

# Intrinsa: testosterone patch for low sexual desire in women

Steve Chaplin MSc, MRPharmS and Nick Panay BSc, MRCOG, MFFP

## KEY POINTS

- Intrinsa is a twice-weekly testosterone patch for the treatment of distressing low sexual desire in women after bilateral oophorectomy
- available as 300µg per 24hr transdermal patch (8, £28)
- women must be taking an oestrogen, but not a conjugated oestrogen
- after 6 months, Intrinsa increased the number of satisfying sexual activities by 1-2 per 4-week period compared with placebo
- the patch also increased other measures of sexual satisfaction and reduced distress
- Intrinsa is associated with a low risk of androgenic side-effects; the commonest adverse event is application-site reaction
- provides an alternative for patients reluctant to consider a testosterone implant



**Intrinsa, a transdermal testosterone patch, is licensed for women with hypoactive sexual desire disorder following bilateral oophorectomy or hysterectomy. Here, Steve Chaplin presents the clinical data relating to its efficacy and adverse effects, and Mr Panay comments on its role in therapy.**

Women who have undergone bilateral oophorectomy have reduced levels of total and bioavailable testosterone (by 40-50 per cent) and androstenedione (by 15 per cent) compared with women of a similar age with intact ovaries.<sup>1</sup> This may be associated with an increased risk of low sexual desire and a corresponding increase in dissatisfaction with sex life and partner relationships.<sup>2</sup>

Distressing low sexual desire, or hypoactive sexual desire disorder (HSDD), is defined as a deficiency or absence of sexual fantasies and desire for sexual activity that results in marked distress or interpersonal difficulty not accounted for by another psychological disorder or medical condition, and is not secondary to other sexual difficulties such as erectile failure or dyspareunia.

Prevalence estimates of low sexual desire in women in the general population range from 7 to 33 per cent, but it is not associated with distress, *ie* meeting criteria for HSDD, in all cases: in one cross-sectional survey of women with low sexual desire, two-thirds aged 20-29 and one-fifth to one-third aged 60-70 reported distress.<sup>3</sup> Surgically menopausal women are twice as likely as premenopausal or naturally menopausal women to have HSDD.<sup>2</sup>

## The technology

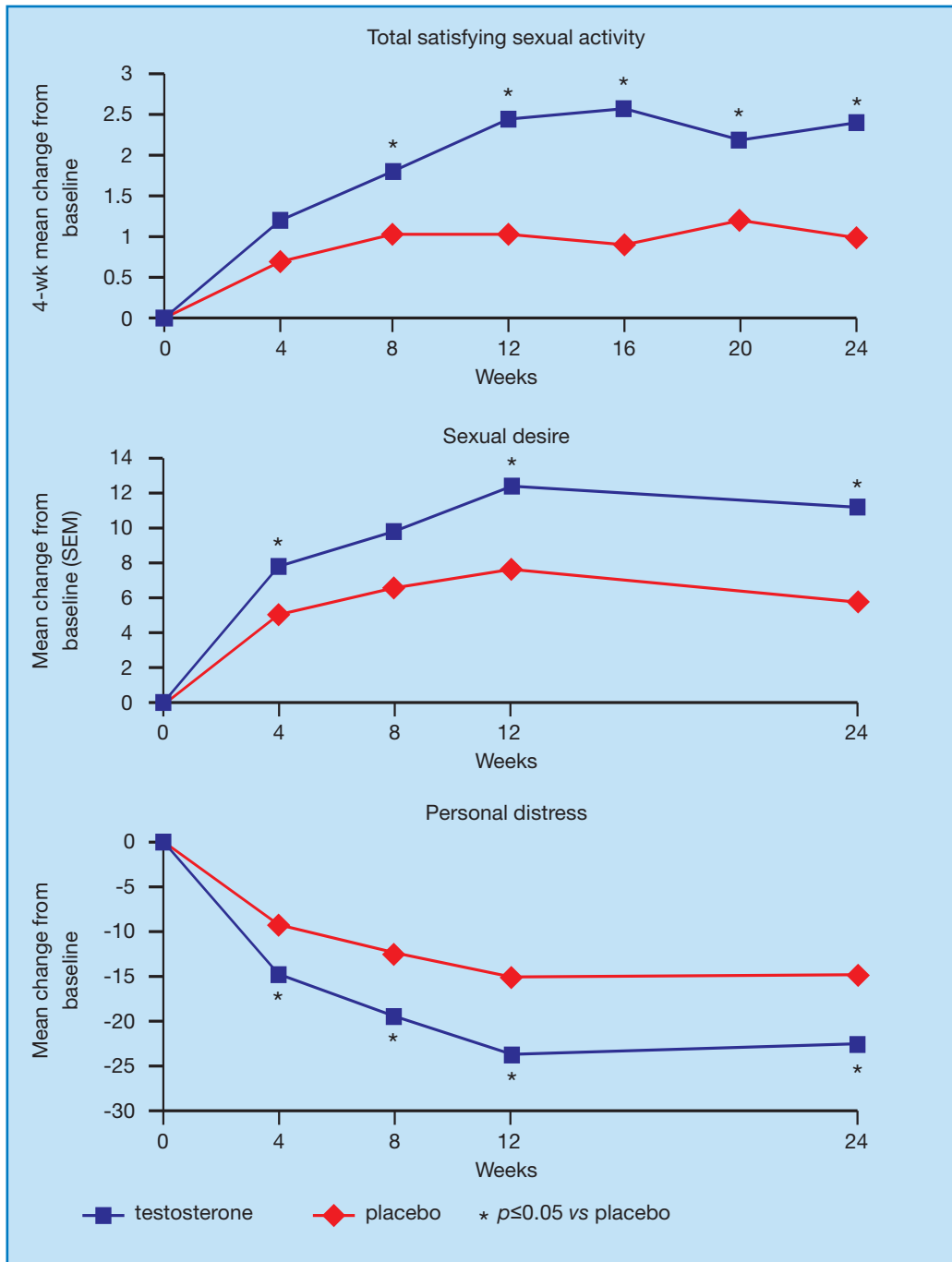
Intrinsa is a transdermal matrix patch delivering testosterone at a dose of 300µg per 24 hours. It is licensed for the treatment of HSDD in bilaterally oophorectomised and hysterectomised (surgically induced menopause) women receiving concomitant

oestrogen therapy. It is not approved for women aged over 60 or use by women taking conjugated oestrogens.

The recommended dose is one patch every three to four days. Treatment should be evaluated after three to six months and every six months thereafter. Testosterone levels during treatment are within the reference range for premenopausal women.<sup>4,5</sup>

## Clinical trials

Two randomised, double-blind, placebo-controlled trials (n=562<sup>4</sup> and 533<sup>5</sup>) provide the key data supporting the use of the testosterone patch. Both included women with HSDD following bilateral oophorectomy at least six months previously (mean age 48-49), in a stable monogamous relationship, who had been taking oestrogen for



**Figure 1.** Response to testosterone patch treatment. At week 24, there was an increase of 2.10 episodes in the final four weeks in the testosterone group in the frequency of total satisfying sexual activity from baseline, compared an increase of 0.98 episodes in the placebo group ( $p=0.0003$ ); the testosterone group also experienced statistically significant improvements in sexual desire and a decrease in distress<sup>4</sup>

at least three months and who did not have other factors possibly affecting sexual desire.

The primary end-point in both 24-week trials was the

change in frequency of total satisfying sexual activity during the final four weeks. In the first trial, the mean frequency of total satisfying sexual activity was approxi-

mately three episodes during the final four weeks at baseline, increasing to four with placebo and five with the patch (mean increase 0.98 placebo, 2.10 patch,  $p=0.0003$ ; see Figure 1).<sup>4</sup> Baseline data were not reported in the second trial but mean increases in this end-point were 0.73 episodes with placebo and 1.56 with the patch ( $p=0.001$ ) over the four-week period.<sup>5</sup> Differences between the two groups were statistically significant from week 5 in both trials.

There were also improvements in secondary end-points including sexual desire and quality of sexual experience, and a reduction in distress (see Figure 1).

#### Adverse effects

The commonest adverse event reported in clinical trials was application-site reaction, occurring in about 30 per cent with both placebo and testosterone patches. There was no significant difference in the incidence of androgenic events, *ie* acne, alopecia, unwanted hair growth and deep voice. Other adverse reactions possibly associated with the patch include migraine, breast pain, increased weight and insomnia.

#### References

1. Laughlin GA, Barrett-Connor E, Kritz-Silverstein D, *et al*. Hysterectomy, oophorectomy, and endogenous sex hormone levels in older women: The Rancho Bernardo Study. *J Clin Endocrinol Metab* 2000; 645-51.
2. Dennerstein L, Koochaki P, Barton I, *et al*. Hypoactive sexual desire disorder in menopausal women: a survey of Western European women. *J Sex Med* 2006;3:212-22.
3. Hayes RD, Dennerstein L, Bennett CM, *et al*. Relationship between hypoactive sexual desire disorder and aging. *Fertil Steril* 2007;87: 107-12.

4. Simon J, Braunstein G, Nachtigell L, *et al.* Testosterone patch increases sexual activity and desire in surgically menopausal women with hypoactive sexual desire disorder. *J Clin Endocrinol Metab* 2005;90:5226-33.
5. Buster JE, Kingsberg SA, Aguirre O, *et al.* Testosterone patch for

low sexual desire in surgically menopausal women: a randomized trial. *Obstet Gynecol* 2005;105:944-52.

*By Steve Chaplin, a pharmacist who specialises in writing on therapeutics*

---

## Place in therapy

Healthy young women produce approximately three to four times more testosterone than oestrogen, around 100-400µg per day. About half is derived from the ovaries and half from the adrenal glands. Testosterone levels begin to decline naturally from the late 20s onwards.<sup>1</sup> In surgically menopausal women, testosterone production decreases by 50 per cent within days of the operation.<sup>2</sup> This decline can have profound effects on sexual desire, arousal and orgasm, as well as general energy levels and well-being.

Until recently, only testosterone implants were licensed for androgen replacement in women. Tibolone (Livial), a synthetic type of HRT, also has some androgenic benefits.

A 300µg-per-day testosterone patch (Intrinsa) is now licensed for use in surgically menopausal women with HSDD. The patient must be undergoing concomitant oestrogen therapy (not conjugated equine oestrogens). Although testosterone levels are increased by the treatment, they usually remain within the physiological range and the incidence of androgenic side-effects is not significantly different to placebo in recent studies.

Benefits are seen within four to eight weeks of therapy with a mean increase in sexual activity and desire of approximately 60-70 per

cent, compared to 30-40 per cent in the placebo groups.<sup>3-4</sup>

Transdermal testosterone is a welcome addition to the available HRT options as it provides an alternative for patients reluctant to consider a testosterone implant. Although tibolone is an alternative, its progestogenic effects are unnecessary in hysterectomised women. A careful psychosexual history should be taken before prescription, with specialist advice sought where necessary.

Experts in psychosexual disorders and HRT have occasionally prescribed the patch off-label for both naturally menopausal women and for women not on concomitant oestrogen. Although there are data for efficacy and safety in these situations,<sup>5-6</sup> it is advised that prescription of transdermal testosterone in primary care should only be initiated in line with the licensed indication.

## References

1. Davison SL, Bell S, Donath S, *et al.* Androgen levels in adult females: changes with age, menopause, and oophorectomy. *J Clin Endocrinol Metab* 2005;90(7):3847-53.
2. Judd HL, Lucas WE, Yen SS. Effect of oophorectomy on circulating testosterone and androstenedione levels in patients with endometrial cancer. *Am J Obstet Gynecol* 1974;118:793-8.
3. Buster JE, Kingsberg SA, Aguirre O, *et al.* Testosterone patch for low sexual desire in surgically menopausal women: a randomized trial. *Obstet Gynecol* 2005;105:944-52.

4. Simon J, Braunstein G, Nachtigall L, *et al.* Testosterone patch increases sexual activity and desire in surgically menopausal women with hypoactive sexual desire disorder. *J Clin Endocrinol Metab* 2005;90:5226-33.

5. Shifren JL, Davis SR, Moreau M, *et al.* Testosterone patch for the treatment of hypoactive sexual desire disorder in naturally menopausal

women: results from the INTIMATE NM1 study. *Menopause* 2006;13:770-9.

6. Davis SR, Moreau M, Kroll R, *et al.* The efficacy and safety of testosterone patches for the treatment of hypoactive sexual desire disorder in menopausal women not receiving systemic estrogen or estrogen plus progestin therapy: results of the

APHRODITE Trial. *NEJM* 2007; (submitted).

*By Mr Panay, a consultant gynaecologist and subspecialist in reproductive medicine and surgery at Queen Charlotte's and Chelsea and Chelsea and Westminster Hospitals, and honorary senior lecturer at Imperial College London*

## InfoPOEMs



### CPAP associated with decreased CV risk

#### Bottom Line:

The use of continuous positive airway pressure (CPAP) in patients with mild to moderate obstructive sleep apnoea (OSA) is associated with a decreased risk of fatal and nonfatal cardiovascular events. Since we also have data that CPAP decreases motor vehicle accidents, it is reasonable to recommend CPAP until we have randomised controlled trial data that show its use to be harmful. (LOE = 2b)

#### Reference:

Buchner NJ, Sanner BM, Borgel J, *et al.* Continuous positive airway pressure treatment of mild to moderate obstructive sleep apnea reduces cardiovascular risk. *Am J Respir Crit Care Med* 2007;176(12):1274-80.

**Study Design:** Cohort (prospective) **Funding:** Unknown/not stated **Setting:** Outpatient (specialty)

#### Synopsis:

CPAP has been shown to improve daytime alertness and decrease motor vehicle accidents in patients with OSA. Additionally, patients with severe OSA treated with CPAP have a decrease in cardiovascular events. These researchers wanted to see if there might also be a cardiovascular benefit in patients with mild to moderate OSA.

They recruited all patients who came to their sleep centre over a five-year period and enrolled a total of 288 patients with mild to moderate OSA. OSA was considered present when no air flow was measured for more than 10 seconds in the presence of paradoxical chest wall motion. Hypopnoea was

defined as a 50 per cent reduction in airflow for more than 10 seconds. Mild OSA was defined as having 5-15 episodes of apnoea or hypopnoea per hour and moderate OSA was 15-30 episodes per hour. The physicians recommended CPAP in patients with moderate to severe OSA and to patients with mild OSA who also had severe daytime hypersomnolence. Patients could choose to use CPAP, oral appliances or no treatment. The researchers evaluated the patients annually with a standardised set of surveys. When patients died during the follow-up period, the researchers checked death certificates and autopsy reports. The median follow-up was six years. At the onset, the patients treated with CPAP had higher body mass index (31 vs 29kg per m<sup>2</sup>). Otherwise, the groups were similar for other cardiovascular risk factors.

Twenty of the 78 patients (25.3 per cent) with mild to moderate OSA who were not treated had fatal or nonfatal cardiovascular events compared with 30 of the 209 who chose to use CPAP (14.4 per cent;  $p=0.024$ ).

Although these findings are consistent with what has been seen in severe OSA, this is not a randomised trial, so the results could be explained by other factors that could not be accounted for.

POEM (Patient Orientated Evidence that Matters) editors review more than 1200 studies monthly from over 100 medical journals, presenting only the best as InfoPOEMs. The POEMs process applies specific criteria for validity and relevance to clinical practice. About 1 in 40 studies qualifies. For more information visit: [www.info poems.com](http://www.info poems.com)