ŁOŚ, Dawid, NOWAK, Aleksandra, JANUS, Anita, KAPTUR, Agata and DZIEDZIŃSKI, Dawid. Peyronie's disease - a condition affecting many. Quality in Sport. 2024;15:52623. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.15.52623
https://apcz.umk.pl/QS/article/view/52623

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 14.06.2024. Revised: 25.05.2024. Accepted: 03.07.2024. Published: 06.07.2024.

Peyronie's disease - a condition affecting many

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ABSTRACT

Introduction

Peyronie's Disease (PD) is an acquired connective tissue disorder resulting in abnormal healing of the tunica albuginea causing abnormal curvature, narrowing and shortening of the penis, can also lead to difficulties in coitus. In affecting up to 13% of the adult male population, it can also be a major psychological issue, therefore many of existing therapeutic options are worth looking into. This article provides a review of current knowledge about etiology and ways of treatment as well as a closer look into the impact on mental health among males affected with PD

Review methods

English-language scientific literature found in PubMed was used for the review. Articles were searched based on keywords. Each article was analyzed for knowledge currency and relevance for use in the review.

Description of the State of Knowledge

After searching the articles, 32 articles were selected for final analysis. The collected data provided the latest information on Peyronie's disease while showing the connection between Peyronie's disease and overexpression of HLA-B7 antigen, TGF-β1, anti DNA, antinuclear and anti elastin antibodies. The treatment could be non-invasive, intralesional or surgical.

Summary

Peyronie's disease is a condition that requires a holistic approach with physical difficulties being as important as a patient's mental health.

Keywords: Peyronie disease, penile curvature

INTRODUCTION AND OBJECTIVE

Peyronie's Disease (PD) is an acquired connective tissue disorder resulting in abnormal healing of the tunica albuginea causing abnormal curvature, narrowing and shortening of the penis, can also lead to difficulties in coitus. In affecting up to 13% of the adult male population, it can also be a major psychological issue, therefore many of existing therapeutic options are worth looking into.

The purpose of this review is to provide an up-to-date overview of the current knowledge on the subject with the aim of increasing clinician's awareness of PD.

MATERIALS AND METHODS

For this review we conducted a manual search of the PubMed database for english articles on Peyronie's disease. We used the keywords 'Peyronie disease', 'penile curvature'. Our search was limited to english articles published between 2011 and 2024 along with their references. The evaluation was based on titles, abstracts and full texts. Only the ones properly matching and describing the topic were included.

REVIEW

Epidemiology and etiology

The prevalence of PD is not well known, as the studies are limited and inconsistent. Different estimates have ranged from 0,39% to about 20% depending on the inclusion of patients. There

is, however, a concern that the true prevalence might be underreported due to the psychological burden that could be associated with this issue. [1, 2]

It usually occurs in Caucasian patients between 40 and 60 years of age. About 10% of patients, however, are younger than 40 years and those are the ones more likely to have pain and to progress. [3]

The common symptoms the patients are presenting are curvature of the penis or other type of deformity, especially during erection and associated with pain, erectile dysfunction (ED) and a palpable plaque. The deformity is usually the first of the symptoms noticed by patients. Most patients would present a palpable plaque along with the penile curvature.

There has been a strong link between PD and Dupuytren's disease (DD). The prevalence of PD symptoms in DD patients in studies ranges from 22-26%. Other conditions connected to PD include Paget's disease of the bone, Ledderhose disease, hypogonadism, diabetes, urethral manipulation and radical prostatectomy

There have been studies that reported low testosterone levels in almost 75% of the patients taking part in the study and hypogonadal men have more penile curvature than eugonadal PD patients

We are not sure about the exact etiology of PD. The most common concept refers to trauma or repeated microtrauma to the erect penis in genetically susceptible individuals causing inflammation, damage of the elastic fibers and deposition of fibrin. The thought of this concept being true is helped by the fact of epidemiologic association of PD with traumatic events. It has been also suggested that vascular trauma could lead to osteoid formation with the action of osteoblast-like cells originating from the vascular lumen. Also, the upregulation of osteoblast specific factor 1 is said to play a role in plaque calcification. Another theory of the influence of cavernosal hypoxia inducing collagen deposition and fibrosis could explain the morphological changes of the penis with development of PD following radical prostatectomy. [4]

There have been few different hypotheses about genetic etiology of PD: familial aggregation and genetic transmission mode via HLA-B7 cross-reacting group; chromosomal abnormalities

like duplication of chromosome 7 and 8 and deletion of chromosome Y; single nucleotide polymorphism leading to elevated levels of transforming TGF-β1; overexpression of gene pleiotrophin and monocyte chemotactic precursor protein-1 gene; epigenetic regulation by histone deacetylases. The familial aggregation and genetic transmission mode via HLA-B7 cross-reacting group theory, among all the theories, is accepted and understood. Aneuploidy of chromosomes 7 and 8 was the most common chromosomal abnormality detected. Also, through analysis of three families affected by PD and DD, it's been shown that it is inherited by an autosomal dominant mode with incomplete penetrance. [5, 6]

PD consists of two phases.
First phase is the one of acute inflammatory processes with increased proliferation of the tunical fibroblasts with high deposition of collagen. It is believed that transforming growth factor (TGF)-β1 could play a crucial role in induction of collagen production in development of PD plaques. Studies on animals have shown that TGF-β1 boosts deposition of collagen and forming of the plaques while the suppressors of TGF-β1 cause regression of the plaques. Samples of tissue from human PD plaque contained overexpression of TGF-β1.
In this stage the pain occurs in either flaccid or erect state of the penis and typically resolves after 12-18 months of PD's onset.

The second phase starts 12-18 months from the beginning of the disease with disappearance of the pain and stabilization of plaque and penile deformity. It has been discovered that PD deformity stabilization was more common among older patients and the ones who presented in the first 6 months of symptoms. Improvement rates, however, were higher among younger patients. Chronic inflammation leads to formation of fibrotic plaques which can progress to calcification or ossification although we are uncertain of the exact mechanism of the process. [7]

Diagnosis

Usually the diagnosis could be made on physical examination and patient's history, which consists of a combination of following conditions: penile pain during erections, curvature of the penis, an hourglass deformity caused at the site of the plaque due to the indentation of the penile shaft, reduced erectile function due to loss of rigidity, problems with intercourse due to penile buckling caused by the angulation.

The pain in the penis usually resolves with no treatment whatsoever, and while it used to be considered a self-healing feature of PD, the present research suggests it's actually occurring due to death of the nerve fibers innervating the organ caused by extended fibrosis.
The plaque in PD is mostly located in the dorsal midline, therefore the penis gains an upward bend. Dorsal midline with septal extension is another possible location, moreover, the plaque may also extend from the dorsal midline circumferentially around the corporeal bodies. A rarely observed location could be between the corpus spongiosum and the ventral surface of the corpora cavernosa. [8]

While examining a patient, it is very important to take a closer look at his hands and feet to look for symptoms of DD or Ledderhose scarring of the plantar fascia. One should check the appearance of the flaccid penis, whether it's circumcised and measurement of stretch penile length, rigidity, girth and curvature during erection. By stretching the penile shaft one can assess the erectile tissue health. [9]

The degree of curvature can range from 15° to 180°. Palpation is the easiest way to detect a plaque during physical examination as about 80% of plaques have an extension of more than 1,5cm in diameter. Deformities range from "notching" to circumferential hourglass defects and a shortening of the penis is also a common symptom.
No specific blood tests are available. Even though a correlation between PD and overexpression of HLA-B7 antigen, TGF-β1, anti DNA, antinuclear and anti elastin antibodies has been spotted, those particles cannot be thought of as the markers for the disease. In case of the imaging, in the diagnosis of PD it is important to spot calcification in the plaque, as it signifies the end of chronic PD, and there is no angulation occurring past that point. An X-ray radiograph can show calcification/plaque in the soft tissue, however computerized tomography could visualize non-calcified plaque. High resolution USG is considered as a good tool for defining the extent of the plaque. It's the method of choice for demonstrating plaque calcifications. MRI is another diagnostic tool that could be helpful, despite its high costs, because of its ability to identify the plaque in the early stages. Computed tomography is an excellent imaging method for the detection of calcified plaques, but it is known that soft-fibrotic plaques are not well visualized. [10]

Non-invasive treatment

The main goal of non-surgical treatment is alleviating pain at the early stage of the disease. It is also used to decrease the progression of the disease, stabilize inflammation, penile plaque and deformity. Oral pharmacotherapy, intralesional injection therapy, among others, could be used with that purpose. [11]

L-arginine

L-arginine is working in the mechanism of reducing the expression of collagen I, increasing production of nitric oxide (NO) and inhibiting the extracellular matrix synthesis in the fibrotic's plaques. It also shows efficacy in improving the curvature of the penis. Overall, data shows a positive role in managing PD, especially in combination regimen [12]

Pentoxifylline

Pentoxifylline plays a role in reducing TGF-β1 level in tissue, therefore having an anti-fibrotic role. In vitro, it has shown abilities to attenuate the deposition of collagen in tunica albuginea and reduce the secretion of tumor necrosis factor (TNF) by T-cells associated with PD pathogenesis. It also could enhance regeneration of the nerve and improve erectile function

Tamoxifen

Tamoxifen can serve in treatment of PD because of its anti-fibrotic effects through inhibition of TGF-β1. It has shown anti-fibrotic effects in animal models, however the trials among patients with PD have shown inconsistent results. [13]

Phosphodiesterase Type 5 Inhibitors

Phosphodiesterase Type 5 (PDE5) Inhibitors have been widely used for treatment of ED with the support of previous studies. Long-term administration of PDE5 inhibitors could inhibit the fibrotic process through decreasing the degradation of cGMP and thus increasing NO

downstream signaling. PDE5 inhibitors could also inhibit corporal fibrosis at a genetic level which has been shown in animal studies. [14]

Intralesional medication

It is used to deliver agents into the pathological site with relative high concentration while also avoiding the systemic side effects. One of the pros of that type of treatment is also the fact that it does not require the compliance or time commitment, the oral treatment does. It has, however, some intrinsic limitations and the potential risk of injection-related complications, such as rupture of tunica albuginea, hemorrhage and hematoma. [15]

Verapamil

Verapamil ‘s role in treatment of PD is to block the transportation of calcium into fibroblasts, thus inhibiting the transfer of proline into the matrix and stimulating the phenotype transformation of fibroblasts to produce collagenase. Studies show improvement on clinical features, such as curvature of the penis, size of the plaque and sexual function in patients treated by intralesional medication of verapamil. However, one single-blind randomized controlled trial has shown ineffectiveness of that method compared with the control group. Overall, existing evidence suggests that intralesional verapamil might be beneficial to a subset of patients, especially those in acute phase with minimal calcification. [16, 17]

Interferon-α2b

Interferon is a kind of molecular weight protein characterized by modulating immune function in anti-proliferative or anti-neoplasm effects. Its application in PD is based on the fact that in vitro it has been proved to decrease fibroblasts proliferation and reduce the collagen synthesis and deposition while also increasing collagenase activity in fibrotic plaques. It also has the advantage of treating ventral curvatures, while other intralesional therapies are contraindicated for that purpose. The side effects, however, present as influenza-like symptoms, and are well tolerated [18]

Corticosteroids

Corticosteroids are known for inhibiting inflammation and that is the reason their use has been considered in PD. An observational study in 2000 has shown that local injection of betamethasone could be effective while presenting a low rate of severe complications. The study, however, limited the group of patients to those with medical history less than 12 months and with a plaque of a size less than 20mm. [19]

Hyaluronic Acid

Hyaluronic acid (HA) is a key participant in tissue regeneration and has been demonstrated to have multiple roles in the wound-healing process. In 2017 a multi-center randomized controlled trial compared intralesional hyaluronic acid with verapamil in PD's treatment. It has shown greater effectiveness on improvement of penile curvature and patient's satisfaction in those treated with hyaluronic acid. A 2020 prospective clinical study has proven HA to be an effective option of treatment in the acute phase of the disease while also helping patient's erectile function [20]

Collagenase Clostridium Histolyticum

Collagenase clostridium histolyticum (CCH) is an anti-fibrotic agent which degrades the collagen and is the only FDA approved intralesional drug for treatment of PD. Two large randomized controlled trials were performed on the subject of the efficacy of CCH in treatment of PD. The deformity has been corrected for the average of 17° while also greater satisfaction of the International Index of Erectile Function was achieved. Moreover, a multi-institutional retrospective analysis has confirmed the safety and efficacy with low rate of adverse effects. This indicates CCH to be an effective agent in management of PD with moderate penile curvature. However, it's not the first line medication for PD patients with painful or calcific plaque, penile curvature more than 90° and hourglass deformities. [21, 22, 23]

Mechanical therapy

Traction and vacuum therapies have their place in the treatment of PD. The reasoning behind it seems to be an attempt of remodelling the extracellular matrix of the plaque via mechanically-induced signal transduction pathways and gene regulatory mechanisms. Overstretching the penile plaques can increase the level of degradative enzymes. [24, 25]

Surgical treatment

The technique of surgical treatment should be chosen individually for each patient. Factors such as penile rigidity, degree of curvature, shaft narrowing and erectile response have to be taken into consideration. Potential adverse events related to PD surgery include: de novo ED, worsening of preexisting ED, curvature recurrence, glans hypoesthesia, palpable sutures/material and graft bulging. [26, 27]

Penile plication

It involves the placement of sutures on the opposite side of the plaque to pull the penis into straighter shape. It is offered to patients with adequate penile rigidity for coitus. It is considered to be a safe and straightforward procedure with minimal chance of inducing ED or decreased sensation. Some studies have had 93% of patients reporting straight erections at 6 months postoperatively. Also, the results are very good in complex deformities with different types of curvature [28, 29]

Plaque incision or excision with or without grafting

It is an alternative surgical technique offered to patients with adequate rigidity for coitus. It is recommended for patients with severe deformities, significant hourglass deformities or plaque burden. Procedure is reported to have complication rates of about 67% for postoperative ED and 20% for decreased sensitivity and 18-43% for penile shortening. Despite the risks, the satisfaction rates soar up to 97% at the follow up in 20 months following the incision. [30]

Penile prosthesis

The surgery could be offered to patients suffering from PD with coexisting ED or penile deformity sufficient to impair sexual intercourse despite non-surgical treatment as it offers resolution to both these problems at once. Studies show that inflatable penile prostheses produce a high rate of satisfaction reaching over 80% and decreases the rate of depression in patients. Combining inflatable prosthesis with penile plication or graft excision/incision has also provided good results [31, 32]

CONCLUSION

Peyronie's disease is a condition which requires holistic approach and complex solutions.

With the prevalence of up to 20% it affects many males and could put them in a state of psychological trauma.

Patients have to be educated about different symptoms such as: curvature of the penis - especially during erection and associated with pain, erectile dysfunction and a palpable plaque.

Treatment methods could be non-invasive, intralesional, tractional or surgical and the method of treatment should be chosen in regards to the patient's best interest.

Statement of the author's contribution

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Receiving funding - no specific funding.

All authors have read and agreed with the published version of the manuscript.

Financing Statement
This Research Received No External Funding

Institutional Review Board Statement
Not Applicable

Informed Consent Statement
Not Applicable

Data Availability Statement

Not Applicable

Conflict Of Interest

The authors deny any conflict of interest.

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