Estradiol reduces connexin43 gap junctions in the uterus during adenomyosis in cows

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Abstract

Adenomyosis is defined as the presence of glandular foci external to the endometrium of the uterus, either in the myometrium or/and perimetrium, depending on the progress of this dysfunction. To date, we showed that steroids secretion and prolactin expression and proliferative processes are disturbed during uterine adenomyosis in cows. During endometriosis in eutopic endometrium in women, gap junctions are down regulated. The transmembrane gap junction protein, connexin (Cx43) is necessary for endometrial morphological, biochemical and angiogenic functions. The aim of this study is recognition of adenomyosis etiology by determination of the role of Cx43 in this process. Immunolocalization and comparison of Cx43 mRNA and protein expression in healthy (N=9) and adenomyotic uterine tissue (N=9), and Cx43 mRNA expression (real time PCR) in uterine stromal – myometrium co-culture under 24-hour stimulation with 17-beta estradiol (10^-7M) isolated from healthy (N=5) and adenomyotic (N=5) cows were determined.

Cx43 was localized in healthy and adenomyotic uteri. mRNA and protein expression was down-regulated in uterine tissue in adenomyotic compared with healthy cows (p<0.05). Estradiol stimulated Cx43 mRNA expression in myometrial cell culture and co-culture of stromal and myometrial cells in adenomyotic compared with healthy cows (p<0.05). In summary, down-regulation of Cx43 expression in the junction zone might play an important role in pathogenesis of adenomyosis. Estradiol modulates gap junctions during adenomyosis.

Key words: uterus, gap junction, connexin, adenomyosis, cow

Introduction

Adenomyosis is a uterine dysfunction characterized by the presence of endometrial glands with stromal elements in the myometrium (Azziz 1989, Campo et al. 2012) but the etiology of this disorder is still unclear (Ferency 1998, Korzekwa et al. 2014). Our previous studies showed that in cows the frequency and progression of adenomyosis are positively correlated with age, what is consistent with studies on women. The cows older than 5 years had advanced stages of adenomyosis (approx. 40% of animals; Korzekwa et al. 2013). Moreover, the presence of adenomyosis did not differ based on the sampling location in the uterus. The glandular nests in adenomyotic cows were present in myometrial layer of both uterine

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