Evaluation of a rapid test for detection of *insulin-like growth factor binding protein-1* (IGFBP-1) for the diagnostic of premature rupture of membranes

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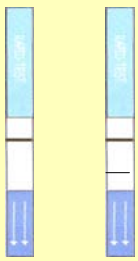
Premature rupture of membranes (PRM) is a common obstetrical event which may be the cause of severe materno-fetal complications. In the case of subclinical forms, a rapid biological diagnostic is of high value. The detection of IGFBP-1 (insulin-like growth factor binding protein-1) in cervicovaginal secretions (by immunochromatographic dipstick) is a recognized, rapid and reliable test.

Our study focused on the analytical validation of Amnioquick® strips (Biosynex, France) and on comparison to the Actim® PROM test (Biochemia Medix, Finland distributed in France by Fumouze) currently used in routine laboratory of Medical Biochemistry Laboratory, CHU Estaing of Clermont-Ferrand.

1. Protocol for use of Actim® PROM & Amnioquick®

• In the clinical department : the secretions in the vaginal fornix were collected with a sterile polyester swab supplied with the kit, which is then immersed for 10 seconds in the extraction buffer.



negative positive

• In the laboratory:

-immersion of test strips into tubes containing 500 mL of extraction buffer (10 minutes for Amnioquick® and 30 seconds for Actim® PROM)

-reading of the result immediately after removing the strip for Amnioquick® and after 5 minutes for Actim® PROM

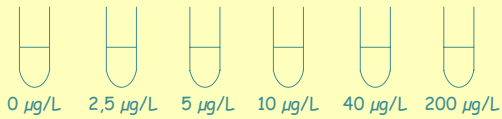
⇒ Negative result : a positive control of reaction is included on each strip exhibiting a grey control band to validate the analytical stage.

⇒ Positive result : appearance of a grey band even of low intensity, reflecting the binding of IGFBP-1 from the sample on the specific anti-IGFBP-1 immobilized onto the strip.

2. Repeatability test of Amnioquick® strips

• Repeatability conditions: independent assays, same method, same laboratory, same operator, same equipment within short intervals of time.

Establishment of dilution cascade of IGFBP-1 from 5 to 200 µg / L in the Amnioquick® buffer after reconstitution of 1 µg of lyophilized recombinant IGFBP-1 (Milllegen, Meylan, France) in 1 mL of distilled water.



⇒ Repeatability test on n=10 for each concentration

The repeatability is 100% for each concentration tested

3. Comparison of sensitivity of Amnioquick® vs. Actim®PROM

• From serial dilution of recombinant IGFBP-1 performed in the respective buffers of the 2 tests to determine their analytical threshold.

•From 2 samples of amniotic fluid (AF) diluted in NaCl solution in order to simulate a possible dilution of AF in pregnant women with vaginal discharges or other physiological substances

		AMNIOQUICK®	Actim® PROM
sensitivity threshold (µg of IGFBP-1/L)	theorical threshold given by the manufacturer	5	25
	thresholds obtained from the dilution ranges	5	40
Last positive dilution of AF	AF n°1	1/640	1/80
	AF n°2	1/640	1/160

⇒the results of these two trials are in accordance and show a difference of sensitivity ranging from a factor 4 to 8

Experimentally, the Amnioquick® strips are at least 4 times more sensitive than the Actim® PROM strips

4. Samples of patients

• A retrospective study on 223 patient samples collected between July and November 2009 and whose Actim® PROM test has been made at the time of prescription.

•Analysis of discordant cases according to clinical response and outcome of pregnancy

		AMNIOQUICK®		TOTAL
		positive	negative	
ACTIM® PROM	positive	44 (19.7%)	10 (4.5%)	54
	negative	**4 (1.8%)**	165 (74%)	169
TOTAL		48	175	223

⇒there are 14 discordant results confirmed) or 6.3%

3 analyzed cases
⇒ No PROM for 2/3 of cases

9 analyzed cases
⇒ 8 proven ruptures

In 10 of the 12 cases studied, Actim ® PROM is more related to the clinical findings

Conclusion

Amnioquick® strips have excellent repeatability and are more sensitive than the Actim® PROM test (factor 4 to 8). Nevertheless, it appears that lowering the threshold does not bring more information in terms of correlation with pregnancy outcomes of women tested for premature rupture of membranes.
Other strategies using the combined detection of new markers with IGFBP-1 could be an interesting development, to associate a higher sensitivity while maintaining excellent correlation with clinical outcome.