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THE VAGINAL ABSORPTION OF OESTROGENS IN POST-MENOPAUSAL WOMEN

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Serum E_1, E_2 and E_3 concentrations and E_2/E_1 ratio were measured after vaginal application of conjugated oestrogens, micronized 17β-oestradiol and oestriol. 2.4 mg of conjugated oestrogens caused a prompt elevation in the serum E_1 concentration; the E_2 level changed only slightly. After vaginal application of 2 mg micronized 17β-oestradiol the main serum oestrogen is E_2 and the conversion of E_2 to E_1, as in oral administration, does not occur. A significant elevation in the serum E_3 concentration was noted 2 h after the vaginal application of 0.5 mg oestriol. The E_2/E_1 ratio changed little after the application of conjugated oestrogens but increased considerably after the vaginal administration of 2 mg micronized 17β-oestradiol.

(Key words: Vaginal absorption – conjugated oestrogens, 17β-oestradiol, Oestriol)

INTRODUCTION

The vaginal application of oestrogens is in common use in the treatment of vaginal atrophy and related conditions due to oestrogen deficiency. Even small doses produce proliferation of the vaginal epithelium, and systemic effects are also possible [1,2]. The incremental changes caused by various oestrogens and their duration appear to be related to both the dose and the type of oestrogen cream used [3].

In the present study we have investigated the vaginal absorption of two creams containing conjugated oestrogens and micronized oestradiol and ovula containing oestriol. For the latter only few recent reports exist [4].

SUBJECTS AND METHODS

15 oestrogen-deficient women (age range 50 to 71 yr) participated in the study. None of the patients had received hormone therapy for at least 2 wk before the start of the study, and none of them had a vaginal infection. 5 of the patients received intravaginally 2.4 mg conjugated oestrogens (Senikolp®, Star, Finland), for 5 patients the treatment was a cream containing 2 mg micronized oestradiol (Leiras, Finland) and for 5 it consisted of ovula containing 0.5 mg oestriol (Organon, The Netherlands). The total serum oestrone (E_1), 17β-oestriol (E_2) and oestriol (E_3) were determined by means of radioimmunoassay

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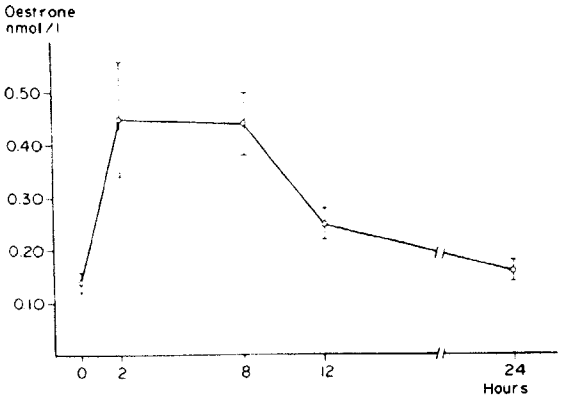

Fig. 1. Serum oestrone concentrations after vaginal application of 2.4 mg of conjugated oestrogens. Mean ± SEM.

[5,6] prior to the oestrogen application 2, 8, 12 and 24 h afterwards. The E_2/E_1 ratio was measured for the corresponding times.

RESULTS

The serum E_1 level rose significantly ($P < 0.05$) 2 h after intravaginal application of 2.4 mg conjugated oestrogens (Fig. 1). It remained at the same level for 6 h. 12 h after application the E_1 level was still higher ($P < 0.05$) than before the application. By the time 24 h had elapsed, it was back at the pre-treatment level. The corresponding E_1 values after the application of 2 mg micronized oestradiol are shown in Figure 2. The highest concentration was noted 8 h after application and even after 12 h this level was higher ($P < 0.05$) than before application.

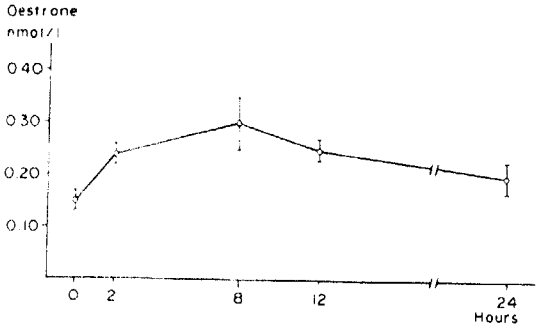

Fig. 2. Serum oestrone concentrations after vaginal application of 2 mg of micronized 17β-oestradiol. Mean ± SEM.

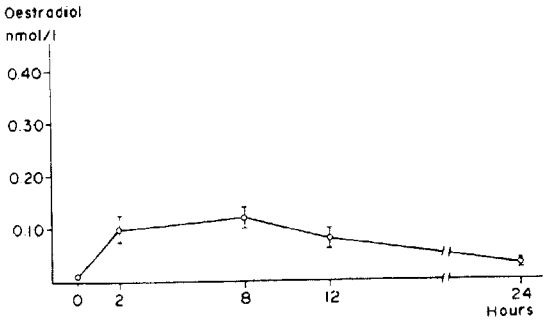

Fig. 3. Serum oestradiol concentrations after vaginal application of 2.4 mg of conjugated oestrogens. Mean ± SEM.

The serum E_2 concentration changed only slightly after the application of conjugated oestrogens (Fig. 3). Micronized oestradiol caused a distinct elevation in the serum E_2 level 2 h after application ($P < 0.05$). The other measurements did not differ from the pre-treatment value (Fig. 4). Serum E_3 concentrations in both treatment groups were low and did not differ from each other (Figs. 5 and 6).

In patients with intravaginal oestriol, the serum E_3 level increased significantly ($P < 0.05$) 2 h after application (Fig. 7); the other values were at the pre-treatment level. The serum E_1 and E_2 concentrations were low and did not change during this treatment.

The E_2/E_1 ratios for various treatment groups are shown in Table I.

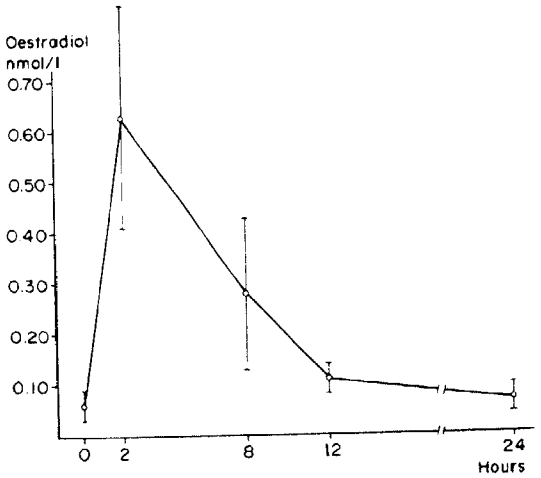

Fig. 4. Serum oestradiol concentrations after vaginal application of 2 mg of micronized 17β-oestradiol. Mean ± SEM.

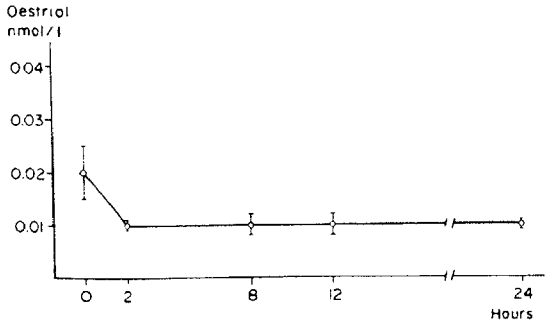

Fig. 5. Serum oestriol concentrations after vaginal application of 2.4 mg of conjugated oestrogens. Mean ± SEM.

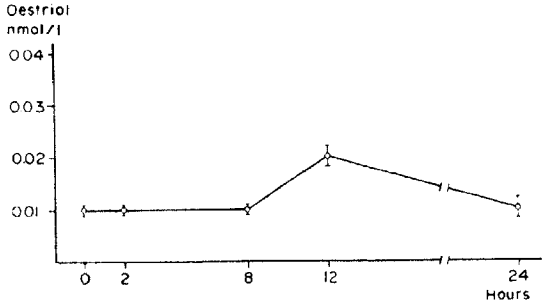

Fig. 6. Serum oestriol concentrations after vaginal application of 2 mg of micronized 17β-oestradiol. Mean ± SEM.

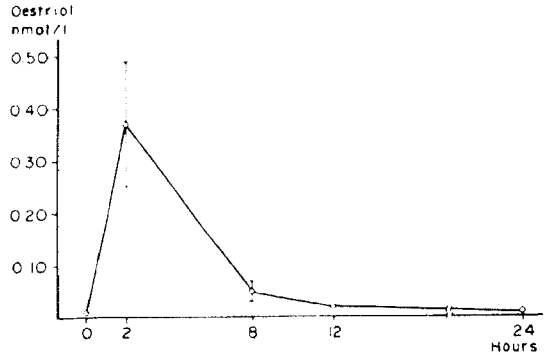

Fig. 7. Serum oestriol concentrations after vaginal application of 0.5 mg oestriol. Mean ± SEM.

TABLE 1

The E_2/E_1 ratio in various treatment groups.

	Pre-treatment	2 h	8 h	12 h	24 h
Conjugated oestrogens	0.10	0.22	0.27	0.32	0.19
Oestradiol	0.40	2.62	0.93	0.44	0.35
Oestriol	0.15	0.11	0.12	0.09	0.13

DISCUSSION

Before the beginning of the treatment, serum E_1, E_2 and E_3 concentrations were low in all cases and similar to those in castrated women [7–10].

The absorption after vaginal application of oestrogens is fast and effective, and the elevation of serum concentrations has been noted even 30 min after application [11]. The biological effect of intravaginally administered oestrogens takes place principally through delivery to target cells by circulation. The significance of the possible topical effect is evidently relatively minor [3].

Conjugated oestrogens consist principally of natrium oestrone sulphate and cause a distinct elevation in the serum E_1 concentration. Endometrial proliferation and bleeding has been described after vaginal treatment with conjugated oestrogens [1,2]. The effects on the gonadotrophin levels are similar with the intravaginal and oral routes of administration [12,13].

After vaginal administration of micronized 17β-oestradiol, the main serum oestrogen is E_2. The primary effect of the oral administration of micronized 17β-oestradiol on the other hand is in the elevation of the serum E_1 concentration, with a much lesser increase in E_2 [11]. Quite similar are the results of our previous studies with oral oestradiol-valerate [8]. These changes are based on the conversion of E_2 to E_1 by the mucosa of the small bowel.

The vaginal administration of oestriol caused an elevation in the serum E_3 concentration without any effect on E_1 and E_2 levels. It has been shown that oral oestriol treatment does not promote endometrial proliferation when administered in low doses to post-menopausal women [14]. The treatment, however, counteracts atrophic changes in the vaginal epithelium. Generally it is possible to use oestriol, though the other oestrogens are contraindicated [4].

The E_2/E_1 ratio changed only slightly after the application of conjugated oestrogens; all the E_2 values measured were low. On the other hand the E_2/E_1 ratio was considerably elevated following the application of micronized 17β-oestradiol, and was similar to that caused by intramuscular oestradiol valerate [9].

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