Erectile dysfunction

'Highs' and 'lows' of sublingual treatment for ED

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Since 1998, the availability of effective non-invasive pharmacological approaches to treating men with diabetes with erectile dysfunction (ED) have turned into reality, and there is no doubt the oral phosphodiesterase type 5 (PDE5) inhibitors have revolutionised treatment. However, in a few people with diabetes, either response to oral PDE5 inhibitors has been disappointing or this class of drugs has not been tolerated. In others it has been contraindicated, particularly those with active coronary disease or those taking nitrate preparations.

It was with great interest that we saw an alternative therapeutic agent become available – sublingual (SL) apomorphine. This is a centrally acting selective D_1-,D_2-like dopamine agonist that appears to enhance the normal neurological signalling in response to sexual stimulation. Its mechanism of action and side-effect profile is different to PDE5 inhibitors and can be cautiously used in patients with stable coronary disease concomitantly prescribed nitrate therapy (British National Formulary, 2004).

Until now there have been no prospective studies assessing the efficacy of SL apomorphine in patients with diabetes – as is so often the case, its benefit was assumed from retrospective sub-analyses of people with diabetes extracted from a larger whole population cohort. It is helpful to see the outcome of a well-designed study of 130 patients with diabetes (85 % had type 2 diabetes) with ED, that examines the effects of treatment with SL apomorphine or placebo (Gontero et al, 2004, see right). Disappointingly, however, the response rate was only 22 % after apomorphine SL compared with 17 % with placebo, suggesting the drug has limited use in males with diabetes and ED. Although patients only received a maximum of four 3 mg tablets of apomorphine SL and it is recognised that response rates may increase with greater use, this response rate is still considerably lower in *de novo* users compared with oral PDE5 inhibitors.

On a more positive note, Deveci et al (2004, see below) have examined the effects of SL sildenafil in the treatment of ED based on the premise that this mode of administration avoids the limited bioavailability of oral sildenafil (in the region of 41 %) due to first pass metabolism. The sample size in this study was small and there was no within-study comparison with patients taking oral PDE5 inhibitors. However, the results suggest that SL sildenafil, through greater bioavailability, may work faster, require a lower dosage than is conventionally used orally and may be associated with reduced frequency of side-effects. These findings are worthy of further evaluation in larger studies. Given the relatively poor outcome associated with apomorphine alone in men with diabetes, perhaps a combined preparation of SL PDE5 inhibitor and apomorphine warrants investigation?

British National Formulary 47 (2004) Drugs for Erectile Dysfunction: 403–05

Deveci S, Peskircioglu L, Aygun C et al (2004) Sublingual sildenafil in the treatment of erectile dysfunction: faster onset of action with less dose. *International Journal of Urology* **11:** 989–92

Gontero P, D'Antonio R, Fontana F et al (2004) Clinical efficacy of apomorphine SL in erectile dysfunction of diabetic men. *International Journal of Impotence Research* 1–6

INTERNATIONAL JOURNAL OF UROLOGY

SL sildenafil: faster with smaller dose

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 This study aimed to show the safety and efficacy of sublingual sildenafil and determine if the same effect and faster onset of action was caused by lower doses of sublingual sildenafil.

2 Forty consecutive men (aged 25–55 years) presenting with ED of a longer duration than three months were included in the study.

3 In all participants erectile function scores, serum glucose and testosterone levels and lipid profiles were obtained; 20 patients were given 20 mg of sublingual sildenafil and 20 received placebo.

4 Sildenafil had a significantly higher effect on erection than placebo with 13 men (65 %) taking sildenafil achieving erections for satisfactory intercourse compared to three (15 %) of those on placebo.

5 With sildenafil, mean onset of action was 15.5 minutes and lasted for 40 minutes on average.

6 Side-effects experienced included minimal headaches, sweating and flushing.

7 In erectile dysfunction, sublingual sildenafil 20 mg is effective and safe. It enters the circulation quickly and is not effected by food ingestion and so compared to oral sildnafil has a faster onset of action with a lower dose.

8 Sublingual sildenafil may be more cost-effective and may provide a more predictable onset of action.

Deveci S, Peskircioglu L, Aygün M et al (2004) Sublingual sildenafil in the treatment of erectile dysfunction: faster onset of action with less dose. International Journal of Urology **11**: 989–92

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Apomorphine SL has a limited use for men with ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The objective of this study was to assess the efficacy of apomorphine SL in men with diabetes and ED, and to identify factors to predict people who might benefit from the treatment.

2 Participants comprised 130 people who were randomised to receive placebo or four tablets of 3 mg apomorphine.

3 The erectile function domain of the International Index of Erectile Function and the one-item global efficacy question assessed efficacy.

4 The response rate was 17 % post-placebo and 22 % post-apomorphine SL.

5 Younger age and lower HbA_{1c} were significantly linked to the status of responder in the apomorphine group.

6 Apomorphine SL showed no statistically significant benefit over placebo, suggesting it has a limited use for men with ED and diabetes.

Gontero P, D'Antonio R, Pretti G et al (2005) Clinical efficacy of Apomorphine SL in erectile dysfunction of diabetic men. International Journal of Impotence Research **17**: 80–85

'Alterations in riding habits that have been previously suggested may not change the prevalence of ED among the cycling community.'

'This study provides age-specific estimates of change in sexual functioning over a 9-year period in a cohort of unselected men, so filling a gap in the literature.'

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Smokers have higher risk of ED

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

1 This study estimated the effects of smoking on the risk and prognosis of ED and of ED on smoking behaviour.

2 The researchers estimated the effect of smoking on incidence of ED in 1130 men without ED, ED on risk to start smoking in 502 non-smokers, smoking on the prognosis of ED in 312 men with ED and ED on quitting smoking in 292 smokers.

4 Risk of ED increased non-significantly with smoking, while ED recovery reduced; quitting and starting smoking were rare and non-significantly higher in men with ED.

5 Smokers had a higher risk of ED than non-smokers; men with ED were more likely to start smoking than those without ED.

6 Recovery from ED was less in smokers than in non-smokers, and current smokers with ED were more likely to stop smoking than those with no ED.

Shiri R, Hakama M, Hakkinen J, Tammela TLJ, Auvinen A, Koskimaki J (2004) Relationship between smoking and erectile dysfunction. International Journal of Impotence Research E-pub October 28

JOURNAL OF THE AMERICAN GERIATRIC SOCIETY

Decline in sexual function more pronounced with age

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 This study aimed to describe within-individual change in sexual function over a nine-year period, and to determine whether the amount of change differs by age group.

2 Participants in this cohort comprised 1085 men aged 40–70 years who were interviewed at baseline (1987–97) and follow-up (1995–97).

3 Analyses showed significant longitudinal changes over the nine-year period in erection frequency, sexual intercourse, sexual desire, satisfaction with sex and difficulty with orgasm.

4 After adjusting for baseline sexual function, within-person change in all outcomes was strongly related to age; decline in sexual function became more pronounced with increasing age.

5 This study provides age-specific estimates of change in sexual functioning over a nine-year period in a cohort of unselected men, so filling a gap in the literature.

Araujo AB, Mohr BA, McKinlay JB (2004) Changes in sexual function in middle-aged and older men: longitudinal data from the Massachusetts Male Aging Study. Journal of the American Geriatric Society **52**: 1502–09

THE JOURNAL OF UROLOGY

Bicycle riding does not affect ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 Risk factors within cycling that may put riders at risk of developing ED were investigated.

2 An Internet-based survey of cyclists examined factors associated with cycling that could contribute to ED (as defined by the International Index of Erectile Function).

3 Participants comprised 688 cyclists aged 18–77 years.

4 ED prevalence was 17 %, but although results from univariate analysis indicated a correlation between ED and several tested variables, none were statistically significant after controlling for age.

5 The overall prevalence of ED among cyclists does not seem to be greater than that of historical controls.

6 Alterations in riding habits that have been previously suggested may not change the prevalence of ED among the cycling community.

Taylor III, JA, Kao T-C, Albertsen PC, Shabsigh R (2004) Bicycle riding and its relationship to the development of erectile dysfunction. The Journal of Urology **172**: 1028–31

UROLOGY

Success with tadalafil increases with use

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This post-hoc integrated analysis studied the first-dose success, cumulative success by dose, and maintenance of success in men taking tadalafil.

2 Men were randomised to placebo (n=308), tadalafil 10 mg (n=321) or tadalafil 20 mg (n=258) as a fixed dose in five double-blind, placebo-controlled, 12-week studies.

3 The Sexual Encounter Profile (SEP) diary questions assessed success from three perspectives: (a) first-dose success; (b) cumulative proportion of men with first success by dose; and (c) maintenance of success in men with first-dose success.

4 With the fist dose, more men taking tadalafil 10 mg and 20 mg doses versus placebo achieved successful erection, intercourse, and were satisfied overall with their sexual experience.

5 The proportion of men achieving first success increased with continued dosing, and reached a plateau between doses four and eight at approximately 95 % (SEP-Q2), 90 % (SEP-Q3) and 81 % (SEP-Q5).

6 For those men who had first dose success, the subsequent success rate in the 12-week study was significantly greater for men taking tadalafil 10 mg and 20 mg vs placebo.

7 The majority of men who took tadalafil achieved successful erection, penetration and intercourse after one dose and maintained the success over time.

8 Men who do not initially respond should continue treatment as success increased with continued use.

Schulman CC, Shen W, Stothard DR, Schmitt H (2004) Integrated analysis examining first-dose success, success by dose, and maintenance of success among men taking tadalafil for erectile dysfunction. Urology **64**: 783–88