Abstract

Studies on the pathogenesis of the retention of fetal membranes in cows that have been conducted for years have not yet explained the mechanisms of detachment of the maternal and fetal parts during parturition, as well as the creation of a connection between the mother and the embryo during implantation and placentation. As possible causes of fetal membrane retention, changes in hormonal profile, oxidative stress, genetic disorders and dietary deficiencies are considered, inter alia. On the basis of the available literature, it can be concluded that in order to understand the mechanisms occurring in physiological and pathological conditions, one should focus on the analysis of the range of changes occurring during the remodeling of connective tissue and on the examination of factors influencing the changes in the amount of proteins and their activity.

In early pregnancy and in the periparturient period, significant changes in the composition and distribution of extracellular matrix (ECM) components are observed. ECM, also known as extracellular substance, consists mainly of glycoproteins and proteoglycans, thus providing a suitable environment for placental cells. In addition to its structural function, its role is also to regulate physiological and pathological processes through participation in signaling, proliferation, migration and invasion of cells. The main protein component of ECM are collagens and fibronectin, which are involved in placental maturation and the normal development of pregnancy. ECM is also a rich source of proteoglycans, which, by interacting with cell surface receptors, modulate their migration, proliferation, differentiation and adhesion. One of the proteins is decorin (DCN), a low molecular weight leucine-rich proteoglycan with a mass of approximately 100 kDa, composed of a protein core (approximately 40 kDa) and a chain of glycosaminoglycans, which can be additionally glycosylated. Under physiological conditions, the protein core of decorin and its sugar chain may exhibit separate functions, and changes in gene expression of this protein may be associated with placental maturation and pregnancy development. The role of decorin during the remodeling of the placenta is to regulate collagen concentration at transcriptional and translational levels, to modulate collagenase activity and to stabilize fetal membranes in the early stages of fetal development and later pregnancy. Based on available sources of information, it is suspected that this protein may not only participate in adhesion of the placenta

during pregnancy, but also its excretion during delivery. However, this mechanism is not fully understood.

Throughout pregnancy, placental cells are under exact hormonal control, which regulates the concentration and activity of specific proteins. Among the hormones that concentrations in the bloodstream and fetal membranes change during pregnancy are progesterone and prostaglandin $F_{2\alpha}$. These hormones differ in structure and regulate different signaling pathways, therefore they perform different functions in placental tissue.

Taking into account the lack of unequivocal information about the role of decorin, progesterone and $PGF_{2\alpha}$ in the adhesion of placental cells during pregnancy in cows, it has been decided to verify the research hypothesis about their possible effect on the adhesion of pregnant endometrial cells. In addition, based on numerous reports on the significant impact of the glycosylation process during pregnancy, it has been also decided to assess the effect of inhibitors of this process on the adhesion of cells. For this purpose, as a model for the research, self-derived epithelial cell lines were used, which are a direct contact point of the maternal and fetal parts of the placenta. Cells were incubated with decorin, progesterone, $PGF_{2\alpha}$ and glycosylation inhibitors - 2-acetamido-2-deoxy-α-D-galactopyranoside and tunicamycin, followed by an adhesion test to the fibronectin matrix.

The results obtained in this study indicate that decorin affects the adhesion of pregnant endometrial cells in cows. Thus, the analyzes carried out allowed for positive verification of the research hypothesis. Incubation of cells with decorin and prostaglandin $F_{2\alpha}$ reduces cell adhesion to the fibronectin matrix. Progesterone does not affect cell adhesion, but masks the anti-adhesive properties of decorin. In addition, it was found that the glycosylation process modulates the adhesion of pregnant endometrial cells in cows. N-glycosylation seems to be an important modification of proteins for adhesion processes, because the use of its tunicamycin inhibitor inhibits the adhesion of pregnant endometrial cells in cows. In turn, O-glycosylation may be a factor limiting cell adhesion - administration of its inhibitor - benzyl 2-acetamido-2-deoxy-α-D-galactopyranoside - stimulates the adhesion of the cells studied.

The obtained results confirm the research hypotheses put forward in this doctoral thesis on the modulating effect of decorin, progesterone, prostaglandin $F_{2\alpha}$ and glycosylation process on the adhesion of endometrial cells in cows during pregnancy.

Key words: Placenta, decorin, pregnancy, adhesion, cow