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Prostaglandin E_1 in the medical management of erectile dysfunction in a genito-urinary medicine clinic

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SUMMARY

Fifty consecutive patients with erectile failure who had previously proved refractory to papaverine and phentolamine intracavernosal therapy or were inappropriate candidates for such treatment were treated with intracavernosal prostaglandin E_1. Forty patients (80%) achieved an erection sufficient for sexual intercourse and after a mean follow-up period of 5.9 months, 32 patients were continuing to use treatment successfully. The average dose was 14 micrograms (range 2.5 to 30 micrograms). There were no cases of priapism or cavernosal fibrosis and no systemic side effects. A low incidence (8%) of local discomfort was reported. We conclude that prostaglandin is a safe and effective vasoactive agent for the treatment of erectile failure in a genito-urinary outpatient clinic.

INTRODUCTION

The use of intracavernous vasoactive agents has been shown to be effective in the medical treatment of erectile dysfunction. Virag [1] originally described the use of the smooth muscle relaxant papaverine while Brindley [2] demonstrated the effectiveness of the alpha adrenergic receptor blocker phenoxybenzamine. A combination of papaverine plus phentolamine (an alpha-blocker) was subsequently shown to be more effective than either agent alone [3,4]. Ishii [5] has described the use of prostaglandin E_1, and studies have since demonstrated its efficacy in association with a reduced incidence of serious side effects [6,7,8]. We are unaware of reports of the use of this drug in a genito-urinary clinic, and describe our experience.

PATIENTS AND METHODS

Patients with erectile dysfunction were referred to the Genito-Urinary Medicine Clinic, which provides a weekly clinic for erectile dysfunction, from their general practitioners or from consultant staff within the Northern Ireland hospital system. After a detailed sexual and medical history a full physical examination was performed and blood was taken for haemoglobin concentration, erythrocyte sedimentation rate, plasma glucose, liver function tests, testo-

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sterone and prolactin measurement. Intracavernous Prostaglandin E_1 was first used in this clinic in November 1991, and this paper describes the first 50 patients. Those selected fulfilled one or more of the following criteria:

(1) Previous failure to achieve satisfactory erectile response to papaverine 30 mg plus phentolamine 1 mg.

(2) Previous priapism associated with papaverine plus phentolamine treatment or

(3) Patients with a history of serious ischaemic heart disease but who were currently stable.

The latter group of patients were assessed by a consultant cardiologist to ensure that treatment for their impotence was appropriate.

Intracavernous injection of 10 μg of prostaglandin was given with a fine bore needle (26 gauge) into the lateral aspect of one of the corpora cavernosa at a site 1-2 cms proximal to the coronal sulcus. It was not our routine practice to use a constricting band at the base of the penis at the time of injection. The drug was supplied in 1 ml ampoules containing 10 μg prostaglandin E_1. These were individually prepared at the pharmacy of the Royal Victoria Hospital from 500 μg ampoules (Upjohn). The initial dosage was 10 μg with appropriate titration according to response up to a maximum of 30 μg. Once an erection sufficient for sexual intercourse was achieved the patient was instructed in the technique of self-injection and supervised to ensure that their technique was correct. A supply of needles, syringes and prostaglandin E_1, was then provided for home use with advice that the injection should not be used more than twice per week; the patient attended on a regular basis to monitor effectiveness, side effects and to provide new supplies. Those who did not achieve an erection sufficient for sexual intercourse despite maximal dosage of 30 μg were assessed for a mechanical suction device.

RESULTS

Fifty patients satisfied the criteria for treatment between November 1991 and September 1992. This represented approximately one third of patients on intracavernosal treatment. Their average age was 52.5 years (range 25-74) with a mean duration of impotence of 5.7 years (range 6 months – 30 years). The aetiology was organic in 44 cases, psychogenic in 3 cases and uncertain in three cases (Table 1). Five patients had had previous episodes of priapism.

TABLE 1

Aetiology of impotence

Aetiology	*Number of patients*	*(%)*
Vasculogenic	31	(62)
Diabetes	6	(12)
Neurgenic	5	(10)
Psychogenic	3	(6)
Idiopathic	3	(6)
Alcohol-related	2	(4)

Forty patients (80%) achieved an erection sufficient for sexual intercourse; ten failed. In those treated successfully the average dose was 14 μg (range 2.5-30), the average duration of erection being 80 minutes (range 20 minutes – 4 hours). Of the original 40 patients with a satisfactory response 32 are still attending and regularly using injection therapy after a mean follow-up period of 5.9 months (range 1-11 months). Eight patients have failed to continue to attend for unknown reasons.

Four patients complained of local pain in the penis, usually burning in nature and associated with the erection. The aetiology of erectile failure in these cases was vasculogenic in two, diabetic in one and psychogenic in one. In the diabetic case local pain necessitated reduction of the dose from 10 to 5 μg. His erectile response was still satisfactory at the lower dose. To date there have been no systemic side effects and no cases of priapism or corporeal fibrosis.

DISCUSSION

Prostaglandin E_1 is an endogenous prostaglandin whose mode of action has yet to be fully elucidated. It acts as a powerful smooth muscle relaxant leading to dilatation of the cavernosal arteries and relaxation of the cavernosal sinusoidal smooth muscle. Its efficacy has been well documented, with erections sufficient for sexual intercourse reported in 68-86% of patients in unselected series [5, 9, 10]. The response rate is highest in those of psychogenic and neurogenic origin, [7, 8] reaching almost 100% in some series [7, 8]. A significantly lower rate of positive response occurs in cases of vasculogenic or diabetic impotence [5, 11]. Our own series was a selected group in terms of aetiology in that failure to respond to papaverine plus phentolamine tended to favour patients with a vasculogenic aetiology and this subgroup formed 60% of the total patient population. The aetiological diagnosis was presumptive on the basis of the clinical history, the presence of coexisting or previous significant medical conditions and thorough physical examination. Angiography was not available for further assessment of presumed vasculogenic cases and it is probable that there was some overlap in the categories, most notably in diabetic cases where both vasculogenic and neurogenic components are commonly present. The idiopathic group were patients in whom no overt organic risk factor for erectile dysfunction could be identified but who at the same time demonstrated no clear evidence of psychological problems. More intensive psychological and physical assessment might allow a more accurate classification of such patients. In this study the overall response rate of 80% demonstrates the superior efficacy of prostaglandin E_1 in the treatment of vasculogenic impotence. In the ten cases where treatment was unsuccessful the presumed aetiology was vasculogenic in seven, idiopathic in two and diabetic in one.

The use of papaverine has two principal complications, priapism and corporeal fibrosis. With the introduction of a combination of papaverine plus an alpha-blocking agent the dosage of papaverine required to induce an erectile response was significantly lowered, but despite this priapism and fibrosis remain important clinical side effects. Ten percent of our patients were commenced on prostaglandin E_1 because of previous priapism associated with papaverine and phentolamine treatment.

Prostaglandin E_1 is a physiological agent partially metabolized locally within the cavernous tissue, and approximately 70% eliminated in a single passage

through the lungs [12]. It is this rapid elimination which is believed to account for the absence of systemic side effects even in the presence of venous leakage. Many reports on its clinical use have shown a notable absence of priapism or fibrosis [5, 8, 9]. Some authors, however, have documented priapism requiring treatment with metaraminol [10], the most vulnerable group being those with a non-vasculogenic aetiology. Cases of sustained erections of up to 11 hours have also been described where spontaneous detumescence ultimately occurred [6, 10]. In our own series there were no cases of priapism or sustained erection and this may be related to the selection of patients with vasculogenic disease. Corporeal fibrosis and fibrotic thickening of the tunica albuginea have been reported with papaverine injections and may be related to a number of factors including repetitive needle trauma, organization of haematomas associated with vascular puncture, or a local toxic reaction to papaverine solution which is of low pH [13-16]. We found no cases of corporeal fibrosis although the period of follow-up at present is relatively short.

In previous studies the most commonly described side effect of prostaglandin E_1 is the occurrence of localized pain in the penis, varying in intensity from mild discomfort to a severe burning sensation prohibiting sexual intercourse. The reported incidence varies from 11% up to 75% [6-10], but was a complaint in only four patients (8%) in our own series. In only one was a dose reduction required to ameliorate this problem. Localized pain appears to occur more commonly in those individuals whose impotence is non-vasculogenic in origin [10], which may explain the low incidence of this series. Intracavernous prostaglandin E_1 has proved an effective and safe alternative agent for the treatment of erectile failure with particular application to those patients where treatment with papaverine and phentolamine had been ineffective or inappropriate.

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