Analytical and operational test of the ROM-Plus test for rupture of fetal membranes

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Abstract

Background: ROM-Plus (Clinical Innovations) is a recently approved test for rupture of fetal membranes, intended for use at point-of-care. The test is a lateral flow sandwich immunoassay for detection of either placental protein 12 (PP12) or insulin-like growth factor binding protein-1 (IGFBP-1) or alpha-fetoprotein (AFP) in vaginal pool fluid, as markers for presence of amniotic fluid. We investigated analytical and operational characteristics of the assay: sensitivity for detection of controls, stability of controls, dilution factor of swab samples, and titre of near-term amniotic fluid and of biological fluids other than amniotic fluid.

Methods: Operation of the assay was according to manufacturer's instructions, using either direct application (DA) of fluids to the application point (as for controls) or by after swab transfer (ST) to diluent (as for samples), as noted. Controls are provided in sealed glass ampules with plastic applicators. For positive control, release of lysate by breakage of the ampule subsequently dissociates tyrosylated protein within the holder. This holder is also a dropper device for direct application of fluid to the application point. For vaginal pool samples, a plastic holder with diluent is provided wherein a swab sample is placed for solution of sample from the swab. After score point-breakage of the tip which then remains in the fluid, the holder has an attached dropper cap within swab sample is applied. A dye-diffusion timer on the device is activated by finger. Samples are to be read as positive or negative by appearance of a line at the test position no more than 20 min after sample application.

Results: Mass-carrying capability of swab for 7 g aliquot is an average 78±13 g (n = 6), given diluent volume of 380 μL, this indicated an application minimum dilution for ST samples of 18%. Positive control (stated concentrations [AFP] = 600 ng/mL, PP12 = 20 ng/mL, IGFBP-1 = 5 ng/mL) was positive (DA) to 1:30 dilution, consistent with stated device analytical sensitivity ([AFP] = 150 ng/mL, PP12 = 5 ng/mL, IGFBP-1 = 3 ng/mL) for ST when accounting for ST dilution. Control 1:8 remained positive (DA) after 10 days storage either refrigerated or frozen. By 14 days, ST pregnancy pooled, previously frozen amniotic fluid (submitted for fetal lung maturity testing) was positive to titre less than 1:3000. EDTA-whole blood samples from males, non-pregnant females (<36 years of age), and first-trimester pregnant females were all positives by ST.

Conclusions: Positive ROM-Plus ST results for samples other than amniotic fluid are likely due to high test sensitivity for IGFBP. Specifically, the validity of test-positive samples were unlikely to be due to PP12.

References