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Fetal membrane patch and biomimetic adhesive coacervates as a sealant for fetoscopic defects

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ABSTRACT

Iatrogenic preterm premature rupture of membranes after fetoscopic procedures affects 10–47% of patients, secondary to the non-healing nature of membranes and the separation of layers during the entry. In this study we developed an in vitro model to mimic the uterine wall–fetal membrane interface using a water column with one end sealed with human fetal membranes and poultry breast, and a defect was created with an 11 French trocar. Further, a fetal membrane patch in conjunction with multiphase adhesive coacervates modeled after the sandcastle worm bioadhesive was tested for sealing of an iatrogenic defect. The sealant withstood an additional traction of 12 g for 30–60 min and turbulence of the water column without leakage of fluid or slippage. The adhesive is non-toxic when in direct contact with human fetal membranes in an organ culture setting. A fetal membrane patch with multiphase adhesive complex coacervates may help to seal the defect and prevent iatrogenic preterm premature rupture of the membranes.

1. Introduction

Iatrogenic preterm premature rupture of the membranes (iPPROM) after a fetal intervention procedure is a major complication, affecting 10–47% of procedures [1–5]. iPPROM leads to an increased risk of preterm labor and worsens the perinatal mortality, undermining the true benefit of such interventions [6]. There are two possible explanations for the increased risk for iPPROM after invasive fetal procedures. One is the innate non-healing nature of the fetal membranes, as demonstrated in both in vivo and in vitro studies [7,8]. The other is that separation of the amnion from the chorio-decidual layers that occurs during the introduction of instrumentation into the uterine cavity can cause a persistent parting of membranes with subsequent leakage of amniotic fluid [9]. There have been several attempts to study sealants at the site of the fetal membrane defect, both in vitro and in vivo [10–12]. However, there is no ideal in vitro model to simulate the relationship of the uterine wall, the fetal membranes and the amniotic fluid environment. There is evidence to suggest that a decellularized fetal membrane scaffold can promote cellular proliferation at the defect site [13]; however, no method to introduce a fetal membrane patch through a narrow operative cannula and deliver it to the site of the defect has ever been described. Additionally, after the patch has been deployed, the challenge of fixation to the membranes and the uterine wall remains due to the dynamic nature of the amniotic fluid and uterine musculature. An underwater adhesive that would fix a tissue scaffold to the edges of the defect in place for the remainder of the pregnancy would be an ideal solution to the problem of iPPROM; however, no adhesive suitable for this task is available.

Development of medical adhesives for the wet interior of the body is both chemically and biologically challenging. The adhesive must be delivered, bonded and cured in the presence of moisture, must be non-toxic, and must not provoke a severe foreign body response. One approach to achieve underwater bonding is to study natural biological underwater adhesives, identify their key chemical features and copy that chemistry using non-toxic, biocompatible and cost-effective synthetic polymers. Numerous aquatic organisms produce working underwater adhesives as part of their

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