ELSEVIER

EJC Supplements Vol 2 No. 9 (2004) 70–71

EJC Supplements

www.ejconline.com

E24. Low-dose intrauterine levonorgestrel release protects the endometrium during oestrogen replacement: an update

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1. Introduction

The frameless Fibroplant™-levonorgestrel (LNG) intrauterine system (IUS) is an anchored levonorgestrel-releasing device releasing approximately 14 μg of LNG per day. The system is effective for at least three years. The anchor is implanted into the myometrium of the uterine fundus using an insertion instrument. The LNG IUS is frameless, completely flexible and adapts to cavities of every size and shape. Clinical experience with the system in peri- and post-menopausal women has been published previously in [1,2].

2. Patients and methods

Sixty-two post-menopausal women using continuous oestrogen (percutaneous 17 oestradiol, 1.5 mg daily, or an equivalent dose by patch or oral oestrogen) combined with the frameless intrauterine LNG were evaluated. After having used the regimen for a minimum period of three years, they were examined by transvaginal ultrasound examination (TVU) (Ultramark® 4Plus, ATL Inc., USA) and endometrial biopsy (Probet®, Gynetics, Belgium) in order to assess endometrial safety. The use of the LNG IUS was approved by the Ethics Committee of the University in Ghent, Belgium, and written informed consent was obtained. All women were screened according to the World Health Organisation (WHO) eligibility criteria prior to entering the study. The thickness of the endometrium at baseline, assessed according to the measures used by Fleischer et al. [3], showed a thin endometrium (<5 mm) at the start of the study in all women. The endometrial samples were drawn from all parts of the uterus to get a representative sample. Biopsies were placed in phosphate-buffered formaldehyde (4%) immediately upon collection and stained with haematoxylin and eosin for examination. They were examined by two independent pathologists, who did not have any knowledge about the study, according to the diagnostic categories set by Hendrickson and Kempson [4].

3. Results

Histological examinations were conducted in 62 post-menopausal women after an average period of use of the method of 43 months (range 36–50 months). They showed predominantly inactive endometrium characterised by pseudodecidual reaction of the endometrial stroma with endometrial atrophia. There were no specimens showing signs of proliferation. At follow-up, a thin endometrium (<5 mm in thickness), as assessed by transvaginal ultrasound, was found in all post-menopausal women in this study.

4. Discussion

In the 62 women in our study, no hyperplasia was detected. A similar low incidence (0%) of hyperplasia in post-menopausal women receiving estrogen therapy (ET) and a low-dose LNG IUS has been observed in

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1359-6349/$ - see front matter
doi:10.1016/j.ejcsup.2004.08.025

other studies [5]. Intrauterine progestogen delivery, particularly LNG, is probably more effective in postmenopausal women in preventing endometrial proliferation than oral treatment because of the uniform suppression of the endometrium throughout the whole thickness of the mucosa caused by the high tissue concentrations when the hormone is applied locally [6]. However, with sequential therapy, there may be a higher rate of hyperplasia, including complex and atypical hyperplasia [7]. As far as prevention of endometrial hyperplasia is concerned, the duration of the progestogen administration seems more important than the daily dose [8]. The promising results in this study suggest that continuous, intrauterine progestogen delivery could be ideal.

TVU, conducted in all subjects in this study appeared to correlate well with the histological findings. This corresponds with previous studies that found a good correlation if the endometrium is thin (4 or 5 mm) [9].

Conflict of interest

Dirk Wildemeersch is a Belgian gynaecologist and Medical Director of *Contrel Research*, Belgium. *Contrel* is the manufacturer of FibroPlant-LNG IUS in cooperation with the University of Ghent, Belgium.

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