

## Incidence, pathophysiology and treatment of prolonged erections

C. G. Stief<sup>1</sup>, W. Bühren<sup>2</sup>, H. Gall<sup>3</sup>, and W. Scherb<sup>4</sup>Departments of <sup>1</sup>Urology, <sup>2</sup>Radiology, <sup>3</sup>Dermatology and <sup>4</sup>Neurology and Psychiatry, BWK, Academic Hospital of the University of Ulm, FRG

**Summary.** Prolonged erections (pharmacologically induced erections over 6 hours) are the most inconvenient side effects encountered in the diagnosis and therapy of erectile dysfunction with intracavernous injection of vasoactive drugs. Out of a total of 29 prolonged erections, 26 were seen after diagnostic use in 300 patients and 3 after therapeutic application in more than 4800 protocolled autoinjection of a standardized vasoactive solution (papaverine hydrochloride 15 mg/ml and phentolamine mesylate 0.5 mg/ml). In 25 of these 29 prolonged erections intracavernous injections of the alpha-receptor stimulant metaraminol was done and led to flaccidity in all cases. Another patient with a papaverine-induced erection lasting 26 h did not respond to intracavernous metaraminol and required puncture and aspiration; he lost spontaneous erectability and cavernosal response to vasoactive drugs. Metaraminol was also injected intracavernosally in a further 32 patients with pharmacologically induced full erections: flaccidity was obtained in all patients.

Since intracavernous injection of vasoactive substances has proven easy to manage, safe and effective in the diagnosis and therapy of erectile dysfunction, it has found widespread use in patients with erectile failure [1, 2, 9–13]. However, as an untoward side effect, prolonged erection (pharmacologically induced erection lasting over 6 h) has been observed with increasing frequency [2, 3, 9–13]. At first Brindley reported prolonged erections in 16 patients responding to intracavernous administration of phenoxybenzamine, which ceased spontaneously after 22 h [2]. Later he mentioned another patients with prolonged erections lasting up to 40 h. Every patient was treated successfully with intracavernous injection of the alpha-receptor stimulant metaraminol [3]. Zorogniotti reported a prolonged erection in 1 of 65 patients after intracavernous autoinjection of papaverine-phentolamine [13]. He recommended treatment with puncture and aspiration. We report our experience with incidence,

pathophysiology and treatment of prolonged erections in the diagnosis and treatment of erectile dysfunction with vasoactive drugs. The control of this serious and frequent side effect is an indispensable requirement for therapy with intracavernous injection of vasoactive drugs.

### Patients and methods

The intracavernous injection of the alpha-receptor stimulant metaraminol was used to counteract 1 TUR- and 58 pharmacologically induced erections. The patients were divided into 6 groups as described below, with 10 healthy men serving as controls (Table 1).

To prevent hematomas as a result of puncture, aspiration or injection, a swab was pressed for 5 min on the site where the needle had penetrated. Blood pressure, pulse rate and ECG were monitored closely over 30 min in each patient of all 6 groups. Changes in arterial inflow and blood gases were documented by Doppler tests and blood gas analyses performed on 12 patients.

#### Group 1 (control group)

Metaraminol was used in a reference group of 10 potent young men (average age 24 years) to interrupt a complete 2-h erection induced by phentolamine mesylate 0.25 mg and papaverine hydrochloride 7.5 mg.

#### Group 2 (prolonged erection during diagnosis)

Between February 1985 and January 1987, 300 patients with erectile dysfunction underwent multidisciplinary examinations at the BWK-hospital in Ulm to elucidate the origin of their erectile failure. Due to the fact that vasoactive substances were used for diagnosis, patients with arterio-occlusive disease (AOD), starting with stage III, cardiac dysrhythmia, severe liver or kidney diseases or patients older than 65 years were excluded because adverse reactions were anticipated.

**Table 1.** A total of 63 erections treated in 61 patients by either aspiration and puncture (4 patients of group 2) or intracavernous injection of metaraminol (58 patients). Patients were assigned to 6 groups according to their etiology

Group No.		Patients No.	Erections No.
1.	Control group	10	10 Full erections
2.	Diagnostic injections	24	26 Prolonged erections
3.	Auto-injection therapy	3	3 Prolonged erections
4.	Impotent patients	20	20 Full erections
5.	Potent patients	3	3 Prolonged erections
6.	TUR-P	1	1 Full erection

After obtaining a comprehensive history with the aid of a questionnaire, the following tests were performed: physical examination, blood tests including fats, glucose tolerance and hormones (testosterone, prolactin; if applicable FSH, LH), sexual anamnesis and psychometry (MMPI: Minnesota Multiphasic Psychoinventory FPI: Freiburger Psychoinventory), bulbo-cavernosus reflex (BCR) latency and somatosensory-evoked potentials (SSEP), ultrasonography of abdomen and large vessels, Doppler and penile-brachial index (PBI) [5]. Selective angiography of the pelvis and penis [4] was performed on 59 patients, dynamic cavernosography on 94. Subsequently, i.c. pharmaacotesting was done.

After informed consent was obtained, each patient received an injection of papaverine hydrochloride (7.5 mg) and phentolamine mesylate (0.25 mg) in the right proximal corpus cavernosum by means of a 26-gauge needle. In 24 of the 300 patients, intracavernous injection of this mixture led to prolonged erections (persisting 6 h), associated with painful tension of the penile shaft in 3 cases (Table 1). Although only 3.7 mg papaverine and 0.12 mg phentolamine were injected the following day, another prolonged erection occurred in 2 of the 24 patients.

The first 4 cases of prolonged erection were treated by aspiration and lateral puncture of the proximal third of both corpora cavernosa using a 19-gauge needle. The other 20 patients were administered metaminiol intracavernosally, the first 7 being injected with 2.5 mg using a 26-gauge cannula, the remaining with 2.0 mg in the right proximal corpus cavernosum. Previous aspiration of blood was omitted.

#### *Group 3 (prolonged erection during auto-injection therapy)*

During auto-injection therapy at home, only 3 patients reported the occurrence of 1 prolonged erection each, persisting for 6–12½ h (mean = 8 h). A total of 4813 auto-injections were documented. The prolonged erections occurred despite individual dosing for induction of an erection of 30–90 min duration. In each of the 3 cases, the patient had self-injected a second dose after thinking the first injection was unsuccessful.

#### *Group 4 (interruption of erection due to injection of vasoactive substances)*

To unveil possible circulatory side effects of the intracavernous injection of metaminiol, 20 patients with erectile dysfunction responding to the intracavernous injection of papaverine and phentolamine with a full erection were injected 2 mg metaminiol intracavernosally following diagnostic injection (average dosage 13.5 mg papaverine and 0.45 mg phentolamine). Metaminiol was injected after half of the expected individual duration of erection (72 min). Each of these patients consented to this study.

#### *Group 5 (accidental prolonged erection in potent men)*

Two potent men (24 and 41 years) self-administered an intracavernous injection of a vasoactive mixture „in order to achieve greater satisfaction for the sex partner“. Both men injected a solution of papaverine hydrochloride (7.5 mg) and phentolamine mesylate (0.25 mg) that had been supplied by other hospitals. The injections produced erections persisting for 6 and 18.5 h respectively. The second patient experienced painful tension of the penile shaft after 12 h of erection.

A third, 60-year-old, patient, capable of having normal coitus with full erections every 14 days, was injected papaverine hydrochloride (30 mg) by his urologist. As there was no effect within 10 min after administration, another 30 mg were injected and the patient was sent home with a complete erection. After 24 h he returned with a painful prolonged erection. At the office, intracavernous injection of 4 mg metaminiol had no effect. After 2 more hours, he was admitted to our hospital with a palpable, complete, painful erection.

#### *Group 6 (erection during TUR)*

A 71-year-old patient with a history of unimpaired sexual potency and coronary heart disease was to undergo transurethral resection for benign prostatic hyperplasia (BPH). Introduction of the resectoscope caused an erection with palpable full rigidity persisting for 15 min, which made transurethral resection impossible. In order to interrupt the

erection, metaminiol (2 mg) was injected in the right proximal corpus cavernosum.

## Results

### *Group 1 (control group)*

All 10 potent men exhibited complete flaccidity 9–22 min (mean = 13.1 min) after intracavernous injection of metaminiol (2 mg) in the right proximal corpus cavernosum. The ability to have spontaneous erections on the next day was not impaired.

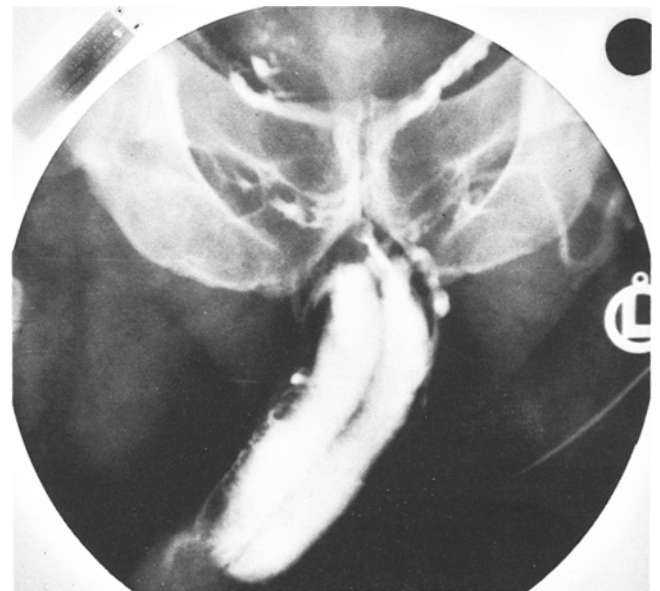
### *Group 2 (prolonged erection during diagnosis)*

In the first 4 prolonged erections aspiration of 210–400 ml (mean = 315 ml) of unclotted blood produced constant flaccidity in all cases. Residual spontaneous activity and the response to intracavernous injection of vasoactive substances on the third day after puncture were unchanged as compared with the previous state, i.e., before the prolonged erection.

The following 22 prolonged erections subsided after intracavernous metaminiol (2.5 or 2.0 mg). Complete flaccidity was attained after 7–20 min (mean = 14.4 min); the difference between the two doses was not statistically significant. The response to intracavernous injection of vasoactive drugs on the next day was not impaired.

### *Group 3 (prolonged erection during auto-injection therapy)*

Intracavernous injection of metaminiol (2.5 mg) in the right proximal corpus cavernosum did not reduce rigidity in any of the three patients. The erection did not subside



**Fig. 1.** Dynamic cavernosography 48 h after treatment of a 26-h prolonged erection by puncture and aspiration. Maintenance-flow = 148 ml/min

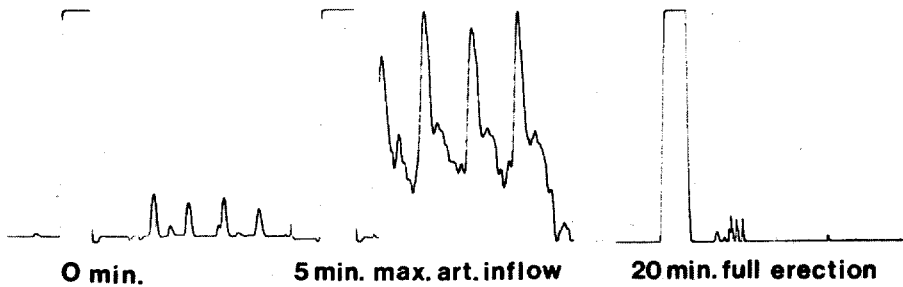


Fig. 2. Doppler sonography before, and 5 and 20 min after erection induced by vasoactive drugs

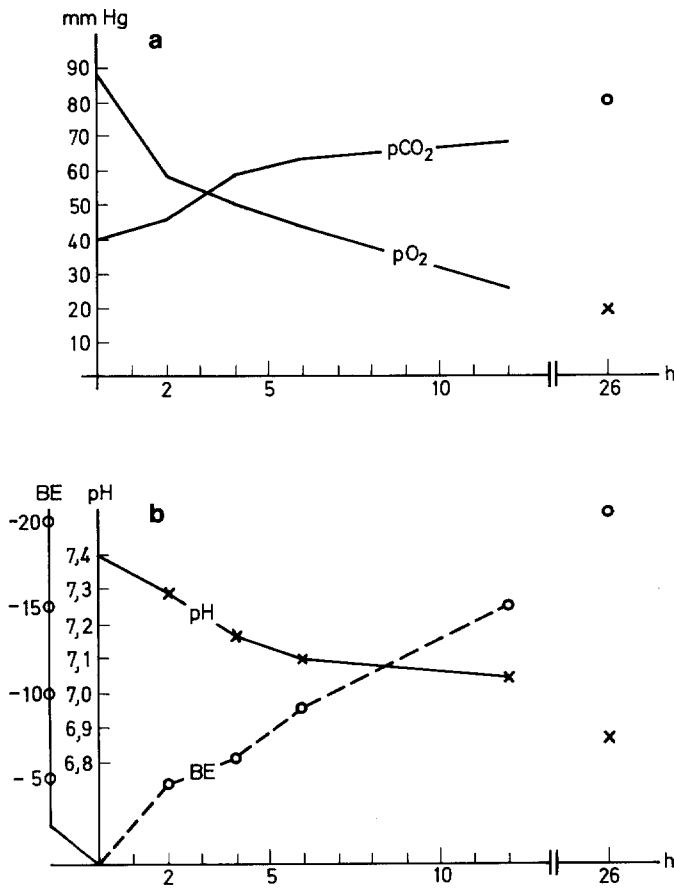


Fig. 3a, b. Intracavernous blood gas analysis performed in 12 patients with pharmacologically induced full erections. The analysis was done in 3 patients after 2 h, in 3 patients after 4 h, in 3 patients after 6 h, in 2 patients after 12 h and in 1 patient after 26 h. **a** With duration of the full erection,  $pO_2$  decreases and  $pCO_2$  increases significantly. **b** Simultaneous to the changes in Fig. 3a, pH decreases and the negative base excess increases dramatically

until, 10 min later, 1 mg of metamaminol was additionally injected into the proximal left corpus cavernosum. Complete flaccidity was attained ca. 15 min after the second injection.

#### Group 4 (interruption of erection due to injection of vasoactive substances)

Intracavernosal injection of metamaminol (2 mg) in the right proximal corpus cavernosum caused complete flac-

idity within 3.5–12 min (mean = 7.7 min) in all 20 patients.

#### Group 5 (accidental prolonged erection in potent men)

In the first two subjects, the erection subsided after metamaminol (2 mg) had been injected in the right proximal corpus cavernosum; flaccidity was attained after about 10 min.

The third subject, who had received the papaverine dose twice had been administered an injection of metamaminol (4 mg) in the right corpus cavernosum by his urologist. As there was no apparent decrease in rigidity within 1 h, he was referred to our hospital.

The blood gas analysis performed after 26 h of complete erection yielded a pH of 6.87,  $pO_2$  of 19 mmHg,  $pCO_2$  of 73 mmHg and a base excess of -25. As the injection of metamaminol (3 mg) in the left corpus cavernosum did not produce any decrease in rigidity within 15 min, both corpora cavernosa were punctured with a 19-gauge cannula using an antibiotic for prophylaxis (Ceftacidin 2 g i.v.). Aspiration led to immediate detumescence; 520 ml of dark, unclotted blood was withdrawn (the blood clotted in the kidney dish within 7 min). Thereafter, the following blood gas values were obtained: pH 7.44,  $pO_2$  77 mmHg,  $pCO_2$  35 mmHg, base excess +1.0. Before the cannulas were removed, metamaminol (2 mg) was injected into the right corpus cavernosum. No spontaneous erection occurred within the next 24 h. Cavernosography showed pathologic venous outflow 48 h following puncture without any evidence of thrombotic obliteration of the venous drains (Fig. 1).

After 3 months, the patient reported complete loss of spontaneous full erectability. He did not respond to maximal doses (3 ml) of a standardized vasoactive solution (papaverine hydrochloride 15 mg/ml and phentolamine mesylate 0.5 mg/ml) with full erection.

#### Group 6 (erection during TUR)

Intracavernosal injection of metamaminol (2 mg) led to complete flaccidity within 5½ min. The ECG 3 min after injection showed atrial extrasystoles for about 140 sec, which did not call for treatment and ceased without therapy. During this time, the systolic blood pressure increased by 15 mmHg.

## Discussion

Under the precondition of adequate neurogenic stimulation, dilatation of the penile arteries, particularly of the aa. profundae penis, relaxation of the cavernosal sinusoids and constriction or compression of the penile veins results in an erection with full rigidity [6]. The apparent hemodynamic changes caused by neurogenic stimulation correspond to those seen after intracavernous injection of vasoactive substances [8].

Our Doppler tests performed on the a. profunda penis show that the intracavernous injection of vasoactive substances causes a strong increase in blood flow within 30 sec. This flow increase reaches a maximum after 4–6 min, but is no longer detectable by Doppler ultrasonography 20 min after a complete erection has been achieved (Fig. 2). This, together with blood gas analysis, which deteriorates with the duration of the erection (Fig. 3), gives the characteristic picture of a low-flow or even no-flow priapism [7].

This condition is likely to have its origin in a maximal relaxation of the intracavernosal smooth muscles. This maximal relaxation can be interrupted by intracavernous injection of alpha-sympathomimetics, as our results have been able to demonstrate. When, however, pronounced ischemic changes associated with a low tissue pH are present in the corpus cavernosum as a result of a persisting erection, it seems that the low pH blocks the effect of the alpha-receptor stimulant. This condition calls for an invasive procedure with puncture of the corpora cavernosa and aspiration of ischemic blood. The introduction of a glandulocavernosal shunt was not necessary in our patients.

The absence of subjective and objective adverse cardiovascular effects to the intracavernous injection of metaraminol (2.0 and 2.5 mg) is due on the one hand to the low doses used and, on the other, to preselection of the population as patients with severe cardiovascular disease were excluded. Possible untoward effects affecting the heart, which was noted in the one patients of group 6, justify rigid preselection criteria, all the more so, since severe paroxysmal hypertension and allergic reactions following intravenous doses of metaraminol have been described [1].

The prolonged erections during diagnosis and therapy did not cause any of the patients to reject or discontinue auto-injection therapy. The three cases of prolonged erections under home treatment occurred during the first 6 months in which this kind of therapy was used at our hospital. Since, on the basis of this experience, we now warn our patients not to apply more than one auto-injection per day, even if the injection appears to be unsuccessful, we have received no further reports on persisting erections during home treatment within the last 17 months.

## Conclusion

Prolonged erections resulting from intracavernous injection of vasoactive substances should be stopped after 3 h and in no case be allowed to persist for more than 6 h, as they involve the risk of ischemic damage to the cavernous tissue with resulting irreversible erectile impotence. A simple method is the intracavernous injection of 2 mg metaraminol. When repeated injection of 1 mg metaraminol fails to produce flaccidity in the case of persisting rigidity, puncture and aspiration of the corpora cavernosa are required.

The use of vasoactive substances for diagnostic and therapeutic purposes in patients with erectile dysfunction as well as the administration of antagonistic alpha-sympathomimetics require careful preselection of the population, cooperation of the individual patient, and the full responsibility of the treating physician, who must be aware that he is working with highly potent drugs.

## References

1. Altwein JE, Bähren W, Stief CG, Thon W (1987) Rationelle Diagnostik und Stellenwert der SKAT-Testung. In: Proceedings of the 10th International Symposium, Ludwig Boltzmann Institut, Wien, pp 345–350
2. Brindley GS (1983) Cavernosal alpha-blockade: new technique for investigating and treating erectile impotence. *Br J Psych* 143:332–337
3. Brindley GS (1984) A new treatment for priapism. *Lancet* ii:220–221
4. Ginestie JF, Romieu A (1977) L'exploration radiologique de l'impotence. Maloine, Paris
5. Jevtich MJ (1984) Non-invasive vascular and neurogenic tests in use for evaluation of angiogenic impotence. *International Angiology* 3:225–232
6. Juenemann KP, Luo J-A, Lue TF, Tanagho EA (1986) Further evidence of venous outflow reduction during erection. *Br J Urol* 58:320–324
7. Juenemann KP, Lue TF, Abozeid M, Hellstrom WJG, Tanagho EA (1986) Blood gas analysis in drug-induced penile erection. *Urologia Internationalis* 41:207–211
8. Lue TF, Hricak H, Schmidt RA, Tanagho EA (1986) Functional evaluation of penile veins by cavernosography in papaverine-induced erection. *J Urol* 135:479–482
9. Robinette MA, Moffat MJ (1986) Intracorporal injection of papaverine and phentolamine in the management of impotence. *Br J Urol* 58:692–695
10. Sidi AA, Cameron JS, Duffy LM, Lange PH (1986) Intracavernous drug-induced erections in the management of male erectile dysfunction: experience with 100 patients. *J Urol* 135:704–706
11. Stief CG, Bähren W, Gall H, Scherb W, Gallwitz A, Altwein JE (1986) Schwellkörper-Autoinjektionstherapie (SKAT): erste Erfahrungen bei erektiler Dysfunktion. *Urologe A* 25:63–66
12. Virag R (1982) Intracavernous injection of papaverine for erectile failure. *Lancet* i:938
13. Zorniootti AW, Lefleur RS (1985) Auto-injection of the corpus cavernosum with a vasoactive drug combination for vasculogenic impotence. *J Urol* 133:39–41