Investigating the Effects of High-Dose Phenylephrine in the Management of Prolonged Ischaemic Priapism

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ABSTRACT

Introduction. Acute priapism can be managed by corporal blood aspirations and the instillation of α adrenergic agonists such as phenylephrine if patients present early. Following prolonged ischaemic priapism, this regimen is often unsuccessful, and the use of phenylephrine is limited due to systemic cardiovascular side effects.
Aim. To investigate the effects of high-dose phenylephrine on human corpus cavernosal smooth muscle obtained from patients presenting with refractory ischaemic priapism.
Methods. Strips of corpus cavernosum were obtained from six patients presenting with prolonged ischaemic priapism (duration 60–240 hours), where detumescence was refractory to conventional doses of phenylephrine. The smooth muscle contractile response to high doses of phenylephrine were then compared with that of normal control corpus cavernosum obtained from four patients undergoing a penectomy for penile cancer. The tissue was then analyzed using TUNEL (terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling) to assess its viability.
Main Outcome Measures. The in vitro response to high-dose phenylephrine of corpus cavernosum smooth muscle obtained from patients with refractory priapism compared with normal human corpus cavernosum.
Results. Corporal blood gas analysis confirmed hypoxia (pO_2 1.5–2.3 kPa), acidosis (pH 6.9–7.1), and glucopenia (0–0.3 mmol/L) in all six patients confirming the ischaemic nature of the priapism. Application of high doses of phenylephrine produced a marked muscle contraction in the control tissue, but there was no contractile response at all in any of the priapism patients. Analysis with TUNEL indicated widespread smooth muscle cell apoptosis in all the priapism tissue.
Conclusions. This study has shown that patients with ischaemic priapism that fails to respond to conventional doses of an α-agonist are unlikely to benefit from continual or high-dose phenylephrine administration, as there is usually widespread apoptosis of the cavernosal smooth muscle preventing further contraction. **Muneer A, Minhas S, Freeman A, Kumar P, and Ralph DJ. Investigating the effects of high-dose phenylephrine in the management of prolonged ischaemic priapism. J Sex Med 2008;5:2152–2159.**

Key Words. Corpus Cavernosum; Priapism; Erectile Dysfunction; Smooth Muscle; Penis; Phenylephrine

Introduction

Priapism is defined as a prolonged penile erection in the absence of sexual stimulation and persists despite orgasm. Although a rare condition, it often presents as a delayed medical emergency [1]. Traditionally, a time period of 4 hours is recommended where by patients should seek active medical treatment if there is a failure of detumescence [2]. In reality, patients often seek medical attention after a much longer time period [1].

The most common subtypes are ischaemic and nonischaemic priapism. Ischaemic priapism, a medical emergency, is characterized by a prolonged stagnation of blood within the corpus cavernosum that becomes increasingly hypoxic and acidotic [1]. High-flow priapism is less common and is characterized by an increase in the penile

arterial flow within the corpus cavernosum, and is well oxygenated in the absence of acidosis, and, therefore, the management is less urgent.

The medical management of ischaemic priapism includes conservative methods initially, such as ice packs, cold baths, sedatives, and further ejaculation. These therapeutic measures are through anecdotal reports and individual experiences. Failing this, aspiration of blood from the corpus cavernosum is performed. If the erection persists despite these measures, then the instillation of α-adrenergic agonists is performed. As the duration of priapism increases, α-agonists such as phenylephrine become less efficacious in achieving successful detumescence. Alternative pharmacotherapies such as methylene blue [3] and terbutaline[4] have been used with anecdotal reports of success. Eventually surgical options in the form of shunt surgery is required [5,6].

Animal models reproducing these conditions of acidosis, hypoxia, and glucopenia have demonstrated an impairment in cavernosal smooth muscle contraction to α-agonists [7–10]. Studies on the effects of higher doses of phenylephrine in vivo have been limited due to the systemic side effects. A study utilizing high-dose phenylephrine (bolus doses of phenylephrine up to 1,000 μg repeated every 5 minutes) have been reported to achieve successful detumescence in 17 patients suffering from iatrogenic priapism lasting up to 48 hours in some cases [11].

The aim of this in vitro study, therefore, was to investigate the effects of high concentrations of phenylephrine on human cavernosal smooth muscle from patients presenting with prolonged ischaemic priapism refractory to conventional medical treatment.

Aims

The study aims to identify parameters common to priapism patients failing to respond to phenylephrine treatment, then to undertake an in vitro investigation into the effects of high-dose phenylephrine on human corpus cavernosal smooth muscle obtained from patients presenting with refractory ischaemic priapism. The tissue will then be analyzed histologically in order to identify the cause for the refractory priapism.

Materials and Methods

Normal Human Corpus Cavernosum

Normal human corpus cavernosum was obtained from four patients (mean age 48, range 42–53) undergoing a partial or total penile amputation for penile carcinoma. The use of human tissue was approved by the University College London/University College London Hospitals (UCL/UCLH) Ethics Committee. All of these patients had a penile carcinoma that was located distally, and all of the patients reported normal erectile function preoperatively. Therefore, for the purposes of this study, we obtained tissue from the most proximal part of the corpus cavernosum, as this was considered functionally normal.

At the time of the operation, a small piece of corpus cavernosum was dissected well away from any macroscopic tumor and the tissue was immediately placed into ice-cold modified Kreb's solution.

Human Corpus Cavernosum Obtained from Patients Presenting with Prolonged Priapism

Patients presenting with prolonged ischaemic priapism (N = 6) had an initial Duplex Doppler ultrasound using a 10 MHz probe in order to establish the diagnosis. This was followed by corporal blood aspiration and infusion of phenylephrine (repeated doses of 200 μg up to a maximum of 1,000 μg). The phenylephrine dose was limited as some patients had already undergone phenylephrine infusion up to 1,000 μg at the initial hospital of presentation, and our protocol limited the use because of systemic side effects. If the priapism failed to resolve, then these patients were offered the option of having the immediate insertion of a penile prosthesis pending the results of an on-table frozen section biopsy of the cavernosal smooth muscle. The duration of their priapism ranged from 60–240 hours. Immediately prior to the operation, corporal blood aspirates were analyzed for pO_2 levels, pH and glucose concentration using an automated blood gas analysis chamber. A corporotomy was performed and tissue was obtained for histological analysis with strips being placed immediately in ice-cold modified Krebs solution.

Functional Study

Experiments were performed in order to compare the response of normal human corpus cavernosum and that from priapism patients with phenylephrine. Normal human corpus cavernosum strips or tissue strips from priapism patients (3 × 8 mm) were mounted horizontally in superfusion chambers between two ring electrodes 4 mm in diameter as described previously [12]. The double-jacketed chambers were maintained at 37°C. The chambers were perfused with modified Kreb's solution at a constant flow rate of 1 mL per minute