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Vaginal microbiota in women with preterm labor and intact membranes

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Objective

Spontaneous preterm birth (sPTB) is one of the major problems in Maternal and Fetal Medicine being intra-amniotic infection and sterile intra-amniotic inflammation (IAI) leading causes of sPTB at early gestational ages. Ascending pathway is considered the most common dissemination pathway to the amniotic fluid. With vaginal sequencing of 16S rRNA gene we aim to evaluate, in women with preterm labor (PTL), whether vaginal microbiota differs among the different infectious/inflammatory phenotypes reported in women with preterm labor (PTL).

Methods

Women with singleton pregnancies admitted with PTL <34. 0 weeks with an amniocentesis to rule out intra-amniotic infection/IAI were included. Vaginal fluid was collected in the vaginal fornix within 24 h after amniocentesis. Intra-amniotic infection was diagnosed in women with a positive amniotic fluid (AF) aerobic/anaerobic/genital mycoplasma cultures and/or a positive AF PCR of 16S rRNA gene. Sterile IAI was diagnosed in women with a negative AF culture and a negative AF PCR of 16S rRNA gene but with high levels of AF interleukin-6 (≥13. 4 ng/mL). We defined 5 vaginal community types (CST): CSTs I, II, III and V were dominated by Lactobacillus crispatus, Lactobacillus gasseri, Lactobacillus iners, and Lactobacillus jensenii, respectively. CST IV was characterized by higher proportions of anaerobic bacteria with low levels of Lactobacillus spp. Vaginal sequencing of 16S rRNA gene was performed using MiSeq platform, targeting the V3 and V4 hypervariable regions. Data cleaning, processing and taxonomic affiliations were performed using QIIME. Statistical analyses and graphics were performed using R (v3. 4. 2), Calypso (v8. 56) and SPSS program (v24. 0).

Results

From 2013 to 2016, 69 women were included being 19 (27. 5%) women diagnosed of intra-amniotic infection and 6 (8. 7%) of sterile IAI. Most common microorganisms isolated in the amniotic fluid were Ureaplasma parvum 8/19 (42. 1%), Mycoplasma hominis 3/19 (15. 8%) and Streptococcus spp. 2/19 (10. 5%). Only one woman with intra-amniotic infection had low levels of IL-6. Presence of Lactobacillus spp. in the vagina was significantly more common in women without intra-amniotic infection or sterile IAI. Interestingly, and despite the absence of a positive AF culture/PCR of 16S rRNA gene, women with sterile IAI presented a similar vaginal microbiota than women with intra-amniotic infection being this microbiota dominated by bacteria commonly associated to CST IV. Vaginal microbiota diversity (Alpha diversity or Shannon index) was significantly higher in women with intra-amniotic infection or with sterile IAI than in women without infection or IAI. We did not observe differences on vaginal microbiota diversity between women with intra-amniotic infection and women with sterile IAI. In women with intra-amniotic infection, Ureaplasma parvum, Burkholderia cepacia and Peptoniphilus harei were the most common species found in vaginal microbiota being Atopobium vaginae, Haemophilus influenzae, Gardnerella vaginalis and Prevotella amnii those species more frequently found in vaginal microbiota of women with sterile IAI. We also found a positive correlation between vaginal microbial diversity and levels of AF IL-6 ($R = 0.27$, $p = 0.023$), and a negative correlation with glucose levels ($R = -0.3$, $p = 0.014$).

Conclusion

A vaginal microbiota dominated by lactobacillus spp. was found in women without infection or IAI. However, in women with intra-amniotic infection we observed a higher vaginal microbiota diversity dominated by Ureaplasma spp. highlighting the importance of ascending pathway. Regardless of the absence of a negative AF culture/PCR of 16S rRNA gene, women with sterile IAI presented similar vaginal microbiota diversity than women with intra-amniotic infection. Whether vaginal Lactobacillus spp. dominance plays a protective role against the occurrence of intra-amniotic infection and sterile IAI is unknown but merits to be further evaluated in the future.