#392 Pharmacokinetics of oestradiol cream using quantitative liquid chromatography tandem mass spectrometry

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Introduction

- Vaginal oestrogen is often prescribed by Urologists and Urogynaecologists to treat women with urinary incontinence, prolapse, and/or recurrent cystitis
- After the publication of the association between oral oestrogen and breast cancer (1), patients often query its safety
- Previous studies demonstrating that oestriol (E3) cream is safe, relied on demonstrating serum E3 levels below the nominal postmenopausal threshold of 100 pmol/L in current cream users (2)
- These measurements were performed using radiolmmunoassay (RIA), originally developed for infertility investigations and known to have low specificity and sensitivity

Methods and Materials

- Women had been using E3 cream for a median of 26 months (IQR 12-46)
- Median vaginal pH levels measured 4.7 (IQR 4.4-5)
- E3 was absorbed rapidly in most patients (Fig. 1): Median peak serum E3 concentration 416 pmol/L at 2 hours (range 1.5-8 hours, Table 1).
- E3 levels fell to <100 pmol/L in the majority of women (6/10) within 8 hours
- At 24 hours 9/10 women demonstrated oestriol levels <10 pmol/L
- Interindividual variability for peak levels was high: range 245.1-1066.4 pmol/L
- Intraindividual variations were less marked in 5 women that repeated the PK study, with similar peaks during the two 24-hour periods
- No association was found between levels of E2 and BMI

Results

- There were wide variations in individual cream users can be measured much more accurately than with the previously used RIA

Discussion

- We have developed a highly precise analytical technique to assess E3 serum PK levels
- Oestradiol in postmenopausal women is almost absent or below the LLOQ of a sensitive and specific assay to detect (<5 pmol/L)
- There are wide variations in individual response to oestriol cream with median peak values reaching 416 pmol/L at 2 hours
- Rapidity returning to baseline levels (in undetectable) within 24 hours in the majority of women
- There was much less intraindividual variation in the repeated patients (n=5)
- A woman’s capacity to replicate the absorption profile suggests that local factors influence absorption in chronic users of topical E3 in a predictable way and that dosing of E3 cream to local symptoms and serum levels could titrate the amount of E3 absorbed topically
- Chronic users were thought to have less E3 absorption following adaptation/ corrosion of the epithelium from E3 exposure

Conclusion

- In this novel study we found serum E3 levels of women using E3 cream as a chronic treatment to vary greatly between users
- This was less so within single users who were measured twice
- The majority of women had E3 levels below 100 pmol/L after 8 hours and undetectable levels within 24 hours

Table 1. E3 levels in pmol/L. NS = no sample. a and b are the test-retest samples of same patient.

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References