SUMMARY

Preterm labor with intact membranes (PTL) is responsible for approximately 40% of all preterm deliveries. PTL is frequently complicated by intra-amniotic inflammation (IAI), characterized by the elevation of inflammatory mediators in the amniotic fluid. Based on the presence or absence of microbial invasion of the amniotic cavity (MIAC), two different clinical phenotypes of IAI are distinguished: i) intra-amniotic infection, when microorganisms are present in the amniotic fluid, and ii) sterile IAI, when there are no microorganisms in the amniotic fluid. The clinical severity of both phenotypes of IAI is underlined by their association with adverse neonatal outcomes.

In addition to the presence or absence of MIAC, there are also differences between the phenotypes of IAI in terms of their intra-amniotic inflammatory status characteristics. The clinical part of this thesis has addressed these differences in women with PTL. The first specific aim of this clinical study was to determine the concentration of interleukin (IL)-6 in the cervical fluid of women with PTL complicated by intra-amniotic infection and sterile IAI. The second specific aim was to determine the concentration of IgGFc-binding protein (FcgammaBP) in the amniotic and cervical fluids of women with PTL complicated by intra-amniotic infection and sterile IAI.

Both specific aims of the clinical part of this thesis were investigated in the same study population, consisting of 79 women with PTL. The presence of both phenotypes of IAI was associated with a higher concentration of IL-6 in the cervical fluid than the absence of IAI. However, there were no differences in the concentration of IL-6 in the cervical fluid between the phenotypes of IAI. The concentration of FcgammaBP in amniotic fluid was elevated in the presence of both phenotypes of intra-amniotic inflammation, being more pronounced in the presence of intra-amniotic infection. The concentration of FcgammaBP in the cervical fluid was not altered by the presence of either phenotype of IAI.

Animal models of IAI represent a unique tool in the research of preterm delivery, enabling the study of aspects that cannot be evaluated in human clinical studies. Therefore, the objective of this thesis was to develop a rat model of IAI established by ultrasound-guided intra-amniotic administration of an inflammatory agent. The first specific aim of the experimental part of this thesis was to perform a systematic review of literature on methods of intra-amniotic administration of infectious and/or inflammatory agents to develop a rodent model of inflammation-driven preterm delivery. The second specific aim was to assess the effect of

ultrasound-guided intra-amniotic administration of lipopolysaccharide (LPS) on the concentration of IL-6 in the amniotic fluid of rats. The third specific aim was to define a detailed protocol for ultrasound-guided intra-amniotic administration of an agent in a rat.

A systematic review of the literature revealed that intra-amniotic administration of triggering agents was used to model intra-amniotic infection/inflammation in rodents. Intra-amniotic administration under ultrasound guidance has been described in mice, but not in rats. Our experiments performed on seven rat dams showed that ultrasound-guided intra-amniotic administration of an agent was feasible in rats. Administration of 10 μg of *Escherichia coli* LPS serotype O55:B5 per gestational sac resulted in the development of IAI and did not induce labor or fetal mortality. The processes of ultrasound-guided intra-amniotic administration of an agent in a rat were summarized as a protocol to offer detailed guidelines supporting the feasibility and reproducibility of this technique for future research.