PEYRONIE'S DISEASE

Evaluation of Oral Pentoxifylline, Colchicine, and Penile Traction for the Management of Peyronie's Disease

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ABSTRACT

Introduction: Currently, there are several treatment options for Peyronie disease (PD). Although surgical interventions have better reported outcomes than conservative therapy, surgery is not suitable for all patients with PD. Therefore, oral therapy for PD is still a frequently used treatment due to low cost, convenience and limited side effects. However, current literature on the efficacy of oral therapy in PD is inconclusive. Pentoxifylline and colchicine have both shown some promise though further studies are required to confirm their effectiveness.

Aim: The aim of this study was to assess the efficacy of oral therapy for PD, including pentoxifylline and colchicine, coupled with the Andropenis penile traction therapy (PTT) extender on degree of penile curvature and plaque size.

Methods: Between March 2015 and June 2018, a prospectively collected database for patients receiving oral therapy for PD (pentoxifylline and/or colchicine) was reviewed.

Main Outcome Measure: Collected data variables were compared at baseline and after 6 months of treatment, including degree of curvature, plaque size, and penile Doppler ultrasound parameters (peak systolic velocity, minimum diastolic velocity, and pulsatility index). PTT was applied by the patient for a total of 1 hour per day for 6 months.

Results: A total of 46 patients were involved in this study. Mean age was 56 ± 10 years. There was a significant decrease in the degree of penile curvature after 6 months (55.8° ± 20° vs 41.4° ± 20.8°; $P = .03$). Likewise, the plaque size decreased significantly from 5.42 ± 2.7 to 2.42 ± 1.71 cm^2; $P = .0001$. There was a significant increase in the peak systolic velocity from 29.8 ± 10.02 to 38.2 ± 11cm/sec; $P = .02$, whereas no statistically significant difference could be detected regarding end diastolic velocity ($M = 0.56 \pm 3.1$ vs 1.59; $P = .415$) or pulsatility index ($M_{diff} = 0.03$; CI = -0.06 to 0.12; $P = .473$). Furthermore, there was no statistically significant difference in medication type of pentoxifylline or colchicine ($M_{diff} = 17.23$; CI = -3.31 to 37.77; $P = .09$).

Conclusion: Altogether, pentoxifylline and colchicine, taken with concomitant PTT, present a potentially convenient, low cost, and effective treatment for penile curvature and plaque resulting from PD. Prospective randomized trials are still required for better evaluation of the course of PD with patients undergoing conservative management. **Ibrahim A, Gazzard L, Alharbi M, et al. Evaluation of Oral Pentoxifylline, Colchicine, and Penile Traction for the Management of Peyronie's Disease. Sex Med 2019;7:459–463.**

Key Words: Peyronie's Disease; Erectile Dysfunction; Pentoxifylline; Colchicine; Penile Traction

INTRODUCTION

The occurrence of Peyronie's disease (PD) is quite common, with a prevalence ranging from 0.4–13% of the general population and affecting 8% of patients with erectile dysfunction.[1–4] PD can physically and psychologically hinder sexual intercourse due to various symptoms, including penile pain, loss of penile length, curvature deformities, and erectile dysfunction.[5]

Currently, there are several treatment options that exist for PD. Although surgical interventions have better reported outcomes

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than conservative therapy, surgery is not suitable for all patients with PD. Surgical intervention is only indicated in patients with stable disease, significant penile curvature, erectile and sexual dysfunction, or resistance to nonsurgical interventions.[6] Therefore, minimally invasive therapy may provide a reasonable alternative to those who are ineligible for surgical interventions or who wish to pursue a more conservative course of treatment. Despite inconclusive data supporting the use of oral therapy for PD with concomitant penile traction therapy (PTT), this type of treatment is still frequently used due to low cost, convenience, and limited side effects.[7] A rationale for using PTT for PD comes from Dupuytren's contracture, a disease involving hand deformation with potential gene and pathophysiological commonalities with PD, which has been shown to improve with traction therapy.[8] This remodeling is thought to occur through the reorientation of tissues, such as collagen fibrils, and an increase in collagen turnover. However, this does not seem to be the case when PTT is used alone.[9] Nevertheless, current literature on the efficacy of oral therapy in PD is inconclusive. Pentoxifylline and colchicine, both which are off-label treatments, have both shown some promise, although further studies are required to confirm their effectiveness.[10] Our aim is, therefore, to assess the effect of oral therapy for PD, including pentoxifylline or colchicine coupled with the Andropenis PTT extender on degree of penile curvature and plaque size.

Patients and Methods

After obtaining ethics approval by our local committee of the McGill University, between March 2016 and June 2018, a prospectively collected database for patients receiving oral therapy for PD (pentoxifylline and/or colchicine) was retrospectively reviewed. Collected data variables were compared at baseline and after 6 months of treatment, including degree of curvature, plaque size, and penile Doppler ultrasound parameters (peak systolic velocity, end diastolic velocity, and pulsatility index). PTT was applied by the patient for a total of 1 hour per day for 6 months (Table 1).

Measures and Procedures

At the baseline assessment (t_1), urologist first measured the size and location of the plaque using a physical examination and ultrasound and then injected 10 μg of prostaglandin E1 to facilitate penile erection. Five minutes after the administration of the injection, duplex Doppler ultrasound was used to measure the patients' arterial diameter, peak systolic velocity, minimum diastolic velocity, and the pulsatility index. The patients were subsequently instructed to privately self-stimulate to elicit an erection. Once achieved, the urologist measured the degree of curvature, and repeated the measurement of the peak systolic velocity, end diastolic velocity, and pulsatility index. The patients were prescribed the Andropenis extender to be worn a minimum of 1 hour per day, and either 400 mg of pentoxifylline twice daily for those presented without erectile pain or could not tolerate colchicine, whereas colchicine (0.6 mg twice daily) was prescribed for patients who presented with pain at the baseline.

Table 1. Demographic and perioperative data with long-term complications

Variables	Mean ± SD, no. (%)
Mean age, years	70 ± 7.5
Clinical presentations*	
Penile pain	26 (57.8)
Penile curvature	23 (51.1)
Erectile dysfunction	21 (46.7)
Type of penile curvature	
Dorsal	18 (40)
Ventral	4 (8.9)
Right	11 (24.4)
Left	12 (26.7)
Type of medication	
Pentoxifylline	27 (60)
Colchicine	18 (40)
Mean plaque size, cm^2	5.4 ± 2.7

*Some patients had multiple clinical presentations.

At the 6 month follow-up (t_2), the same procedure of measurements was repeated for comparison. Data from both assessments were documented in the patients' medical record chart.

Design

The study is a quasi-experimental between-subject design, with a statistical analysis (mean, SD, CI, and Hedge's *g*) of degree of curvature, plaque size, peak systolic velocity, minimum diastolic velocity, and the pulsatility index at t_1 vs t_2.

Data Analysis

Prior to generating the statistics, the dataset was checked for the following exclusionary factors: participant attrition, medication intolerance, and missing data. As a result, 18 patients were excluded from the final analysis.

In order to analyze the treatment effects, results from t_2 were compared to t_1. Determining a decrease in curvature involved dividing the curvature into 3 sides (eg, dorsal, right, and left). The patient with ventral curvature was excluded from analysis as only 1 participant presented in this manner. The plaque size was defined as the area in cm^2, and the peak systolic velocity and end diastolic velocity were measured in cm/s in both the right and left corpora cavernosa. The pulsatility index is defined by the following equation: (peak systolic velocity − end diastolic velocity) / (peak systolic velocity). The mean, SD, CIs, and Hedge's *g* were calculated for the following: the change in *degree of curvature* for the dorsal, right and left sides, the change in *plaque size*, difference in *peak systolic velocity for the right* corpus cavernosum, difference in *peak systolic velocity for the left* corpus cavernosum, difference in *end diastolic velocity for the right* corpus cavernosum, difference in *end diastolic velocity for the left* corpus cavernosum, difference in *pulsatility index for the right*

corpus cavernosum, and difference in *pulsatility index for the left* corpus cavernosum.

RESULTS

After exclusion of 18 cases with incomplete data, a total of 46 patients were included in the present study. Each participant was specifically referred for the treatment of PD to our tertiary care center. The mean age was 55 ± 10.4 years ranging from 33−70 years of age.

The following statistics involve the measurements taken at t_1 compared to those taken at t_2, 6 months after the Andropenis extender and oral therapy were prescribed.

There was a significant decrease in the degree of penile curvature after 6 months (55.8° ± 20 vs 41.4° ± 20.8, CI = 0.82−28.11; $P = .03$). Likewise, the plaque size decreased significantly from 5.42 cm^2 ± 2.7 to 2.42 cm^2 ± 1.71; CI = 1.64−4.37; $P = .0001$. There was a significant increase in the peak systolic velocity from 29.8 cm/s ± 10.02 to 38.2 cm/s ± 11, CI = -12.03 to 2.97; $P = .02$, whereas no statistically significant difference could be detected regarding end diastolic velocity (0.56 cm/s ± 3.1 vs 1.59 ± 4.1 cm/s; CI = -3.39 to 2.27; $P = .415$). Similarly, no statistically significant difference could be detected regarding pulsatility index (M_{diff} = 0.03, CI = -0.06 to 0.12; $P = .473$) (Table 2).

Type of Medications (Pentoxifylline vs Colchicine)

A comparison of both the pentoxifylline and colchicine t_2 results indicated that there was no statistically significant difference in medication type for dorsal (M_{diff} = 17.23; CI = -3.31 to 37.77; $P = .095$; $g = 0.87$), or left curvatures (M_{diff} = -12.67; CI = -32.47 to 7.13; $P = .169$; $g = 1.14$). The right curvature could not be compared, as all patients with a right curve at t_2 had been treated with pentoxifylline. No statistically significant difference was observed between those prescribed pentoxifylline or colchicine for plaque size (M_{diff} = -0.10; CI = -1.66 to 1.46; $P = .897$; $g = 0.06$), right corpus cavernosum peak systolic velocity (M_{diff} = -8.89; CI = -21.31 to 3.52; $P = .148$; $g = 0.87$), left corpus cavernosum peak systolic velocity (M_{diff} = -7.19; CI = -21.22 to 6.85; $P = .293$; $g = 0.62$), right corpus cavernosum minimum diastolic velocity (M_{diff} = 0.44; CI = -5.60 to 6.47; $P = .879$; $g = 0.09$), left corpus cavernosum minimum diastolic velocity (M_{diff} = 0.08; CI = -5.31 to 5.48; $P = .974$; $g = 0.02$), right corpus cavernosum pulsatility index (M_{diff} = 0.01; CI = -0.15 to 0.17; $P = .892$; $g = 0.08$), or the left corpus cavernosum pulsatility index (M_{diff} = -0.03; CI = -0.17 to 0.11; $P = .640$; $g = 0.27$).

Table 2. Outcomes and penile Doppler ultrasound parameters

Variables	Baseline data	After 6 months of treatment	
Peak systolic velocity, cm/s	29.8 ± 10.02	38.2 ± 11	0.03
End diastolic velocity, cm/s	0.56 ± 3.1	1.59 ± 4.1	0.415
Plaque size, cm^2	5.42 ± 2.7	2.42,± 1.71	0.001
Penile curvature	55.8° ± 20°	41.4° ± 20.8°	0.03
Pulsatility index	(M_{diff} = 0.03; CI = −0.06 to 0.12; 0.473		0.473

DISCUSSION

Establishing effective treatments for PD is crucial, as the individual is affected physically, psychologically, and interpersonally. Although cases of spontaneous remission have been reported in 3−13% of cases if left untreated, the disease tends to worsen and become chronic in its prognosis. Treatments for PD aim to limit the disease progression and decrease the plaque and penile curvature in order to improve erectile and sexual comfort. Current treatment options include pharmacological therapies, which are more suitable at the early stage of the disease, minimally invasive therapies, such as Collagenase Clostridium Histolyticum (CCH), which has a high level of evidence supporting its efficacy, as well as surgical correction, which is suitable only after disease stability.[10] Despite better outcomes reported after surgical interventions than after conservative therapy, surgery is a more invasive option that many patients avoid, especially those with milder disease and limited sexual dysfunction. Furthermore, despite proven effectiveness, CCH may be very costly and time-consuming for some patients.

One of the minimally invasive options is oral therapy for PD, which is still frequently used due to low cost, convenience, and limited side effects. However, current literature on the efficacy of oral therapy in PD is inconclusive. In comparison to invasive surgical procedures, clinical trials involving oral therapies may elucidate a beneficial, minimally invasive, widely available, and low cost treatment for PD. In the interest of adding to this body of literature, this study seeks to test the hypothesis that pentoxifylline or colchicine coupled with the Andropenis PTT extender will lead to significant reductions in penile curvature and plaque size. Therefore, the aim of this study was to determine if pentoxifylline or colchicine coupled with PTT would significantly decrease the degree of penile curvature and plaque size.

Based on the statistical analysis, it was found that when paired with PTT, pentoxifylline or colchicine may be effective treatments in reducing curvature and plaque size in individuals with PD. Furthermore, these results do not seem to be due to any differences in medication type. In vitro studies of pentoxifylline demonstrated that the drug may increase collagen metabolism, reduce fibrogenesis, and limit elastogenesis in tunica albuginea-derived fibroblasts.[9] Additionally, colchicine, a well-established antimicrotubule agent, is believed to prevent collagen production and wound contraction.[11]

Although there are a limited number of clinical trials that have assessed the effects of pentoxifylline and colchicine on PD symptoms, they are in line with the findings of this study. A case

study conducted by Brant et al.,[12] found that pentoxifylline significantly reduced the patient's curvature and plaque, and improved erectile function. Moreover, a double-blind randomized controlled trial found that pentoxifylline moderately reduced curvature and plaque in patients with beginning stages of chronic PD.[13] Colchicine seems to have mixed results, with 1 study citing no improvement in curvature and plaque compared to placebo;[14] whereas others suggest colchicine was effective for 30−50% of patients.[15−17] This study, coupled with these findings, further supports the need for prospective double-blind randomized controlled trials with these medications.

With regard to blood velocity, there was a significant increase in the peak systolic velocity (29.8 cm/s ± 10.02 to 38.2 cm/s; $P = .02$), whereas no statistically significant difference could be detected regarding end diastolic velocity (0.56 cm/s ± 3.1 vs 1.59 ± 4.1 cm/s; $P = .415$) or pulsatility index ($P = .473$). These results reflect a significant improvement in terms of penile arterial blood circulation compared to the baseline parameters.

Finally, the study is not without its limitations, including its retrospective nature, which does not allow us to control for some variables and emphasis excluding some patients due to incomplete data. Furthermore, perhaps the analysis of erectile rigidity at baseline and at the 6-month follow-up would have provided a greater understanding of the effect of pentoxifylline and colchicine on erectile function. An additional issue with this is that patient motivation may have varied when using the Andropenis extender. Although this study was not designed to specifically assess the effect of length of PTT use, it is recommended that this variable be analyzed in future studies. There is also the possibility that some patients experienced spontaneous remission; however, such remission rates are low. Nevertheless, the present study represents our clinical experience with a specific group of patients who were treated conservatively and with positive effects. Therefore, we believe that future prospective double-blind randomized controlled trials comparing both pentoxifylline and colchicine would also be beneficial in order to better assess long-term effects on PD symptoms.

CONCLUSIONS

Altogether, pentoxifylline and colchicine, taken with concomitant PTT, tend to have a potentially convenient, low cost, and effective treatment for penile curvature and plaque resulting from PD. Prospective randomized trials are still warranted for better evaluation of the course of PD for patients undergoing conservative management.

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