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Intravenous salbutamol treatment for penile erection arising during cystoscopy of cervical spinal cord injury patients

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Two patients with long-standing tetraplegia after spinal cord injury developed reflex penile erection in the operation theatre. One had not received any anaesthesia, and penile erection occurred after introduction of the cystoscope into the urethra, and also *autonomic dysreflexia*. Intravenous salbutamol, in a dose of 10 micrograms, produced immediate and persistent penile detumescence and salbutamol-induced fall in blood pressure was of therapeutic value. In the second patient, penile erection occurred during general anaesthesia prior to cystoscopy. Immediate and persistent penile detumescence was achieved with intravenous salbutamol 20 micrograms. There was transient fall of blood pressure which responded to intravenous infusion of 0.9% sodium chloride. Salbutamol-induced fall in blood pressure is of therapeutic value in those spinal cord injury patients who develop, in addition to penile erection, autonomic dysreflexia precipitated by urethral instrumentation, or bladder distension with the irrigating fluid. Intravenous salbutamol is preferable to intra-cavernosal phenylephrine, noradrenaline, metaraminol, and epinephrine, or intravenous ephedrine which are contra-indicated in patients with hypertension.

Keywords: salbutamol; cystoscopy; spinal cord injury; penile erection; tetraplegia

Introduction

Intra-operative penile erection may occur during any transurethral procedure or during penile surgery, the incidence being 2.4% in able-bodied individuals,[1] and could result in cancellation of the proposed urological endoscopic or penile operative procedure. In tetraplegic patients, urethral instrumentation or penile handling may provoke not only reflex penile erection but also *autonomic dysreflexia* which is associated with an increase in blood pressure. This underscores the need to choose an appropriate drug to treat penile erection in spinal cord injury patients, in contrast to able bodied individuals who never develop autonomic dysreflexia. In the Southport Regional Spinal Injuries Centre, two tetraplegic patients out of the 26 cervical spinal cord injury patients undergoing urological endoscopic procedure over a 2 year period (January 1994 to January 1996) developed penile erection lasting for more than 5 min (7.69%), and they required drug therapy to achieve prompt penile detumescence. Paucity of literature on the management of intra-operative penile erection in the cervical spinal cord injury patients prompted us to report these two cases, and to review the relevance of treatment protocols designed for the treatment of intra-operative penile erection in the able-bodied individuals to cervical spinal cord injury patients, as the latter group of patients may have altered physiology, and pharmaco-kinetic parameters for a number of drugs may be altered as a consequence of spinal cord injury.[2–6]

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Case reports

Case 1

This patient fell downstairs in 1976 and sustained a fracture dislocation of C-5/6 with complete tetraplegia below C-5. In November 1993, a 70 mm Memokath urethral sphincter stent was inserted to facilitate bladder emptying, with success. He was scheduled for elective removal of the stent in October 1994, to be followed by insertion of a new urethral stent at a later date. He received 3 mg of midazolam intravenously to minimize leg spasms. His blood pressure was 150/100 mmHg with a heart rate of 60/min. 2% lignocaine gel was instilled per urethra to anaesthetise the urethral mucosa. As the cystoscope was being inserted in the urethra, he developed a severe degree of penile erection and exhibited features of autonomic dysreflexia: the blood pressure rose to 200/110 mmHg with a heart rate of 50/min. Ketamine 25 mg was administered intravenously to obtain penile detumescence, but there was no

appreciable response within the next 5 min. Therefore, salbutamol 5 microgram was administered intravenously followed by another dose of 5 micrograms 5 min later. The blood pressure fell to 170/95 mmHg and the heart rate increased to 75/min. Within 2 min of administration of 5 mg of salbutamol intravenously, the penile erection began to subside. Complete penile detumescence was achieved immediately after the administration of a total dose of 10 micrograms of salbutamol intravenously. The planned endoscopic procedure was carried out without any further delay, and he made an uneventful recovery, and was discharged home the same afternoon.

Case 2

This patient fell downstairs in 1984 and sustained a hyperextension injury of the cervical spine with fracture dislocation at C-3/4. He had complete absence of touch and pain sensation below C-3 and complete loss of motor power below C-4. Subsequently, there was incomplete sensory recovery and he regained some degree of muscle power in the intercostal and abdominal muscles. He was experiencing psychogenic reflex penile erections. He had been suffering from ankylosing spondylitis for many years. In July 1993, a 60 mm Memokath urethral stent was introduced with a flexible cystoscope under local anaesthesia, without any complications. A follow-up X-ray of the pelvis in January 1996 revealed no calcification around the nickel-titanium urethral sphincter stent. He was scheduled for elective removal of the stent to be followed by insertion of a new sphincter stent for detrusor-sphincter dyssynergia at a later date. Premedication included oral 10 mg of temazepam and 150 mg of ranitidine, 2.5 h prior to anaesthesia, and for prophylaxis against post-operative autonomic dysreflexia, terazosin 3 mg and oxybutynin 5 mg were given by mouth 2 h prior to anaesthesia. On arrival in the operation theatre, his blood pressure was 65/50 mmHg and heart rate 55/min. 0.6 mg of glycopyrrolate was given as the vagolytic agent. With a laryngeal mask, inhalational anaesthesia was administered consisting of oxygen, nitrous oxide, and isoflurane. He was also given intravenously gentamicin 80 mg and cefuroxime 1.5 grams as prophylactic antibiotics. Blood pressure was 110/80 mmHg; heart rate 85/min. Prior to urethral instrumentation/penile handling, he developed penile erection which continued for 5 min. Therefore, he was given salbutamol 10 micrograms intravenously, followed by a further dose of 10 micrograms of salbutamol intravenously 2 min later. Within the next 2 min, complete penile detumescence was achieved. Cystourethroscopy was performed with ice-cold saline and the Memokath was removed without causing any bleeding per urethra. A 14 Fr. Foley catheter was inserted per urethra and clear urine was drained. There was a transient fall of blood pressure to 62/42 mmHg and a rise in heart rate to 100/min. Following intravenous infusion of one litre of 0.9% sodium chloride over 35 min, the blood pressure rose to 75/49 mmHg and the heart rate was 80/min. He has done well since then.

Discussion

Cervical spinal cord injury patients may develop penile erection during the spinal shock phase or, after they have recovered from spinal shock when reflex penile erection is usually induced by penile handling eg urethral catheterisation. Penile erection during the spinal shock phase to innocuous except that urethral catheterisation should be done very gently as urethral bleeding may occur. As no urinary endoscopic procedure is comtemplated at this stage, penile erection during the spinal shock phase is preferably left alone as penile detumescence is achieved spontaneously when the patient recovers from spinal shock.

In cervical spinal cord injury patients who have recovered reflex functions, penile erection may be precipitated by penile handling but, penile erection subsides within the next few minutes when the offending stimulus is removed, and we were usually able to proceed with the intended procedure, be it urethral catheterisation, or flexible cystoscopy, or insertion of a urethral sphincter stent after a delay of 5 to 30 min. Thus we did not have to treat any cervical spinal injury patient for persistent penile erection occurring either during the spinal shock phase or subsequent to their recovery from spinal shock in the ward/out-patient set-up, in our clinical practice spanning more than two decades, while providing comprehensive hospital-based, and community care to the spinal cord injury patients.

In contrast to the above scenario, reflex penile erection may occur in cervical spinal cord injury patients in the operation theatre during general anaesthesia due to (1) psychogenic reflex with afferent stimuli arising from the taste and smell of anaesthetic agents, exaggerated auditory sensation during the second stage of anaesthesia and dreams[7] (which is not surprising, because visual, olfactory, auditory, and imaginative stimuli are known to elicit erectile responses[8]) or, (2) washing, touching, and instrumentation of the area supplied by the pudendal nerve, eg penile handling and cystoscopy. As time is an important factor in the operation theatre set-up, we prefer to institute pharmacological treatment to achieve detumescence promptly in case penile erection does not subside immediately after removing any offending stimulus, eg insertion of a cystoscope. Forcible introduction of a rigid cystoscope into a turgid penis may produce urethral bleeding, perforation of the urethra or even fracture of the penis. Further, reflex penile erection may be associated with the development of autonomic dysreflexia precipitated by urethral instrumentation or distension of the urinary bladder with the irrigating fluid. Autonomic dysreflexia, if present, will require treatment if hypertension persists after the noxious stimulus is

withdrawn eg rapid emptying of the distended bladder or removal of the cystoscope from the urethra. In such patients who have developed penile erection and autonomic dysreflexia, intravenous drug therapy is desirable to achieve penile detumescence and prompt lowering of the blood pressure. Oral terbutaline has been shown to be effective in achieving penile detumescence in spinal cord injury patients with pharmacologically-induced persistent penile erection.[9] Oral medication is not feasible while a patient is under anaesthesia; further, penile detumescence needs to be achieved promptly, whereas oral terbutaline therapy takes 15 to 30 min to achieve complete penile detumescence. Therefore, intravenous drug therapy is essential in the operation theatre set-up. Shantha,[10] administered terbutaline intravenously (0.25 mg in one patient and 0.5 mg in three others) for the management of intra-operative penile erection in able bodied individuals. Complete detumescence was achieved in less than 4 min of terbutaline administration. However, the systolic blood pressure increased from 120 mmHg to 160 mmHg in one patient who received 0.5 mg of terbutaline intravenously and from 88 mmHg to 120 mmHg in another patient following intravenous administration of 0.25 mg of terbutaline. Intravenous administration of salbutamol in 10 healthy subjects (a loading dose of 400 micrograms followed by a constant infusion at a rate of 10 microgram per minute), did not result in any significant change in blood pressure.[11]

We found intravenous salbutamol therapy to be effective in achieving penile detumescence promptly in the two cervical spinal cord injury patients reported herein, but were very conscious of the propensity for intravenous beta-2 agonists to cause profound vasodilatation in spinal cord injured patients. The elimination half-life of salbutamol following its intravenous administration was 3.9 ± 0.8 h, and the renal clearance of salbutamol was 291 ± 70 ml/min.[11] We observed that once penile detumescence was achieved after the intravenous administration of salbutamol, penile erection did not recur later during cystoscopy; thus the initial doses of salbutamol were sufficient to maintain penile detumescence during the entire period of cystoscopy.

Staerman and associates[1] administered phenylephrine intra-cavernosally in a dose of 200 micrograms to 23 able-bodied individuals who developed penile erection during an endoscopic procedure or penile surgery. Penile detumescence occurred in all patients 2 to 3 min after a single intra-cavernosal injection of phenylephrine, but there was a significant increase in the systolic and diastolic blood pressures 10 min after the intra-cavernosal injection of phenylephrine. McNicholas and associates[12] observed a peak rise of blood pressure of 70/60 mmHg (systolic/diastolic) approximately 4 min after the intra-cavernosal injection of 1 mg of phenylephrine in an able-bodied individual developing erection during transurethral instrumentation. Although intra-cavernosal administration of phenylephrine is effective in achieving penile detumescence promptly, its major disadvantages are: (1) the occurrence of significant increase in the systolic and diastolic blood pressures; (2) necessity for a penile injection; (3) a penile haematoma at the site of the needle puncture. Some spinal cord injury patients dislike the idea of an injection into the penis whereas they do not have any objection to an intravenous injection. As cervical spinal cord injury patients are prone to develop autonomic dysreflexia, and have adrenergic receptor supersensitivity, any drug which results in a significant increase in blood pressure may not be the drug of choice for treatment of penile erection in the operation theatre set-up. Thus although intravenous ephedrine (in a dose of 10 mg initially followed by an additional dose of 10 mg injected intravenously and thereafter 20 mg of ephedrine given intravenously over 30 min) produced penile detumescence within 5 min in a 59 year old able-bodied male undergoing transurethral resection of prostate under spinal anaesthesia (with 12.5 mg of 0.5% tetracaine in 10% dextrose, resulting in a sensory level of T-6),[13] it will not be indicated in a cervical spinal cord injury patient for fear of producing hypertension or compounding the untoward cardiovascular symptoms of autonomic dysreflexia.

Miller and Galizia,[14] found the cooling effect of locally applied ethyl chloride spray to be an effective and safer method of achieving detumescence in able-bodied patients developing erection prior to, or during transurethral surgery. The ethyl chloride spray is applied liberally along the shaft of the penis, particularly around the base of the penis. These authors warned that blistering of the penile skin could occur if the skin is frozen with ethyl chloride spray. Thus the safety margin of this therapeutic modality appears to be very narrow, and all physicians caring for spinal cord injury patients wish to avoid at any cost damage to the neuropathic skin. Hence we would be very reluctant to use ethyl chloride spray in our patients for fear of producing blisters over the penis with its sequelae (viz. (1) inability to apply penile condom till such a time the blisters over the penile skin heal completely and even then, the blistered area may be more vulnerable to damage easily during the daily chores of applying and removing penile sheaths; (2) inability to perform sex when the penile skin is damaged).

Dorsal nerve block has been used for management of intra-operative penile erection in a 23 year-old able bodied man who developed persistent rigid erection during sterile preparation of the penis for laser ablation of penile condylomata acuminata under mask general anaesthesia. Injection of 5 ml of 1 : 1 mixture of 1% lidocaine (without epinephrine) and 0.5% bupivacaine into the subcutaneous/subdartos space on each side of the midline at the base of the penis resulted in immediate and persistent detumescence.[15] A potential risk of this procedure is haematoma formation at the injection site. We do

not know whether a dorsal nerve block alone will produce penile detumescence in a cervical spinal cord injury patient with altered physiology of the autonomic nervous system. Tactile or reflexogenic erection is mediated by a sacral spinal reflex with a sensory limb in the dorsal nerve of the penis, and pudendal nerve and, a motor limb consisting of the sacral parasympathetic fibres in the pelvic and cavernous nerves. Psychogenic erection is mediated at supraspinal level with afferent fibres received by, or originating in, thalamic (thalamic nuclei that process somatosensory and visual sensory information), rhinencephalic (including cingulate gyrus, septum, and hippocampus, which receive olfactory information), limbic structures (such as the temporal and frontal cortical lobes and the hippocampus responsible for emotion and memory), and hypothalamic regions of the brain and efferent fibres in the hypogastric and cavernous nerves.[8] The psychogenic stimuli arise from the taste and smell of anaesthetic agents, exaggerated auditory sensation during the second stage of anaesthesia or dreams.[7] Thus only for the tactile or reflexogenic erection, afferent impulses are carried in the dorsal nerve of the penis. Further, the emerging hypothesis is that penile erection may require not just the excitation of nerves promoting tumescence, but also the selective inhibition of the nerves that promote detumescence.[16] Therefore, a dorsal nerve block may not be effective in case of psychogenic penile erection, a pleasurable reflex, which may be experienced by tetraplegic patients with an incomplete spinal cord lesion as in the case number 2 described above.

Intravenous glycopyrrolate given incrementally for a total dose of 0.4 mg produced penile detumescence (2 min after the last glycopyrrolate increment was given) in a 60 year old man scheduled for transurethral resection of recurrent bladder tumour under subarachnoid block with lidocaine HCl in 5% dextrose.[17] It is interesting to observe that patient no. 2, despite receiving 0.6 mg of glycopyyrolate intravenously as the vagolytic agent just prior to the inhalational anaesthesia, developed reflex penile erection prior to urethral instrumentation or penile handling. Thus glycopyrrolate was found to be ineffective in preventing the development of reflex penile erection under anaesthesia in this cervical spinal cord injury patient. Similarly, patient number 1 received ketamine 25 mg intravenously for achieving penile detumescence, but there was no appreciable response in the next 5 min. It is stated by Valley and Sang[17] that the most often used medication for the treatment of intra-operative priapism is ketamine, but doses in excess of 0.5 to 0.75 mg/kg are required to reverse priapism, and sometimes larger doses given incrementally may be required to ensure prolonged relaxation. However, this medication may also produce significant increase in blood pressure, with risk of morbidity or mortality.[17] Therefore, we were reluctant to administer further doses of ketamine and preferred to use salbutamol intravenously.

The mechanism of action of salbutamol in reducing penile tumescence is not clearly understood. It is believed that beta 2-agonists relax the stretched corporeal smooth muscles, causing release of the constricting and collapsing effect on the draining veins, relaxation of the pollsters in the penile veins, widening of the diameter of the corporeal draining veins and removal of impediment to venous blood flow created by contracting pollsters. 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 beta 2-agonists on the cavernous smooth muscle. Thus less blood flows into the cavernous sinusoid and results in reduced blood accumulation in the sinusoid, further contributing to penile detumescence.

Nitric oxide (NO), initially considered to be a mediator of smooth muscle cell relaxation released by endothelial cells, was subsequently demonstrated to be synthesized and released also by neurons. Neural fibres immunoreactive for nitric oxide synthase (NOS), the enzyme that catalyses NO production, have been localized in the trabeculae of the corpora cavernosa and around the deep cavernosal and dorsal penile arteries.[18] Intra-cavernosal injection of NO donors elicits penile erection in man whereas smooth muscle relaxation is blocked by NO scavengers or NOS inhibitors. Pharmacological inhibition of NOS suppresses penile erection induced by cavernous nerve stimulation in the rat.[19] Thus NO scavengers and NOS inhibitors may hold promise for the possible treatment of prolonged penile erection in spinal cord injury patients.

Conclusion

Reflex penile erection may occur in the cervical spinal cord injury patients in the operation theatre during general anaesthesia prior to performance of any procedure in the region supplied by the pudendal nerve. Reflex penile erection may also occur during urological endoscopy or penile surgery and it may be associated with autonomic dysreflexia, in contrast to the able-bodied individuals who never develop autonomic dysreflexia. Penile detumescence is promptly achieved by the intravenous administration of salbutamol, preferably at a dose of 5 micrograms, the same dose being repeated at 2 min intervals if penile erection persisted, up to a total dose of 20 micrograms. Salbutamol-induced hypotension is of therapeutic value in those spinal cord injury patients who develop autonomic dysreflexia including a sudden rise in arterial pressure, often precipitated by urethral instrumentation and/or bladder distension. Salbutamol is preferable to intra-cavernosal phenylephrine, noradrenaline, metaraminol, and epinephrine with mixed alpha and beta effects, which are thus contraindicated in patients with severe hypertension. Even in those spinal cord injury patients without clinical

features of autonomic dysreflexia, salbutamol-induced hypotension at these low doses is of mild degree and it responds to intravenous infusion of 0.9% sodium chloride. Furthermore, salbutamol-induced bronchial dilatation may be of benefit, especially to the cervical spinal cord injury patients with decreased respiratory reserve.

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