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COMBINED ORAL CONTRACEPTIVES- IMPACT ON THE VULVAR VESTIBULAR MUCOSA AND PAIN MECHANISMS

AKADEMISK AVHANDLING
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ABSTRACT

Objective: The main aim of this thesis was to study the impact of combined oral contraceptives (COC) on the vulvar vestibular mucosa and pain mechanisms in healthy women and in women with provoked vestibulodynia (former vulvar vestibulitis syndrome). The somatosensory perception in the vulvar vestibular mucosa of healthy women was studied with the relation to COC. An endogenous pain inhibitory response called diffuse noxious inhibitory controls (DNIC) was examined in healthy women with or without COC and in women with provoked vestibulodynia. The morphology and steroid receptor expression in healthy women during the influence of COC and during the menstrual cycle and in women with provoked vestibulodynia was evaluated.

Material and Methods: Thirty four women with provoked vestibulodynia, 60 healthy women using COC and 64 healthy non COC users participated in the studies. Quantitative sensory tests, including mechanical and thermal pain thresholds of the vulvar vestibule were performed. Pressure pain thresholds (PPTs) were measured before and during a cold pressor test to provoke a DNIC, or "pain inhibits pain" response. Vestibular biopsies were collected for morphological analyses. The amount and distribution of estrogen receptors α and β, progesterone receptors A and B, glucocorticoid receptor, androgen receptor and the proliferation marker Ki67 were estimated using immunohistochemistry followed by computerized image analysis.

Results: The mechanical pain thresholds were significantly lower in women using COC than in non users. An intact DNIC response was present in all three groups as illustrated by a significantly increased PPT during cold noxious stimulation. Compared with the healthy women, the patients displayed lower PPTs, both before and during the cold pressor test. The vulvar vestibular mucosa displayed a larger interdermal papilla distance in the luteal phase compared with the follicular phase. A similar morphological feature was seen in COC users and there was also a larger distance from the dermal papillae to the epithelial surface compared with controls. Histopathological assessments showed a higher amount of superficial blood vessels in the COC users. The vestibular stromal tissue expressed more ERβ in women with COC than in women without. PRB was more abundant in the stromal tissue in the follicular phase than in the luteal phase. There was a significantly higher expression of ERα in both the epithelium and the stroma in the specimens of the vestibulodynia patients compared with that of controls.

Conclusions: COC may induce an increased sensitivity in the vestibular mucosa in healthy women and might be one contributing factor in the development of provoked vestibulodynia. An altered morphological pattern and changes in the expression of various hormone receptors in women using COC and during the luteal phase indicates a gestagenic effect on the mucosa. There is a systemic hypersensitivity in women with provoked vestibulodynia; however the endogenous pain inhibition seems comparable to that of healthy women irrespective of COC use. The increased expression of ERα in women with provoked vestibulodynia, without an effect on the epithelial morphology, may be related to an ongoing neurogenic inflammation in the mucosa.

Key words: combined oral contraceptives, quantitative sensory testing, pain thresholds, DNIC, endogenous pain modulation, provoked vestibulodynia, vulvar vestibulitis syndrome, morphology, vulvar mucosa, steroid receptors

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