SHORT COMMUNICATION

PLASMA ZINC IN PRE- AND POST-MENOPAUSAL WOMEN: ITS RELATIONSHIP TO OESTROGEN THERAPY

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SUMMARY

1. The specific gravity and zinc concentration of plasma obtained during fasting were measured in pre- and post-menopausal women. A number of the latter had been taking 20–40 μg of mestranol daily for at least 1 year.

2. A highly significant correlation was found between plasma zinc concentration and plasma specific gravity in the oophorectomized women who were not receiving oestrogens.

3. The mean plasma zinc concentration was 2 μg/100 ml lower in the pre-menopausal women than in the oophorectomized controls, and this was wholly consistent with the associated fall in plasma specific gravity.

4. The mean plasma zinc concentration in the mestranol-treated women was 12 μg/100 ml lower than that found in the oophorectomized controls, and could not be attributed to the small associated change in plasma specific gravity.

5. It is suggested that the fall in plasma zinc concentration associated with mestranol therapy could be due to either a qualitative change in the plasma proteins or to relative zinc depletion.

Key words: zinc, oestrogen therapy.

Plasma zinc concentrations were reported to be decreased in pregnancy and in normal women taking oral contraceptives (Halsted & Smith, 1970; Schenker, Hellerstein, Jungreis & Polishuk, 1971), or ethinyl oestradiol alone (Briggs, Briggs & Austin, 1971). However, these changes could be explained by a reduction in the total plasma protein concentration, since zinc in the plasma is almost entirely protein bound (Vikbladh, 1951; Prasad & Oberleas, 1968; Boyett & Sullivan, 1970), and it has been shown that plasma specific gravity, which is a good indirect measure of the total plasma protein concentration, is reduced in women taking oestrogens (Aitken, Hart & Wilson, 1972).

Since oestrogens are reported to have specific osteotrophic effects in post-menopausal

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women (Albright, 1947; Wallach & Henneman, 1959; Davis, Strandjord & Lanzl, 1966), it
would be of interest to know if an alteration in zinc metabolism could be in part responsible
for the skeletal wasting characteristically seen in post-menopausal women.

We report here our findings in a large number of pre- and post-menopausal women, in whom
we measured plasma zinc and specific gravity. The relationship between plasma zinc and specific
gravity is examined, and the effect on these parameters of the long-term administration of the
synthetic oestrogen, mestranol, is described.

MATERIALS AND METHODS

One hundred and eighty-one women aged 32–59 years who had undergone hysterectomy and
bilateral salpingo-oophorectomy, and fifty women aged 29–53 years who had undergone
hysterectomy alone, in both instances for non-malignant disease, were studied within 4–8
years of operation. All subjects freely volunteered to participate. Fifty-three of the oophorec-
tomized women had been taking 20–40 μg of mestranol per day for at least 1 year before the
present study started, whereas none of the other subjects were receiving hormone therapy. The
women who had undergone hysterectomy alone were judged clinically to be pre-menopausal on
the grounds of the absence of menopausal symptoms and the presence of a normal vaginal
smear.

Venous blood was obtained with minimal venostasis after an overnight fast. The blood was
drawn into a plastic syringe containing about 0.1 ml of a zinc-free solution of heparin (1000
i.u./ml). Plasma proteins were precipitated with 10% trichloracetic acid as described by Davies,
Musa & Dormandy (1968). The zinc concentration in the protein-free supernatant was
determined using an atomic absorption spectrophotometer, calibrated with aqueous zinc
standards made by diluting each appropriate standard solution 1:1 with 10% trichloracetic
acid. Plasma specific gravity was measured using the copper sulphate technique of Phillips,
Van Slyke, Dole, Emerson, Hamilton & Archibald (1945). All results are given as means ±SD.
The linear regression between plasma zinc and specific gravity was calculated for all the results
obtained from the untreated oophorectomized women using a least-squares fit. Student's t-
test was used to determine the significance of the linear correlation, and also the differences
between means since the data from each group were normally distributed.

RESULTS

The oestrogen-treated oophorectomized women had the lowest mean plasma zinc concentra-
tion at 96·8±10·6 μg/100 ml, this being significantly lower than that found in the oophorecto-
mized women without treatment where the value was 108·9±11·5 μg/100 ml (t = 6·64,
P<0·001). In the women with intact ovaries the mean plasma zinc concentration was 106·8±
11·1 μg/100 ml and was not significantly lower than that found in the oophorectomized controls
(0·4>P>0·3), but was significantly higher than that found in the mestranol-treated women
(t = 4·69, P<0·001).

The relationship between plasma zinc concentration and plasma specific gravity in the
oophorectomized women not receiving oestrogens is shown in Fig. 1. The correlation was
highly significant (t = 4·48, P<0·001). For each 0·001 increment in plasma specific gravity
there was a mean rise in plasma zinc concentration of 4·3 μg/100 ml.
The mean plasma specific gravity was highest in the untreated oophorectomized women at 1.0271±0.0010, being significantly higher than that found in the women with intact ovaries where the value was 1.0267±0.0011 (t = 2.43, P<0.02), and significantly higher than that found in the mestranol-treated women where the value was 1.0265±0.0011 (t = 3.75, P<0.001). No significant difference was found in this respect between the mestranol treated women and the women with intact ovaries (0.3>P>0.2).

**DISCUSSION**

Zinc is a trace element essential for the normal function of a number of important enzyme systems. Collagen synthesis requires the presence of zinc (Fernandez-Madrid, Prasad & Oberleas, 1971) and alkaline phosphatase, which is a zinc-containing metallo-enzyme, is essential for normal bone formation. True zinc-deficiency states, although reported, are rare (Prasad, Halsted & Nadimi, 1961), and the significance of plasma zinc concentrations, which have been measured in a large number of different clinical states remains in doubt (Halsted & Smith, 1970).

The mean plasma zinc concentration found in the pre-menopausal women in this study was about 11 µg/100 ml higher than the mean normal value given by Davies et al. (1968) for non-fasting subjects using this technique, but they state that plasma zinc concentrations are about 12% lower in non-fasting subjects. It is clear that plasma zinc concentrations are intimately affected by changes in the total plasma protein concentration and allowance for this is desirable. The use of plasma specific gravity in this context is, however, rather crude and it would be preferable to use the plasma albumin concentration instead, since most of the zinc in the plasma is bound to albumin (Prasad & Oberleas, 1968; Boyett & Sullivan, 1970).
The post-menopausal women in this study did not have significantly higher plasma zinc concentrations than the pre-menopausal women. Furthermore, the reduction in plasma specific gravity was similar in both the mestranol-treated women and the women with intact ovaries, but the plasma zinc concentration was significantly lower in the mestranol-treated group. This suggests that the mestranol therapy had caused either an important qualitative change in the plasma proteins (Pilgeram & Pickart, 1963; Robertson, 1967), or true zinc depletion.

The mechanism whereby the synthetic oestrogens lower the plasma zinc concentration requires more detailed investigation, but the apparent lack of effect of endogenous oestrogens on plasma zinc in non-pregnant women makes it improbable that an abnormality of zinc metabolism is a contributory factor in the pathogenesis of post-menopausal osteoporosis.

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REFERENCES


