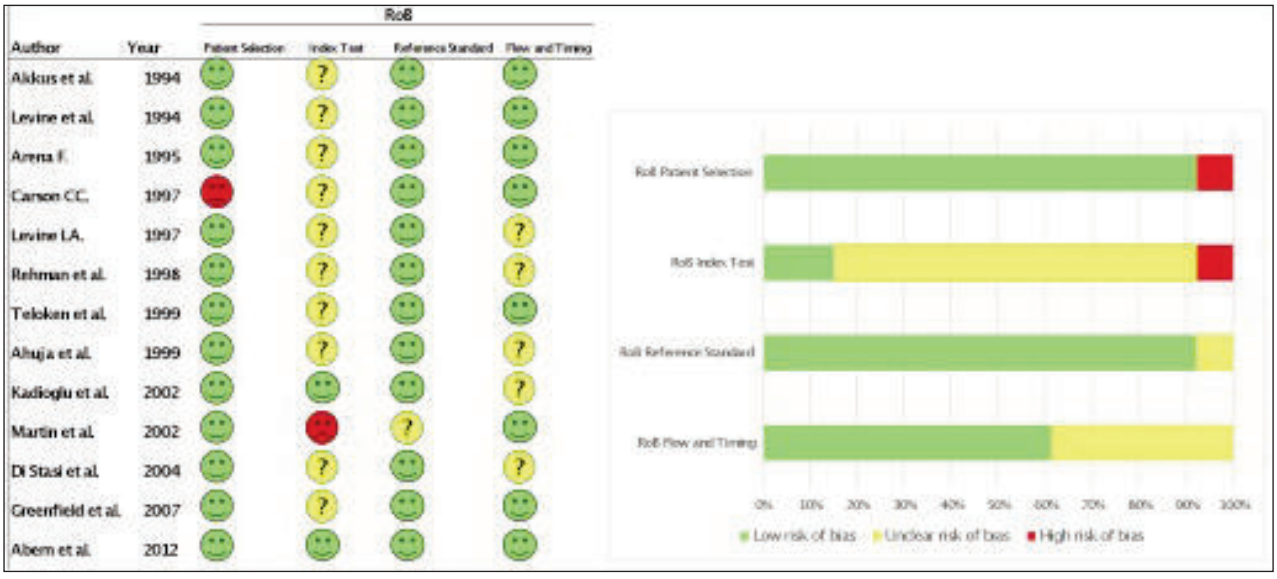

Table 1.
Modality and results of treatment of Peyronie's disease with verapamil.

Reference	No`	Dose (mg)	Treatments per week/ length of treatment (weeks)	I/T/E	% Pain resolved	% Curvature improvement	Sexual function improvement %
Di Stasi SM, et al. (12)	47	5 + 8 mg Dex.	4/6	T+E	Yes	57	51% Regained erectile activity
Levine LA 1997 (15)	38	10	2/24	I	97	76	72% Improvement in sexual function
Levine LA 1994 (16)	14	10	2/24	I	N/A	42	83% Plaque- related changes in erectile function
Rehman J (17)	7	10-27	1/24	I	100	29	43% Quality of erection
Arena F (26)	39	10	2/24	I	90.9	50	23.1% Rigidity improvement
Greenfield JM, et al. (29)	23	10	2/12	E	N/A	65	66% Erectile function satisfaction

"No`" is the number of patients treated with verapamil and completed the study; "I" stands for Injection; "T" for Transdermal; "E" for Electromotive Drug Administration; and "Dex." for Dexamethasone.

treatment of this condition. Further, studies which were deemed irrelevant or repetitive were excluded. We used the revised *Quality Assessment of Diagnostic Accuracy Studies* (QUADAS-2) tool to assess the *risk of bias* (RoB) of the reviewed studies.

Results

The initial search of the databases yielded a total of 1240 studies (*PubMed: 1058; Cochrane: 182*), as of December 2019. Seventy studies were removed due to duplication. Further 986 studies were removed due to not being in English (except for one study by *Arena F.* for which we got a translation form Italian), being about animal experimentations, not being full-text, and not being clinical trials. Likewise, studies not referring at all to verapamil were excluded (148).

From the remaining 36 full-text articles we focused on 13 studies which met the inclusion criteria, mainly being deemed relevant to the context of this study. Figure 1 presents a PRISMA flow diagram of the studies' search and selection.

Figure 2 reports the RoB assessment for each of the individual studies, according to the QUADAS-2 tool. The distribution of RoB (low risk, unclear risk, high risk) is also outlined in Figure 2 across the four different domains of risk (patient selection, index test, reference standard, and flow and timing).

Discussion

Technique

The physician should perform local anaesthesia using a penile block technique with 10 ml bupivacaine 0.5%, should feel and locate the patient's penis plaque and should hold it between two fingers. At one entrance of the skin, the needle should then be passed into and out of the plaque. To prevent haematoma, the patient is asked to compress the penis over the puncture site.

The standard dosage is 10 mg of verapamil diluted in 10 ml of 0.9% saline, while the solution is distributed into the plaque using a 25-gauge needle. It should be noted that Levine et al. were the first authors to report that 10 mg verapamil resulted in the best overall response with no toxicity (16). The patient is asked to avoid sex for the 24 hours following each treatment (15, 16). Blood pressure and heart rate should be monitored throughout the procedure for the first 3 months and may be discontinued later. To prevent incidental injury to the dorsal nerve fibres or dorsal arteries, the needle should be inserted into the dorsolateral or lateral side, depending on the location of the plaque. Precaution should be taken not to inject the drug into the corpus cavernosum. Slight, gentle pressure on the syringe is required for injection into the tunica albuginea, whereas injection into the corpus cavernosum does not require pressure (17). Treatment is recommended once every two weeks; once-a-week treatment can lead to inflammatory reactions (16). The recommended duration of treatment is six months, but if no response is achieved in three months, additional verapamil injections are not recommended (15).

Background, analysis, and findings

The use of the calcium channel blocker verapamil began in the 1980s and has continued into the twentieth century because of its influence on the production of fibroblasts in the extracellular matrix. *Kelly* showed that exocytosis in the extracellular matrix, including of collagen, fibronectin, and glycosaminoglycan, is calcium ion-dependent (21). *Askey et al.* showed that verapamil inhibits fibroblast secretion (22). Experiments on animals have shown that verapamil decreases peritoneal adhesions (23). Other work has shown that verapamil has an effect on the expression of collagen by its excessive activity and that it actually changes the collagenase activity and extracellular matrix structure changes caused by burns (24). *Anderson et al.* investigated the influence of verapamil on fibroblasts derived from excised Peyronie's plaques in a laboratory model, and they found that verapamil had the greatest effect on cell proliferation, compared to other agents, including colchicine, interferon alpha -2b, and prostaglandin E-1 (25). An intracellular balance of ingredients is important so that the production and destruction of fibroblasts play an important role in healing and creating a scar, and the importance of calcium blockers lies in their effect on different levels on fibroblast activity, including production, excretion, and destruction. Therefore, calcium blocker therapy could slow, stop, or even reverse the progression of PD. In 1994, *Levine et al.* published a series of the first cases with injections of verapamil into plaques in cases of PD. Of the cases reported in this series, there was a decrease in pain in 91%, an improvement in the curvature of the penis in 42%, and an improvement in erectile dysfunction in 58%. The injections were given every other week for six months at a dose of 10 mg per treatment (16). A year later, another series showed once again

an improvement in penile curvature as a result of a verapamil injection once every other week for six months, but the improvement was not obvious in cases in which the duration of illness was more than one year (26). Teloken, however, showed that there was no difference between steroids and verapamil injections but emphasised that the injections were near, and not into, the plaques (27). In 1998, *Rehman et al.* published their study, which was the first prospective, randomised study of PD. In that study, verapamil injections were administered into the plaques weekly for six months. According to their results, there was improvement in penile curvature but without statistical significance. Erectile dysfunction improved, penile girth increased, and there was a decrease in plaque volume. The authors concluded that the best results were observed in cases with penile curvature of less than 30 degrees (17).

Levine (1997), studying 46 cases that had been treated with injections of verapamil into the plaques, given every two weeks for six months, found that pain lessened in 97% of the cases, curvature improved in 54% of the cases, and erectile dysfunction improved in 72% of the cases (15). A study of a series of 156 cases with PD showed an improvement in penile curvature in 60% of the cases, an increase in penile girth in 83% of the cases, an improvement in rigidity distal to the plaque in 80% of the cases, and improvement in erectile dysfunction in 71% of the cases (18). Other researchers, due to pain at the injection sites and the fears of the patients, have used local verapamil as a gel (28); because of problems with absorption, however, they applied verapamil gel to the penile skin and simultaneously used a local electric current. In a double-blind, prospective study with a control group (Table 1), comparing verapamil to saline in two groups receiving electrical stimulation to improve the results, there was an improvement in penile curvature but no significant difference between the groups. The authors concluded that verapamil gel treatment with electric stimulation is a therapeutic option for patients with mild penile curvature who do not want to receive injections (29). In another prospective study (Table 1) assessing verapamil and steroid injections, using electrical stimulation at the same time, to improve penetration of the drug into the tunica, compared with lidocaine and electrical stimulation as a control, there was improvement in penile curvature and a decrease in plaque volumes (12). As mentioned before, the studies that examined POTABA, vitamin E, colchicine, tamoxifen, and acetyl-L carnitine failed to show consistent beneficial effects on PD, with the exception of POTABA, which may obtain a decrease of plaque size and curvature. It may be better to use intralesional injection therapy for PD as a first-line therapy, along with oral medication (30). *Abern et al.* used a combination of penile traction, intralesional verapamil, and oral therapies for PD, showed that there was a trend toward measured curvature improvement and a significant gain in stretched penile length. This combination could be an acceptable nonsurgical treatment for PD (31).

A recent study using Penile traction therapy with the new device Penimaster PRO in a group of patients with stable PD, achieved good results including reduction in curvature, increased stretched penile length, and improvement in *International Index of Erectile Function* (IIEF-EF) score with minimal side effects (32). Penile stretching as a treatment for PD was reviewed by *Cowper et al.* who concluded that penile stretching is an effective therapy for PD (33). *Rice et al.* reviewed twelve studies with 1025 patients using *plaque incision and grafting* (PIG). They concluded that PIG is indicated for men with complex or severe penile curvature and, despite a multitude of incision types and grafting materials having been used, no individual technique has proven superiority (34). *Barbosa et al.* concluded that there is no consensus on which surgical technique achieves better results or fewer complications; therefore, the decision on which technique to use is a matter of surgeon preference. Studies comparing distinctive techniques and either opening or not opening the tunica albuginea should be performed to support surgical decision making (35). In a survey, which represents one of the largest studies on the management of PD, members of the *European Society of Sexual Medicine* and of various andrology and urology societies across Europe, with the majority (78%) being urologists, were contacted via e-mail and newsletters and asked to fill in an online questionnaire. The survey comprised 56 items developed by an expert consensus of the educational committee of the E*uropean Society of Sexual Medicine*. In the end, 401 participants responded to the entire survey. Primary treatment options were oral (65%), counseling (57%), and topical/local therapy (30%). Among oral drug users, tadalafil 5 mg was the most commonly used (57%), followed by vitamin E (40%). Regarding intralesional therapy, collagenase clostridium histolyticum was the leading drug (34%), followed by calcium channel blockers (17%). Considering surgical procedures, the original Nesbit technique was the preferred procedure (33%).

The conclusion in the study was that one third of experts and two thirds of patients were dissatisfied with the currently available PD treatment options (36). *Vactosertib*, a novel, orally bioavailable activin receptor-like Kinase 5 inhibitor, promotes regression of fibrotic plaques in a rat model of PD. Vactosertib induced significant regression of fibrotic plaques in PD rats in vivo through reduced infiltration of inflammatory cells and reduced expression of phospho-Smad2, which recovered erectile function. Vactosertib also abrogated TGF-β1-induced enhancement of extracellular matrix protein production and hydroxyproline content in PD fibroblasts in vitro by hindering the TGF-β1-induced Smad2/3 phosphorylation and nuclear translocation, and fibroblast-to-myofibroblast trans-differentiation.

In view of the critical role of TGF-β and the Smad pathway in the pathogenesis of PD, inhibition of this pathway with an ALK5 inhibitor may represent a novel, targeted therapy for PD (37).

Dosage and complications

The therapeutic level for cardiac arrhythmia or hypertension using a calcium channel blocker is between 0.01 and 0.2 micromoles; in contrast, the therapeutic level needed to affect collagen synthesis is 100 micromoles, so to affect collagen synthesis and avoid toxic levels in serum, there is a need in PD to inject the material into

the plaques (38). *Levine and Goldman*, in their 156-case series, reported overall complications in six cases (4%), nausea in three cases, and transient headaches, without any changes in blood pressure and without any cases of cardiac arrhythmia. Three cases noted pain for less than a week. In most cases, there was local ecchymosis with no clinical significance, and no treatment was needed. There were no cardiovascular events (18). Additionally, in *Rehman et al.'s* series, in which the patients received a weekly intralesional injection, there were no long-term complications, neither local nor systemic, although there was some ecchymosis that disappeared a short time later (17).

Conclusions

Peyronie's disease can occur with different combinations of pain and curvature, depending on the levels of plaque in the tunica albuginea or in the dorsal side of the penis, and with erectile dysfunction. The treatment approach is still non-surgical during the first year of the disease. Treatments include common agents, including vitamin E and POTABA, or drug injections into the tunica layers. Treatments with steroids or orgotein are not recommended because there are no prospective studies with control groups. Verapamil treatment has been presented in prospective randomised study with a control group.

Verapamil injection into plaques in PD can affect the activity of fibroblasts on several levels, including the proliferation, synthesis, and secretion of proteins in the extracellular space. It also affects collagen breakdown. These changes can slow, stop, or even reverse the progression of the disease.

Many studies investigating PD and the use of intralesional verapamil injections have shown decreased pain, improvement in penile curvature, improvement in erectile dysfunction, increased penile girth, and postponement of surgery. In cases that were treated with verapamil injections and that were submitted to surgery later, the use of verapamil injections did not compromise the surgical results. Treatment with oral medications has shown negligible improvement of the disease. Treatment with injections into the plaques with verapamil, collagenase or interferon have shown good results, and these injections are considered first-line treatments. For a better understanding of the pathophysiology of the disease, there is a need for more extensive studies on the subject. It may be that the preferred future treatment lies in a combination of drugs.

Patients with localised plaque are the best candidates for intralesional injections of verapamil. The beneficial effects of intralesional verapamil are apparent within the first three months. For patients who respond to treatment, the injections should be continued for six months. Patients who fail to respond to intralesional verapamil or whose angulation is greater than 30° at presentation should be considered candidates for surgery. Injection of verapamil is clinically safe for patients with Peyronie's disease, and it appears to induce a rapid, beneficial effect in patients for the reduction of plaque size. Intralesional verapamil injection for Peyronie's disease could reduce pain, decrease penile curvature, and improve sexual function.

References

1. De La Peyronie F. Sur quelques obstacles qui s'opposent al'ejaculation naturelle de la semence. Mem de l'Acad Roy de Chir. 1743; 1:425-434.

2. Schwarzer U, Sommer F, Klotz T, et al. The prevalence of Peyronie's disease: results of a large survey. BJU Int. 2001; 88:727-730.

3. Mulhall JP, Creech SD, Boorjian SA, et al. Subjective and objective analysis of the prevalence of Peyronie's disease in a population of men presenting for prostate cancer screening. J Urol. 2004; 171:2350-2353.

4. Williams JL, Thomas GG. The natural history of Peyronie's disease. J Urol. 1970; 103:75-76.

5. Gelbard MK, Dorey F, James K. The natural history of Peyronie's disease. J Urol. 1990; 144:1376-1379.

6. Kadioglu A, Tefekli A, Erol B, et al. A retrospective review of 307 men with Peyronie's disease; results of a large survey. J Urol. 2002; 168:1075-1079.

7. Stojic M, Negrojevic M, Josic P, Stojic S. Conservative therapy of Peyronie's disease using vitamin E. Med Pregl. 1987; 40:133-135.

8. Akkus E, Carrier S, Rehman J, et al. Is colchicine effective in Peyronie's disease? A pilot study. Urology. 1994; 44:291-295.

9. Teloken C, Rhoden EL, Grazziotin TM, et al. Tamoxifen vs placebo in the treatment of Peyronie's disease. J Urol. 1999; 162:2003-2005.

10. Carson CC. Potassium para-aminobenzoate for the treatment of Peyronie's disease: is it effective? Tech Urol. 1997; 3:135-139.

11. Gelbard MK, James K, Riach P, Dorey F. Collagenase vs placebo in the treatment of Peyronie's disease: a double-blind study. J Urol. 1993; 149:56-58.

12. Di Stasi SM, Giannantoni A, Stephen RL, et al. A prospective, randomized study using transdermal electromotive administration of verapamil and dexamethasone for Peyronie's disease. J Urol. 2004; 171:1605-1608.

13. Primus G. Orgotein in the treatment of plastic induration of the penis (Peyronie's disease). Int Urol Nephrol. 1993; 25:169-172.

14. Ahuja S, Bivalacqua TJ, Case J, et al. A pilot study demonstrating clinical benefit from intralesional interferon alpha 2B in the treatment of Peyronie's disease. J Androl. 1999; 20:444-448.

15. Levine LA. Treatment of Peyronie's disease with intralesional verapamil injection. J Urol. 1997; 158:1395-1399.

16. Levine LA, Merrick PF, Lee RC. Intralesional verapamil injection for the treatment of Peyronie's disease. J Urol. 1994; 151:1522-1524.

17. Rehman J, Benet A, Melman A. Use of intralesional verapamil to dissolve Peyronie's disease plaque: a long-term single-blind study. Urology. 1998; 51:620-626.

18. Levine LA, Goldman KE. Updated experience with intralesional verapamil injection treatment for Peyronie's disease. J Urol. 2000; 163:170, abstract 751.

19. Bittard H, Schraub S, Bittard M. Treatment of Peyronie's disease by a combination of radiotherapy and surgery. Apropos of 51 cases. Ann Urol. 1988; 22:67-69.

20. Busetto GM. Extracorporeal shock wave therapy in the treatment of Peyronie's disease: Long- term results. Arch Ital Urol Androl. 2010; 82:128-33.

21. Kelly RB. Pathways of protein secretion in eukaryotes. Science. 1985; 230:25- 32.

22. Askey DB, Miller EA, Holguin MA, Albertini D.F. The effect of weak electric fields and verapamil on exocytosis in human fibroblasts. J Cell Biology. 1988; 107:336a, abstract 1905.

23. Kappas AM, Barsoum GH, Ortiz JB, Keighley MR. Prevention of peritoneal adhesions in rats with verapamil, hydrocortisone sodium succinate, and phosphatidylcholine. Eur J Surg. 1992; 158:33-35.

24. Lee RC, Doong H, Jellema, AF. The response of burn scars to intralesional verapamil. Report of five cases. Arch Surg. 1994; 129:107-111.

25. Anderson MS, Shankey TV, Lubrano T, Mulhall JP. Inhibition of Peyronie's plaque fibroblast proliferation by biologic agents. Int J Impot Res. 2000; 12(Suppl 3):S25 -S31.

26. Arena F. Clinical effects of verapamil in the treatment of Peyronie's disease. Acta Biomed Ateneo Parmense. 1995; 66:269-272.

27. Teloken C. Objective evaluation of non-surgical approach for Peyronie's disease. J Urol. 1996; 155:633A, abstract 1290.

28. Martin DJ, Badwan K, Parker M, Mulhall JP. Transdermal application of verapamil gel to the penile shaft fails to infiltrate the tunica albuginea. J Urol. 2002; 168:2483-2485.

29. Greenfield JM, Shah SJ, Levine LA. Verapamil versus saline in electromotive drug administration for Peyronie's disease: a double-blind, placebo controlled trial. J Urol. 2007; 177:972-5.

30. Trost LW, Gur S, Hellstrom WJ. Pharmacological management of Peyronie's disease. Drugs. 2007; 67:527-45.

31. Abern MR, Larsen S, Levine LA. Combination of penile traction, intralesional verapamil, and oral therapies for Peyronie's disease. J Sex Med. 2012; 9:288-95.

32. Moncada I, Krishnappa P, Romero J, et al. Penile traction therapy with the new device 'Penimaster PRO' is effective and safe in the stable phase of Peyronie's disease: a controlled multicentre study. BJU Int. 2019; 123:694-702.

33. Cowper MG, Burkett CB, Le TV, et al. Penile stretching as a treatment for Peyronie's disease: A review. Sex Med Rev. 2019; 7:508-515.

34. Rice PG, Somani BK, Rees RW. Twenty years of plaque incision and grafting for Peyronie's disease: a review of literature. Sex Med. 2019; 7:115-128.

35. Barbosa ARG, Takemura LS, Cha JD, et al. Surgical Treatment of Peyronie's Disease: Systematic review of techniques involving or not tunica albuginea incision. Sex Med Rev. 2019; pii: S2050-0521(19)30082-4.

36. Porst H, Burri A; European Society for Sexual Medicine (ESSM) Educational Committee. Current strategies in the management of Peyronie's disease (PD)-Results of a survey of 401 sexual medicine experts across Europe. J Sex Med. 2019; 16:901-908.

37. Song KM, Chung DY, Choi MJ, et al. Vactosertib, a novel, orally bioavailable activin receptor-like kinase 5 inhibitor, promotes regression of fibrotic plaques in a rat model of Peyronie's disease. World J Mens Health. 2019 Aug 27. doi: 10.5534/wjmh.190071. [Epub ahead of print]

38. Lee RC, Ping JA. Calcium antagonists retard extracellular matrix production in connective tissue equivalent. J Surg Res. 1990; 49:463-466.

Correspondence

Murad Asali, MD (Corresponding Author)
muradasali@hotmail.com
Assuta Medical Center, Ben Gurion University of the Negev
Sokolov 26/99, Beer Sheva 8430905 (Israel)

Muhammad Asali
International School of Economics, Tbilisi (Georgia; IZA, Bonn (Germany);
and School of International and Public Affairs, Columbia University,
New York (United States)