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Journal Title: Br J Obstet Gynecol
Journal Vol: 90
Journal Issue: 
Journal Year: 1983
Article Title: Hormonal treatments of sexually unresponsiveness in postmenopausal women: a comparative study
Article Author: Dow
Article Pages: 361-66

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Hormonal treatments of sexual unresponsiveness in postmenopausal women: a comparative study

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Summary. Forty postmenopausal women, referred for hormone replacement therapy and all of whom reported a significant concern about a decline in their sexual interest, were randomly allocated to one of two hormone implant treatment groups: either oestradiol (50 mg) alone, or oestradiol (50 mg) and testosterone (100 mg). Comparison between the two groups as a whole revealed no significant differences on any measure, both treatments being associated with a significant reduction in the severity of psychological, somatic and vasomotor symptoms, and with a significant improvement in sexual interest and responsiveness. Similar effects were also observed in patients who denied, pretreatment, any concurrent dyspareunia. Although it is not possible to identify the reasons for change, the results indicate no advantages of supplementary testosterone administration over oestradiol alone for sexually unresponsive postmenopausal women.

Although consistent evidence for a relation between the menopause and a decline in sexual interest and responsiveness in women is still lacking, Studd & Parsons (1977) assert that nearly half of all patients presenting at a menopause clinic will offer symptoms of sexual dysfunction among their three main complaints.

Several aetiological theories for this impairment of libido have been advanced and have focused, for the most part, on aspects of adjustment to psychosocial and endocrinological change occurring at this time in a woman’s life (Deykin 1966; Neugarten & Datan 1974). As yet, there is no evidence that diminished sexual responsiveness in postmenopausal women is directly related to either lower oestradiol or androgen levels (Studd et al. 1977b). Controlled studies of the effects of oestrogen therapy suggest an improvement in vasomotor symptoms, vaginal dryness and general wellbeing, but not in libido (Utian 1972; Campbell 1976).

However, oestrogen deficiency may predispose women to an impairment of libido as an indirect function of vasomotor instability and dyspareunia (Van Keep & Gregory 1977). Some evidence consistent with this view is provided by Maoz & Durst (1980) who observed that oral oestrogens facilitated normal sexual activity and satisfaction by lessening painful coitus, hot flushes and depressive symptoms. These results, however, must be interpreted cautiously in view of the inadequate methods of assessing behavioural change and the apparent pretreatment variability of the frequency of sexual activity and degree of sexual satisfaction within the sample of women studied.

Studd et al. (1977a,b) also reported that conjugated equine oestrogen therapy improved sexual satisfaction but only in women with
dyspareunia due to atrophic vaginitis. Sexually dysfunctional women with loss of libido, but no primary coital discomfort, derived little or no sexual benefit from this regimen. In contrast, significant sexual improvement was reported in 80% of these patients with primary loss of libido who received a combined hormone implant of oestradiol (50 mg) and testosterone (100 mg). Despite the uncontrolled nature of this study, Studd & Parsons (1977) subsequently claimed that such patients will respond only to this combined hormone regimen given as a subcutaneous implant.

Unfortunately, the rather general presentation of these findings pre-empts adequate appraisal. Moreover, in contrast to early uncontrolled studies which reported positive effects of exogenous androgens on female libido (Shorr et al. 1938; Greenblatt et al. 1942; Salmon & Geist 1943), the results of recent controlled research have failed to show a significant effect of testosterone in the treatment of general sexual unresponsiveness in premenopausal women (Mathews 1981). It would therefore be of value to re-examine the relative effectiveness of a combined testosterone and oestradiol implant and that of oestradiol alone in sexually unresponsive postmenopausal women.

Patients and methods

Patients

Forty women, who were referred to a hormone replacement clinic by their general practitioners and by other gynaecologists, were recruited to the study. Their mean age was 46·9 years (range 33–61 years) and they had initially presented to the referring practitioners with vasomotor symptoms together with, in varying degrees, a range of other somatic and psychological symptoms. Six of the 40 patients (mean age 50·5, range 49–54 years) had had a natural menopause, the mean time from last menstrual period being 21 (SD 16·9) months. The remaining 34 patients (mean age 46·3 SD 6·2 years) had had a hysterectomy and bilateral oophorectomy on average 3·6 (SD 4·3) years previously.

Criteria for inclusion

Women were included in the study only if the following were applicable.

(a) Loss of libido was a problem. Part of the initial screening of potential subjects involved the use of a menopausal symptoms scale on which the women rated the extent to which they were bothered by each of 22 symptoms, commonly associated with the menopause, on a four-point scale (0—not at all, 3—extremely bothered). Two items relating to sexual unresponsiveness were added to the original scale published by Greene (1976), namely ‘loss of interest in sex’ and ‘difficulty in becoming sexually excited’, and only those patients who indicated at least ‘quite a bit’ of concern about both symptoms (i.e. a rank score of >2 on both items) were included. Thus, the predetermined criterion of concern about libido was deliberately set fairly high to help ensure that this was a clinically relevant area of concern rather than merely a vague sexual dissatisfaction.

(b) They had a regular sexual partner.

(c) The results of routine physical and biochemical assessment (including luteinizing hormone, follicle-stimulating hormone, prolactin, clotting factors, mineral metabolic screens and liver function tests) showed no contraindication to hormonal treatment.

(d) There was no gross primary marital disturbance or significant concurrent psychopathology or physical illness.

(e) There was no concurrent use of medication that might affect libido or interfere with the proposed hormonal treatment.

Treatment

Successful patients who met these criteria were allocated to one of two treatment groups according to a pre-arranged random list and all subjects remained blind throughout as to group membership.

The dosage and method of implantation followed precisely those described by Studd et al. (1977a). In the six patients with an intact uterus unscheduled bleeding and endometrial hyperplasia were prevented by provoking a progestogen withdrawal bleed each month with 5 mg of norethisterone given daily for 7 days each month.

The single implant group, which consisted of 18 surgical and two natural postmenopausal women, received oestradiol (50 mg) only.

The double implant group, comprising 16 surgical and four natural postmenopausal women, received oestradiol (50 mg) and testosterone (100 mg).
Although it is conceded that sample homogeneity, in terms of type of postmenopausal patient, would have been an advantage, the two treatment groups were roughly balanced in this respect.

Rating scales

Only two series of scales of treatment outcome were used.

Menopausal symptoms scale

From factor analysis (a technique that helps identify symptoms that occur together) this scale has been shown to provide a measure of the severity of three groups of symptoms associated with the menopause: psychological, somatic and vasomotor (Greene 1976). Patients were required to rate on a four-point scale, the extent to which they were bothered by each of the symptoms contributing to these three factors.

<table>
<thead>
<tr>
<th>Description of measure</th>
<th>Treatment group</th>
<th>Pretreatment</th>
<th>Post-treatment (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Menopausal symptoms scale (score)a</td>
<td>Oes</td>
<td>26.2 (10.6)</td>
<td>16.8 (12.6)</td>
</tr>
<tr>
<td>Psychological factor</td>
<td>Oes + T</td>
<td>21.6 (11.6)</td>
<td>11.7 (9.4)</td>
</tr>
<tr>
<td>Somatic factor</td>
<td>Oes</td>
<td>10.2 (6.7)</td>
<td>6.4 (4.0)</td>
</tr>
<tr>
<td>Vasomotor factor</td>
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<td>4.7 (4.9)</td>
</tr>
<tr>
<td>Self-rating scale (score)b</td>
<td>Oes</td>
<td>7.8 (2.7)</td>
<td>3.8 (2.5)</td>
</tr>
<tr>
<td>Frequency of sexual interest</td>
<td>Oes + T</td>
<td>8.0 (2.5)</td>
<td>2.9 (2.7)</td>
</tr>
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</table>

Self-rating scales of sexual and marital satisfaction

These included six bipolar seven-point adjectival scales relating to frequency of sexual interest; general satisfaction with the sexual relationship; general satisfaction with the marital relationship; frequency of orgasm during sexual relations (coital or non-coital); ease of responding to sexual stimulation and frequency of dyspareunia.

Results

Table 1 shows the means and standard deviations for each treatment group on the nine dependent variables at each period of assessment. In view of the non-normal distribution of scores, non-parametric analyses were applied throughout. Thus between-groups analyses were

Table 1. Effect of hormone therapy on menopausal symptoms and sexual response scores in two treatment groups. Results are means (SD)

<table>
<thead>
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</table>

**Higher value, greater concern about symptoms.**  
**Higher value, better sexual adjustment.**

Oes, Oestradiol (50 mg); T, testosterone (100 mg).

Significance of differences compared with the pretreatment value in the same treatment group (two-tailed test):  
*P<0.05; **P<0.01; ***P<0.001; NS, not significant.
conducted by Mann–Whitney U-tests on change scores (i.e. pretreatment—2 months, pretreatment—6 months). The results of these analyses showed that there were no significant differences between treatments on any variable at either 2 months or 6 months after treatment.

Examination of the degree of change within each treatment group over the three occasions of testing was conducted by means of Wilcoxon's matched-pairs signed-ranks test. The results are summarized in Table 1.

Significant improvement after 2 months was observed for every variable within each treatment group, with the exception of self-ratings of marital satisfaction. This last finding was, of course, not surprising as there was no reason to suppose that treatment should influence this variable and, in any case, there was no evidence that the sexual difficulties in either group had affected wider aspects of the marital relationship.

Thus, among the sample as a whole, there was no evidence of a differential response to treatments, both of which were associated with widespread significant improvement, largely maintained at 6 months follow-up.

It may be argued that postmenopausal women with low sexual interest do not constitute a homogenous group. Indeed, the specific direct effects of oestrogen reported by Utian (1972) and Campbell (1976) in terms of alleviating vaginal dryness, and the purported superiority of testosterone and oestradiol implants compared with oral oestrogens in patients with loss of libido alone (Studd et al. 1977b) suggest that a distinction in terms of the pretreatment presence or absence of dyspareunia may be relevant to outcome in the present study. Thus, following the findings reported by Studd et al. (1977b) it may be hypothesized that testosterone plus oestradiol would have a greater effect on libido than oestradiol alone in patients without any significant coital discomfort due to atrophic vaginitis or inadequate vaginal lubrication.

Thus all patients whose pretreatment scores on the dyspareunia scale fell within the last two choice points (i.e. 'never' or 'very rarely' experience pain or discomfort during intercourse) were identified. They formed two treatment subgroups of nine patients each and a further comparison between the treatments was made by the same statistical procedures.

Again no significant difference between treatments was observed either at 2 or at 6 months post-treatment for any variable. When pre- to post-treatment change was examined within each treatment group separately, the pattern of results, summarized in Table 2, was shown to be broadly similar to that for the sample as a whole. Thus, each treatment was again shown to be associated with significant improvement on all measures with the exception, of the marital satisfaction and dyspareunia scales. Scores on the somatic factor also did not change significantly, but a clearly positive trend was apparent in each case.

Discussion

Contrary to the findings reported by Studd et al. (1977a,b) the present study failed to indicate any advantage of testosterone and oestradiol implants over those of oestradiol alone in the management of sexual unresponsiveness in postmenopausal women. Moreover the failure to observe any differential treatment response was also apparent in those women whose loss of libido did not appear to be a function of primary dyspareunia, the subgroup for whom the additional use of testosterone had previously been specifically recommended (Studd et al. 1977a,b; Studd & Parsons 1977). In the present study both treatments were shown to be associated with a marked reduction in the severity of a wide range of symptoms occurring at the menopause. More specifically, a significant improvement was evident with respect to psychological, somatic and vasomotor symptoms, as well as general sexual satisfaction, sexual responsiveness, orgasmic capacity, sexual interest and frequency of dyspareunia. These improvements were observed as early as 2 months after treatment and, for the most part, were maintained some 4 months later.

As noted above, however, it is difficult to compare the present results with those of Studd et al. (1977a,b) since their findings are only broadly summarized. It is possible that some of the disparity between the results may be due to differences in the methods of assessment of sexual change and in sample characteristics. The latter factor, in particular, however, seems an unlikely reason for the discrepancies as every effort was made to include only those women who reported a clinically significant impairment of libido.

The present study was clearly not designed to help identify the effective ingredients of therapy and a number of interpretations are possible. Consistent with the views of Van Keep &
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Gregory (1977), concerning the indirect sexual benefits of oestrogen therapy, it is possible that both treatments may have been equally effective in enhancing libido as an indirect function of the control of vasomotor symptoms and an increase in general wellbeing after oestradiol replacement. Fedor-Freybergh (1977) reported that oestrogen replacement had, among other benefits, a positive influence on libido, sexual activity, sexual satisfaction, experience of pleasure, sexual fantasies and orgasmic capacity. Similarly, Dennerstein et al. (1980), in a comparison of the effects of oestradiol, progestogen and placebo on libido in women who had had hysterectomy and oophorectomy, found that oestradiol alone had a significant effect, not only on vaginal dryness, but also on orgasmic frequency, sexual desire and enjoyment. Since the improvement in orgasmic frequency was shown to be unrelated to the control of hot flushes, they interpreted this as suggesting 'a direct influence of hormones on certain aspects of sexuality'. Such an interpretation, however, may not be fully justified at present, since general feelings of wellbeing were also shown in their study to correlate closely with sexual desire. Finally, some or all aspects of the significant widespread and unselective improvement observed in the present study could be of a placebo nature. After a double-blind study of conjugated oestrogens (Campbell 1976), Campbell & Whitehead (1977) reported a highly significant placebo effect on ratings of coital satisfaction. Moreover, given a backdrop of folklore and prejudice about the sexual sequelae of hysterectomy and the menopause itself (Dennerstein et al. 1977), and the demand characteristics of the study (Orne 1962), many of the ingredients are present for a potentially large placebo response. Nevertheless, the aim of our study was to re-examine the claims for the apparently greater sexual benefits of a testosterone supplement in oestradiol replacement, rather than to identify the reasons for change.

Although a wider range of dependent measures, including independent blind ratings and data from the patient’s partner, would have been undoubted refinements in the present preliminary study, the results nevertheless highlight a need for caution before accepting the view that the additional use of testosterone offers a significant advantage over oestradiol alone in the treatment of sexually unresponsive postmenopausal women.
References


Received 8 March 1982
Accepted 5 November 1982