Management of pharmacologically induced prolonged penile erection with oral terbutaline in traumatic paraplegics

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Intracavernosal administration of papaverine or prostaglandin E1 for erectile impotence in paraplegics is being practised widely. One of the complications of this therapeutic regimen is prolonged erection which is at present being treated by aspiration of corporeal blood and intracavernosal administration of alpha-adrenergic agonist such as phenylephrine. We report successful management of pharmacologically-induced prolonged erection in three traumatic paraplegics with oral terbutaline therapy. The indications for oral terbutaline therapy were (1) absence of significant coronary artery disease and (2) full erection persisting for more than 2½ h, but less than 4 h duration. The initial dose of terbutaline was 5 mg and the same dose was repeated after 15 min as full erection persisted. Within the next 15 min, penile detumescence was achieved in two paraplegics with papaverine-induced prolonged erection. However, full erection still persisted 15 min after the second dose of terbutaline in the third patient who had received intracavernosal administration of 3.25 µg of prostaglandin E1. Therefore, he was given the third and final dose of 5 mg of terbutaline under cardiac monitoring. Penile detumescence was achieved within the next 15 min. It was ensured before administration of the third dose of terbutaline that (1) his blood pressure was within the normal range (for his paralysed status), (2) the heart rate was less than 100 per min and (3) there was no cardiac arrhythmia. Occasional premature ventricular contraction was observed only in the patient who received the third dose of terbutaline, but it was transient, self-limiting and did not warrant any treatment. In conclusion, oral terbutaline therapy was effective in achieving penile detumescence in selected cases of pharmacologically induced prolonged penile erections in the spinal cord injured and was devoid of clinically significant side effects.

Keywords: terbutaline; paraplegia; impotence; priapism; penile erection.

Introduction

Intracavernous self injection pharmacotherapy with papaverine for impotence has dramatically altered the therapeutic regimens for erectile dysfunction during the past decade. However, the most significant complication of pharmacologically stimulated erection is a prolonged erection which is dose related and is most frequently observed in men with neuropathic or psychogenic impotence. The incidence of these prolonged erections reported in the literature ranges from 2% to 18%.¹ The standard therapy for pharmacologically in-

duced prolonged erections is a combination of aspiration of up to 70 cc of corporeal blood and intracorporeal injection of alpha-adrenergic agonist and smooth muscle contracting agents, such as phenylephrine, epinephrine, metaraminol and dopamine. Intracavernous use of an alpha-adrenergic agonist should be taken seriously since two patients have died of acute severe hypertension resulting from intracorporeal injection of metaraminol for priapism.² Alternatively, surgical procedures such as Winter's corporoglandular shunt may be carried out to achieve penile detumescence.

Oral medical therapy for the treatment of pharmacologically induced prolonged erections is more attractive than aspiration of corporeal blood, intracavernosal administration of an alpha-adrenergic agonist or a surgically created shunt procedure. Oral medical therapy can be instituted at an earlier time since the medication may be self administered by the patient at home at the appropriate time. It obviates the need for an emergency visit to a hospital for intracorporeal phenylephrine injection and its associated psychological sequelae.

It would be really embarrassing for a man to rush to the emergency department of a hospital in the middle of the night with pharmacologically induced prolonged erection. It has a demoralising effect upon the patient and his spouse as well. Self-administered oral medical therapy for achieving penile detumescence can be practised by the patient himself in his home environment without rushing to a hospital. It is a boon to paraplegics and tetraplegics when they go on a holiday to a remote seaside resort where facilities for emergency transport and medical care are not readily available.

We describe our experience with oral administration of terbutaline for treatment of pharmacologically induced prolonged erection in paraplegics.

Case reports

Case 1

A 32 year old T7 traumatic paraplegic since 1988, who had been enjoying good health otherwise, developed persistent erection after intracavernosal injection of 30 mg papaverine. The duration of prolonged erection was 3 h when he received the first dose of terbutaline 5 mg by mouth. Fifteen min later, full erection persisted and therefore, a second dose of terbutaline 5 mg was administered by mouth. Complete detumescence was achieved within the next 15 min and there was no side effect of terbutaline therapy.

Case 2

A 26 year old T7 traumatic paraplegic since 1991 developed persistent erection after intracavernosal injection of 30 mg papaverine. As erection continued for more than $2\frac{1}{2}$ h, 5 mg of

terbutaline was given by mouth. Fifteen min after the initial dose of terbutaline full erection persisted and therefore a second dose of terbutaline 5 mg was administered by mouth. Complete detumescence was achieved within the next 15 min. After the second dose of terbutaline he was connected to a cardiac monitor. No untoward effect from terbutaline therapy was observed.

Case 3

A 44 year old T12 paraplegic since 1992 received intracavernosal administration of $3.25\text{ }\mu\text{g}$ of prostaglandin E1. Erection persisted for more than $2\frac{1}{2}$ h and therefore, he received terbutaline 5 mg by mouth. Full erection persisted 15 min later and therefore an additional dose of 5 mg terbutaline was given by mouth. Half an hour later, full erection still persisted and he was therefore connected to a cardiac monitor and the third dose of 5 mg of terbutaline was given by mouth. Penile detumescence was achieved within the next 15 min. An occasional ventricular premature contraction was observed in the ECG. The patient was comfortable and there was no clinically significant side effect of terbutaline. He was discharged home after an hour of careful observation of his cardiac status.

Case 4

A 47 year old male reported to the hospital with more than 6 h duration of papaverine induced penile erection. Terbutaline was administered by mouth initially at a dose of 5 mg and the same dose was repeated after 15 min as full erection persisted. Half an hour later full erection still persisted and therefore papaverine induced penile erection was treated by aspiration of corporeal blood and intracavernosal administration of 2 ml phenylephrine ($100\text{ }\mu\text{g}$ per ml).

This case illustrates the inefficacy of oral terbutaline therapy in cases of pharmacologically stimulated penile erection of more than 6 h duration. Preferably, terbutaline should not be administered in such cases as these patients will be treated subsequently with intracavernous phenylephrine to achieve penile detumescence. Prior unsuccessful therapy with terbutaline may only produce cardiovascular side effects such as tachycardia. Cardiovascular side effects are likely to occur again when phenylephrine is administered intracavernosally, thus compounding the problem of arrhythmias.

Discussion

Prolonged erection after intracavernous injection of a vasoactive agent is a result of continuing arterial flow, cavernous smooth muscle relaxation, and venous compression. Terbutaline is a synthetic, sympathomimetic, beta 2-agonist with minor beta 1 effects. The mechanism of action of terbutaline in reducing the penile tumescence is not understood clearly. It is believed that terbutaline relaxes the stretched corporeal smooth muscles, causing release of the constricting and collapsing effect on the draining veins, relaxation of the polsters in the penile veins, widening of the diameter of the corporeal draining veins and removal of impediment to venous blood flow created by contracting polsters. Thus, the penis becomes flaccid. The wide arterial opening at the edge of the cavernous sinuses caused by stretching of these muscles is reduced in size or closed almost completely due to the relaxing effects of terbutaline on the cavernous smooth muscle. Thus, less blood flows into the cavernous sinusoids, and results in reduced blood accumulation in the sinusoids, further contributing to detumescence.

Shantha and associates³ administered terbutaline 0.25 mg subcutaneously every 6 h to achieve penile detumescence in a 19 year old schizophrenic man with priapism. They successfully managed five other patients with terbutaline 5 mg administered by mouth to treat pharmacologically induced penile erection (9 mg papaverine and 0.3 mg phentolamine) lasting longer than 4 h. Oral terbutaline resolved the condition completely within 30 min without recurrence. Gillenwater⁴ used terbutaline in a 7 year old white boy with priapism with outstanding success. This patient had had only temporary response previously to intracorporeal injection of alpha-adrenergic agents. Lowe & Jarow⁵ treated patients who had received intracavernosal administration of prostaglandin E1 in whom full erections persisted for over 2½ h. Terbutaline sulphate (5 mg) was administered by mouth and an additional 5 mg dosage was given if detumescence had not occurred within 15 min. Any patient with a persistent erection 3 h after the initial prostaglandin E-1 injection

received 2-4 ml intracorporeal phenylephrine (100 µg/ml). Penile detumescence was achieved with oral terbutaline in four of the seven patients with neuropathic impotence. Terbutaline was found to be significantly more effective than placebo. These authors recommended initial treatment of pharmacologically induced prolonged erections with oral terbutaline sulfate in patients who do not have significant coronary artery disease.

Controversy exists on (1) the optimum initial dose of terbutaline, (2) the time point at which the first dose of terbutaline should preferably be given and (3) how frequently it should be repeated. In cases of pharmacologically induced prolonged erection, the sooner the oral terbutaline is given, the greater are the chances of it achieving penile detumescence. As illustrated by case 4, when penile erection had persisted for more than 6 h, oral terbutaline therapy was ineffective. In prolonged erections of more than 6 h duration, ischaemia becomes apparent with change of penile blood pH, pO₂ and pCO₂ and oral medication will have little chance of inducing detumescence. Drainage of blood and intracavernous injection of diluted alpha-adrenergic agent should be instituted to reverse the condition and prevent tissue damage.⁶ Oral medical therapy with terbutaline is not recommended in cases of prolonged erection of more than 6 h duration.

In our clinical practice involving the care of spinal cord injured patients, we did not observe spontaneous occurrence of penile detumescence in any of our patients in whom full penile erection persisted at 4 h after intracavernosal administration of papaverine. Hence, we are anxious to institute oral medical therapy as early as possible in order to avoid the deleterious sequelae of persistent penile erection. Understandably, we may be overtreating a few patients, but we believe that the benefits of oral drug therapy in selected cases of pharmacologically induced persistent penile erection outweigh the risks involved, provided the medical therapy is carried out strictly in accordance with the protocol detailed below.

We prefer to start treatment with oral

terbutaline for patients in whom full penile erection persisted for more than 2½ h after intracavernosal administration of papaverine or prostaglandin E1. Provided he does not have significant coronary artery disease, we advocate self administration of an initial dose of 5 mg of terbutaline by mouth. The patient and/or his spouse should review the status of penile tumescence 15 min after oral administration of terbutaline. If penile erection is subsiding, further doses of terbutaline are not required. But a patient in whom full erection persists at 15 min after the initial dose of terbutaline is advised to take a second dose of 5 mg of terbutaline by mouth and to review the status of penile tumescence again after an interval of 15 min. If full erection persisted at 15 min after the second dose of terbutaline, he should go to the spinal injuries unit as quickly as possible.

When he arrives at the spinal injuries unit, a doctor immediately carries out a careful assessment of his clinical status. The patient is attached to a cardiac monitor. If (1) his blood pressure is within the normal range (for his paralysed status), (2) the heart rate is less than 100 per min and (3) there is no evidence of cardiac arrhythmias, (4) full penile erection is still present, (5) the total duration of pharmacologically induced penile erection is not more than 4 h duration and (6) there is no hypokalaemia, he is given the third and final dose of 5 mg of terbutaline by mouth. As illustrated by case 3, this additional dose of terbutaline may help to achieve penile detumescence in selected patients who satisfy all the above mentioned criteria. After administration of the third dose of terbutaline, a physician stays with the patient for at least 1 h carefully observing his cardiac status. Sometimes after oral administration of terbutaline, ventricular premature contractions may be seen as happened in case 3. But as long as their frequency is less than 1 per min and as long as there is no (1) sequential ventricular depolarisations without intervening sinus and beats, (2) multifocal origin of premature ventricular contractions and (3) R on T phenomenon (premature ventricular depolarisation occurs in the T wave of the preceding beat), careful observation

of the patient may suffice; otherwise, suppressive agents should be used. Serum potassium is again checked as overdose of beta-2 agonists may be associated with hypokalaemia which is probably caused by a redistribution of potassium from the plasma and extracellular fluid into the cells mediated by an increase in intracellular 3–5 cAMP concentration. However, in the healthy heart, marked cardiac stimulation and hypokalaemia produced by beta-2 agonists do not necessarily lead to the development of cardiac arrhythmias.

In the unlikely event of full penile erection persisting at 30 min after the third dose of terbutaline, aspiration of corporeal blood and intracavernosal administration of phenylephrine (100 µg of phenylephrine diluted in 1 ml normal saline is administered slowly every 5 min up to a maximum dose of 500 µg or until penile detumescence is achieved, whichever is earlier) are carried out under cardiac monitoring to pharmacologically contract the corporeal smooth muscle. The physician must be familiar with their use and must have vasodilators ready. Phenylephrine must not be given to hypertensive patients and to those with arteriosclerotic coronary artery disease. In patients with significant coronary artery disease who have developed persistent penile erection after intracavernosal administration of papaverine or prostaglandin E1, neither terbutaline nor phenylephrine should be administered. The safest way of managing pharmacologically induced persistent penile erection in such patients is prompt aspiration of corporeal blood which may have to be repeated. If arterial inflow is not reestablished, as evidenced by persistent or recurrent dark corporeal aspirates, surgical shunting to the glans or corpus spongiosum should then be performed. Corporoglandular shunt (Winter's procedure) may be performed with a Trucut needle (Baxter Health Care Ltd, Compton Newbury, UK) under local anaesthesia with lidocaine. Similarly, terbutaline sulfate should not be used for treatment of pharmacologically induced prolonged penile erection in paraplegics who have other concomitant disease(s), such as (1) diabetes mellitus, (2) hypertension, (3) hyperthyroidism, (4) a history

of seizures, or in those spinal cord injured patients who are known to be hypersensitive to sympathomimetic agents.

In conclusion, we recommend initial treatment of selected cases of pharmacologically induced prolonged penile erection with oral terbutaline sulfate; oral terbutaline therapy may obviate the need for an emergency visit to the hospital for intracoporeal phenylephrine injection.

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