Intraamniotic Infection Diagnostic Test in PPROM through the Measurement of Vaginal Fluid C-Reactive Protein Using HS-CRP CHECK-1 (Lateral-Flow Immunoassay Method) with Cobas Integra 400 Plus (Light-scattering Immunoassay method) as a Gold Standard

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ABSTRAK

*Infeksi Intraaamniotic meningkatkan morbiditas dan mortalitas perinatal. Infeksi intraamniotik dapat ditegakkan dari pengukuran konsentrasi CRP pada cairan vagina. Ada beberapa metode untuk mengukur CRP dalam cairan tubuh, salah satu metode yang paling sederhana adalah immunoassay lateral-aliran. Namun keandalan tes ini harus dibandingkan dengan metode yang lebih canggih dengan mengetahui persamaan HS-CRP CHECK-1 ke Plus Cobas Integra 400 dalam mengukur CRP cairan vagina dan mendeteksi infeksi intraamniotik serta mengetahui sensitivitas, spesifisitas, prediksi positif nilai dan nilai prediksi negatif HS-CRP CHECK-1 untuk mendeteksi infeksi intraamniotik. Tujuan dari penelitian ini adalah untuk membuktikan HS-CRP CHECK-1 dapat digunakan untuk mengukur kadar CRP dalam cairan vagina dan dapat digunakan sebagai alat diagnostik untuk infeksi intraamniotik. Ini adalah uji penelitian diagnostik menggunakan 33 sampel cairan vagina dari pasien PPROM yang dianalisis menggunakan HS-CRP CHECK-1 dan Cobas Integra 400 Plus sebagai baku emas. Infeksi intraamniotik ditentukan oleh tingkat CRP> 0,8 mg / L. Hasil tes ini kemudian dibandingkan dan dianalisis. Dari analisis statistik, ditemukan bahwa HS-CRP CHECK-1 setara dengan Ditambah Cobas Integra 400 dalam mengukur CRP cairan vagina dan mendiagnosis infeksi intraamniotik. Sentifity 50%, spesifisitas 100%, nilai prediksi positif 100% dan nilai prediksi negatif 86,2% diperoleh dari HS-CRP CHECK-1 untuk infeksi intraamniotik. Sebagai kesimpulan, HS-CRP CHECK-1 setara dengan Cobas Integra 400 Plus, dan dapat digunakan sebagai tes diagnostik. (**MOG 2011;19:78-80**)*

Kata kunci: *HS-CRP CHECK-1, CRP, infeksi intraamniotik, PPROM*

ABSTRACT

*Intraaamniotic infection increased perinatal morbidity and mortality. Intraamniotic infection can be established from vaginal fluid CRP concentrations measurement. There are several methods to measure CRP in body fluid, one of the simplest method is the lateral-flow immunoassay. However the reliability of this test should be compared to the more sophisticated method by knowing the equality of HS-CRP CHECK-1 to Cobas Integra 400 Plus in measuring vaginal fluid CRP and detecting intraamniotic infection as well as knowing the sensitivity, specificity, positive predictive value and negative predictive value of HS-CRP CHECK-1 for detecting intraamniotic infection. The objective of this study was to prove HS-CRP CHECK-1 can be used to measure the levels of CRP in vaginal fluid and can be used as a diagnostic tool for intraamniotic infection. This was diagnostic test research, 33 sample of vaginal fluid from PPROM patients are analyze using HS-CRP CHECK-1 and Cobas Integra 400 Plus as the gold standart. Intraamniotic infection is determined by CRP level > 0.8 mg/L. Test results were then compared and analyzed. From the statistical analysis, it was found that HS-CRP CHECK-1 is equivalent to Cobas Integra 400 Plus in measuring vaginal fluid CRP and diagnosing intraamniotic infection. Sentifity 50%, spesificity 100%, positive predictive value 100% and negative predictive value 86.2% are obtained from HS-CRP CHECK-1 for intraamniotic infection. In conclusion, HS-CRP CHECK-1 is equivalent to Cobas Integra 400 Plus, and can be used as a diagnostic test. (**MOG 2011;19:78-80**)*

Keywords: *HS-CRP CHECK-1, CRP, Intraamniotic infection, PPROM*

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INTRODUCTION

Fetus exposed to intraamniotic infection have increased morbidity and mortality.[1] Fetal conditions can be predicted by measuring inflammatory mediators in amniotic fluid or fetal blood.[2] 40% of Preterm Premature Rupture of the Membrane have intraamniotic infection.[3,4,5] C-Reactive Protein (CRP) is an acute-phase response protein produced by hepatocytes in the event of inflammatory process and infection.[6,7,8,9] CRP can be found in fetal urine since the beginning of the second trimester of pregnancy.[10] One research showed a significant correlation between CRP levels of amniotic fluid and vaginal fluid as measured by the method of turbidimetry in PPROM patients with positive amniotic fluid culture results indicate the presence of

intraamniotic infection.[2] Cutoff levels of CRP for intraamniotic infection obtained from the study is > 0.8 mg/L. Today there is no rapid test to measure amniotic levels of CRP. Currently, comercially available rapid test is to measure whole blood CRP levels, one of which is the HS-CRP CHECK-1. There are no data about the ability of HS-CRP CHECK-1 to measure CRP levels in amniotic fluid. Researchers aimed to prove HS-CRP CHECK-1 can be used to measure the levels of CRP in amniotic fluid and used as a diagnostic tool for intra-amniotic infection.

MATERIALS AND METHODS

This research is a diagnostic test done by single-blind. Vaginal fluid are taken from PPROM patient with gestasional age 16-36 6/7 weeks in the delivery room of Dr.Soetomo General Hospital Surabaya. For each sample of vaginal fluid CRP levels is measured by two methods. The light-scattering immunoassay using Cobas Integra 400 Plus and the lateral-flow immunoassay using HS-CRP CHECK-1. To determine the ability of HS- CRP CHECK-1 in measuringvaginal fluid CRP levels a comparative test and correlation is carried out using friedman and spearman statistic tests. To determine the ability of HS-CRP CHECK-1 to diagnose intraamniotic infection a test is carried out using McNemar and likelihood ratio statistic tests. To determine sensitifity, spesificity, positive predictive value (PPV) and negative predictive value (NPV) a 2x2 table is used.

RESULTS AND DISCUSSIONS

Thirty-three samples of vaginal fluid are obtained. The average vaginal fluid CRP levels is 1.095 mg/L and the average rectal temperature is 37°C. Spearman correlation test analysis obtained r = 0.877 with p = 0.01, hence the results of HS-CRP CHECK- 1 with Cobas Integra 400 Plus has a strong correlation. Then a comparative analysis of Friedman's test obtained p = 1.00, and hence the results of HS-CRP CHECK-1 with Cobas Integra 400 Plus has no significant difference. Likelihood ratio test correlation analysis obtained p = 0.01, hence the results of HS-CRP CHECK-1 with Cobas Integra 400 Plus has a strong correlation. Then a comparative analysis of the McNemar's test obtained p = 0.125 and hence the results of HS-CRP CHECK-1 with Cobas Integra 400 Plus has no significant difference.

Table 1. Results of vaginal fluid CRP levels using HS-CRP CHECK-1.

CRP		Cobas			Total
		<1 mg/L	1-3 mg/L	>3 mg/L	
Check-1	<1 mg/L	1-3 mg/L	>3mg/L	0	29
	1-3 mg/L	0	3	0	3
	>3 mg/L	0	1	0	1
Total		28	5	0	33

Table 2. Results of HS-CRP CHECK-1 for intraamniotic infection.

Intraamniotic infection		Cobas	Total		
		Infection	No Infection		
Check-1	Infection	4	0	4	PPV 100%
	No Infection	4	25	29	NPV 86.2%
Total		8	25	33	
		Sensitivity 50%	Specificity 100%		Accuracy 87,87%

The results from 2x2 table for diagnosing intraamniotic infection obtained are: accuracy 87.87%, sensitifity 50%, specificity 100%, positive predictive value 100%, and negative predictive value of 86.2%.In diagnostic tests, two different tools is said to be equal if: (1) has no difference in result, to prove it acomparative test is required; (2) the test result correlated, to prove it a correlation test is required. So when the comparative test result is not significant and correlation test result is significant then the two devices can be declared equivalent.

From table 1 comparative analysis results of Friedman's test are not significant (p = 1.00) and Spearman correlation analysis test results are significant (p = 0.01), it can be said that HS-CRP CHECK-1 and Cobas Integra 400 Plus is equivalent in term of measuring the levels of vaginal fluid CRP. And from this study can be concluded that HS-CRP CHECK-1 is also capable of measuring vaginal fluid CRP beside whole blood levels of CRP. So HS-CRP CHECK-1 can replace Cobas Integra 400 Plus for vaginal fluid examination. From table 2 comparative analysis test results of McNemar test is not significant (p = 0.125) and correlation analysis results of likelihood ratio test is significant (p = 0.01), it can be said that HS-CRP CHECK-1 is equivalent to Cobas Integra 400 Plus in terms of intraamniotic infection examination. From table 2 HS-CRP CHECK-1 has a sensitivity of 50% and a spesificity of 100%. HS-CRP CHECK-1 sensitivity is low by being unable to detect the incidence of intraamniotic infection with vaginal fluid CRP levels between 0.8 mg/L to 1 mg/L. because of the low sensitivity HS-CRP CHECK-1 can not be used for screening.

CONCLUSION

HS-CRP CHECK-1 is equivalent to Cobas Integra 400 Plus, and can be used as a diagnostic test.

REFERENCES

1. Merenstein GB and Weisman LE. Premature rupture of the membranes: neonatal consequences. Semin Perinatol. 1996; 20: pp. 375-80.
2. Di Naro E, Ghezzi F, Raio L, Romano F, Mueller MD, McDougall J, et al. C- reactive protein in vaginal fluid of patients with premature rupture of membranes. Acta Obstet Gynecol Scand. 2003; 82: pp. 1072-9.
3. Furman B, Shoham-vardi I, Bashiri A, Erez O, Mazor M. Clinical significance and outcome of preterm prelabor rupture of membranes: population-based study. Eur J Obstet Gynecol Reprod Biol. 2000; 92: pp. 209-16.
4. El-Bastawissi AY, Williams MA, Riley DE, Hitti J, Krieger JN.Amniotic fluid interleukin-6 and preterm delivery: a review. Obstet Gynecol. 2000; 95: pp. 1056–64.
5. Goldenberg RL and McClure EM. The epidemiology of preterm birth. Dalam: Berghella V., 1st ed. Preterm birth: prevention and management. Oxford: Wiley-Blackwell; 2010. Ch. 4.
6. Jaye DL and Waites KB. Clinical applications of C-reactive protein in pediatrics. Pediatr Infect Dis J. 1997; 16: pp. 735–47.
7. Abbas AK and Lichtman AH. Innate immunity: the early defense against infections. In: Abbas AK, Lichtman AH. Basic immunology: functions and disorders of the immune system., 1st ed. Philadelphia; WB Saunders Company; 2001: Ch. 2.
8. Ablij HC and Meinders AE. C-reactive protein: history and revival. Eur J Intern Med 2002; 13: pp. 412-22.
9. Gabay C and Kushner I. Acute-phase proteins and other systemic responses to inflammation. New Engl J Med. 1999; 340(6): pp. 448–54
10. Raio L, Ghezzi F, Mueller MD, McDougall J, Malek A.Evidence of fetal C-reactive protein urinary excretion in early gestation. Obstet Gynecol. 2003; 101(5): pp. 1062-3.