2. Study Descriptor
A Description of the Pioneering Work That Led to the First Approved Agents for ED: Giles Brindley, the Needle, and the Penis (Phenoxybenzamine)

2.1 Key Trial References

2.1.1 Major Publication

2.1.2 Other Important Publications

2.2 Importance of Study
Although some earlier work had been described by Virag, this study really laid down the foundation for the use of therapeutics in the management of ED. It encouraged both patients and physicians to believe that there was a realistic alternative to corrective or implant surgery.

2.3 Study Design
Prospective Trial. n = 15.
The results of 47 cavernosal α-blockade injections in 15 subjects are reported. Phenoxybenzamine was used at dosages of 2.5 to 7mg in 10ml saline.
2.3.1 Outcome Measures
Presence and duration of erection, latency to tumescence, quality of erection (not doublable, not flexible to right angle, fully erect), and occurrence of ejaculation/coitus were recorded, as well as systemic and local adverse events (AEs).

2.3.2 Inclusion Criteria
Potent (n = 4) and impotent (n = 11) men. Subjects were initially assessed for the presence of erections during masturbation and on waking. The age range of the patients was 20 to 64 years, and the duration of impotence ranged from 11 months to 22 years. The 4 potent men were all healthy, but 2 were anorgasmic. Of the impotent men, 5 were healthy, 1 was diabetic, 1 was schizophrenic, 3 had spinal injuries, and 1 had multiple sclerosis.

![Figure 2.1. Phenoxybenzamine injecton trial study design](image)

2.4 KEY RESULTS
- Of 17 injections performed in the 4 potent men (2 of whom were anorgasmic), 10 resulted in full erections, ranging in duration from 1 to 4 hours. Partial erections (penis not “doublable”) were achieved in 16 of the 17 injections, ranging from 1–5 hours.
- Of 30 injections performed in the 11 impotent men, 17 resulted in full erections, ranging in duration from 1–30 hours. Partial erections resulted from 29 of these injections, ranging from 1–30 hours. There was some degree of erectile response from every injection in this group.
- Prolonged full erections occurred in 2 subjects. The first man was had a full erection for 30 hours after 3 of 6 injections but was not distressed and engaged in coitus twice on each occasion. The other man had a full erection for 6 hours on 2 occasions and a prolonged and painful erection for 22 hours on a third occasion, which required intervention.
The erections induced by phenoxybenzamine enabled 6 of the impotent men to have sexual intercourse.

Transient pain was experienced in and around the glans of the penis (distal from the injection site) with these injections, usually nonsevere and lasting 2 to 5 minutes.

Only 2 systemic adverse events (AEs) were noted with this technique; one man noticed sweating on his trunk during and for a few minutes after his first injection, and another had dry orgasms after 2 of 11 injections.

2.5 CONCLUSIONS FROM ORIGINAL REPORTS
Intracavernosal injection of phenoxybenzamine (2.5–7 mg) was effective in producing erections in potent and impotent men.

The duration of erection (<30 hours) produced by this technique is unpredictable, with the risk of prolonged and painful erections. Further understanding of the physiological mechanisms involved in this technique should improve predictability.

2.6 STRENGTHS
The real strength of the study was that, in the absence of any real information, patients were prepared to volunteer.

2.7 WEAKNESSES
The study did not include a placebo and was performed on only 11 patients. However, many subsequent studies have shown the placebo effect to be negligible.
2.8 RELEVANCE
Although phenoxybenzamine has largely been replaced by prostaglandin E₁ (PGE₁) and mixes of vasorelaxant agents, until the arrival of sildenafil intracavernosal administration was the mainstay of therapy. Even after the arrival of sildenafil, there is still relatively widespread use of injectables, and indeed some patients prefer the quality of the erection achieved.