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Stability conditions in estradiol matrix patches; in vitro studies for application in pediatrics

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On behalf of ESPE Turner syndrome working group

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Background

We have previously shown that estradiol (E_2) matrix patches for adults could be cut in smaller pieces to administer low doses for pubertal induction in girls with hypogonadism (1, 2). Using a slow increase of the patch size over a period of few years, serum E_2 concentrations for girls undergoing spontaneous puberty can be closely mimicked.

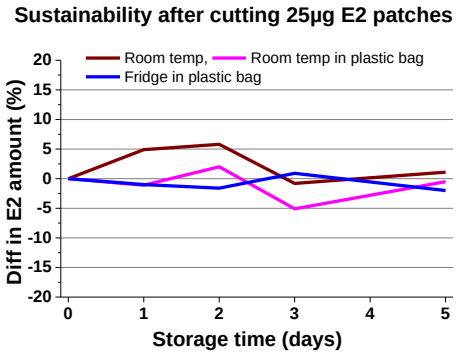
Objective

To confirm that E_2 is evenly distributed over the patch and to assess whether storage conditions have any influence on the amount of E_2 once the patch has been cut.

Conclusions

- The amount of drug E_2 was evenly distributed over the surface.
- In vitro, there were no deterioration of E_2 amount after 5 days of storage in its sachet at room temperature.

Results



In the storage experiment for five consecutive days, no differences were found neither due to storage duration, the way the patches were stored nor how many edges that were exposed. The total coefficient of variation between all the cut pieces was <13%.

Fig 4. Influence of storage on the amount of E_2 compared to an unopened patch sachet.

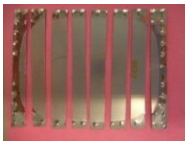


Fig 3. E_2 50µg matrix patch covered with a backing film. The outer edges and six equal pieces have been cut.

Fig 1. E_2 25µg matrix patch covered with a backing film. The two outer edges and two strips has been cut.

Methods

E_2 hemihydrate depot patches 25µg/24h, containing 1.55mg E_2 and 50µg/24h, containing 3.1mg E_2 (Evorel®, Janssen-Cilag) were used.

The left and right hand edges were trimmed off. The aim was to obtain an approximate square size of the patch, to facilitate cutting six strips of equal size.

In the experiment, two pieces were cut from each patch and stored together with the remaining patch in its foil-lined sachet, either (1) in a plastic bag in a fridge (2) in a plastic bag in room temperature or (3) just in room temperature. Storage duration up to 5 days were compared. E_2 concentrations were determined in pieces with two cut edges, pieces with one cut edge and pieces that had no cut edge during storage (Fig 1).

Fig 2. E_2 25µg and 50µg matrix patches

E_2 determination

E_2 was extracted from the patch pieces by a solution of n-hexan and ethylacetat. The samples were thereafter serially diluted. After total evaporation, reconstitution was made using a zero calibrator.

E_2 concentrations were determined by RIA with lower limit of detection 9 pmol/L and total coefficient of variation 9% for 250 pmol/L and above.

References

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