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Research Article

Comparison of Conventional Methods (Nitrazine Test, Ferning Test) and Placental Alpha- Microglobulin1 (Pamg1) in Cervicovaginal Discharge for the Diagnosis of Rupture of Membranes: A case -Control Research Study

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Abstract

Aim/Background: Because of these potential complications, accurate methods are needed for the diagnosis of premature rupture of fetal membranes. This study aimed to compare the diagnostic efficacy of the nitrazine test, ferning test and measurement of placental alpha microgluboline I test in participants with premature rupture of fetal membranes signs and symptoms.

Materials and Methods: Our study was planned as a prospective and observational study. The case and control group consisted of 21 pregnant women. All participants were examined with a detailed history and detailed physical examination. All participants were examined with conventional clinical tests and measurement of placental alpha microgluboline I test.

Results: The relationship between the study and control groups in terms of mean age, gravida, parity, and gestational age at first admission was examined, and it was determined that there was no statistically significant difference The data obtained from our study showed that the PAMG-1 immunoassay has 85% sensitivity, 100% specificity, 100% PPD, and 87.5% NPD. For the nitrazine test, these values were calculated as 90.5% sensitivity, 92.5% specificity, 95.0% PPV and 90.9% NPV, respectively. For the Ferning test, it has 85.7% sensitivity, 100% specificity, 100% PPD, and 87.5% NPD.

Conclusion: The results obtained from our study differed from those obtained from some other studies. It was considered that the difference was due to the number of participants or the difference in practice. It is possible to reach more accurate results with studies to be carried out on larger data sets.

Keywords: premature rupture, fetal membranes, nitrazine test, ferning test, placental alpha microgluboline

Introduction

Premature rupture of fetal membranes (PROM) is the rupture of the gestational membranes before the onset of labor. It is one of the most serious problems of obstetrics. It complicates 5% - 10% of term pregnancies and 30% of preterm births. Although physiological weakening of the membranes, intraamniotic infection, and vaginal bleeding are among the etiological factors, a clear etiological cause is often not found [1]. PROM increases the risk of infectious morbidity in the mother and fetus and may lead to complications such as fetal deformity, pulmonary hypoplasia, and postpartum endometritis. Neonatal deaths and morbidities in PROM are higher than in other pathologies that cause preterm birth. Because of these potential complications, accurate methods are needed for the diagnosis of PROM [1].

Accurate diagnosis and management of PROM requires extensive exploration of pathophysiological pathways and the development of biomolecular markers that can predict PROM. PROM diagnostic tests involve analyzing vaginal secretions to determine if amniotic fluid is present in the vagina. In these analyzes, only substances found in amniotic fluid or certain properties are sought. There is a risk of false results in

these analyzes since vaginal secretions or amniotic fluid may be contaminated [2].

Diagnosis of PROM is a clinical problem in obstetrics. Today, diagnostic tests are invasive. The diagnosis of PROM is often based on the person's history, the amount of amniotic fluids, and the fern appearance detected on microscopic examination. However, the frequency of obtaining false positive and negative results in these examinations is high. Some of the PROM diagnostic tests are listed below:

1. pH testing involves testing the pH of a vaginal fluid sample. Normal vaginal pH is between 4.5 and 6.0, while amniotic fluid is between 7.1 and 7.3.
2. The nitrazine test is based on the principle that the vaginal fluid reacts with the nitrazine dye. Color change is observed in vaginal fluid depending on pH.
3. In the Ferning test, the vaginal fluid is examined under a microscope. If the amniotic fluid is mixed with the fluid, a fern shape is observed [2, 3].

However, these tests can give false-positive results. In cases such as blood or semen mixing in the sample and the presence of infection, the results can be misleading [4].

Measurement of Placental Alpha Microgluboline I (PAMG-1) is one of the newest tests among PROM diagnostic tests. The PAMG-1 test is an easy and fast test to perform. Speculum is not used in this test. The presence of an alkaline vagina and blood has no effect on the test result. In some studies, data have been obtained showing that the PAMG-1 test is more accurate than traditional diagnostic methods [5-7].

This study aimed to compare the diagnostic efficacy of the nitrazine test, ferning test and PAMG-1 test in participants with PROM signs and symptoms. Our study was planned as a prospective and observational study.

Materials and Methods

Our research was carried out in the gynecology and obstetrics clinic of a tertiary education hospital. The case group consisted of 21 pregnant women between the 24th and 40th weeks who applied to our outpatient clinic with signs or symptoms of PROM. The control group consisted of 21 pregnant women without signs or symptoms of PROM. In total, 42 women were included in the study. Participants with active vaginal bleeding, vaginal infection, or a history of sexual activity within 24 hours of admission were excluded from the study [8]. These were accepted as Inclusion/Exclusion criteria. Demographic characteristics of the participants such as age, parity number, gravida, and gestational age at first admission were used as descriptive statistics.

There is no diagnostic method accepted as the gold standard for the diagnosis of PROM. By a review of the literature, demonstration of leakage of amniotic fluid or presence of two of the following three clinical signs by speculum examination was accepted as the gold standard in our study [8].

- Visual collection of fluid in the posterior fornix,
- Positive nitrazine-ferning test,
- Microscopic evidence.

All participants were examined with a detailed history, detailed physical examination including sterile speculum examinations, and transabdominal ultrasound examination. In addition, all participants were examined with conventional clinical tests (nitrazine test, ferning test) and PAMG-1 test. The designated gold standard method for the diagnosis of PROM was applied to all participants. After the examinations, sensitivity, specificity, positive and negative predictive values (PPD and NPD, respectively) were calculated for nitrazine, ferning, and PAMG-1 tests.

Sensitivity is defined as the ability of a test to find cases, while specificity is defined as the ability of a test to find healthy individuals. PPD is the frequency of individuals who have a case among individuals that the test identifies as cases. NPD is the percentage of truly healthy individuals that the test finds to be healthy. Here, the results obtained from the diagnostic method, which is accepted as the gold standard, are accepted as real results [9].

Diagnoses in all participants were confirmed using the designated gold standard method [9]. A sterile Dacron swab was used to collect fluid from the posterior fornix for nitrazine and ferning tests. All cases were clinically managed according to gestational age-specific clinical algorithms.

The participants were informed about the study by the researchers before the start of the study. There was no compulsion to participate in the study. Participation took place on a voluntary basis.

The sensitivity, specificity, positive and negative predictive values were calculated by using the SPSS program.

Results

The relationship between the study and control groups in terms of mean age, gravida, parity, and gestational age at first admission was examined, and it was determined that there was no statistically significant difference ($p>0.05$),

The data obtained from our study showed that the PAMG-1 immunoassay has 85% sensitivity, 100% specificity, 100% PPD, and 87.5% NPD (Table 1).

For the nitrazine test, these values were calculated as 90.5% sensitivity, 92.5% specificity, 95.0% PPV and 90.9% NPV, respectively. For the Ferning test, it has 85.7% sensitivity, 100% specificity, 100% PPD, and 87.5% NPD (Table 1).

	Sensitivity (%)	Specificity (%)	PPD (%)	NPD (%)
PAMG-1	%85.0	%100	%100	%87.5
Nitrazine	%90.5	%92.5	%95.0	%90.9
Ferning	%85.7	%100	%100	%87.5

Table 1: *Sensitivity, specificity, PPD and NPD results of the tests*

The specificity and PPD of the PAMG-1 and Ferning tests were calculated as 100%. The results show that the ability of these two tests to find healthy individuals and all individuals detected as cases are indeed cases. In this area, it was determined that the Nitrazine test gave lower results compared to the other two tests.

When the sensitivity values were examined, it was determined that the results of the Nitrazine test were higher than the other two tests. Accordingly, the Nitrazine test is better than the PAMG-1 and Ferning tests in terms of its ability to detect cases.

The same is true when it comes to NPD. Nitrazine test results are higher compared to the other two tests. Almost all of the individuals identified as healthy by the nitrazine test are healthy. Nitrazine test detects healthy individuals more accurately than the other two tests.

Discussion

The extent to which a test measures the value it should measure is defined as the validity or accuracy of the test. Validity or accuracy is measured by sensitivity and specificity. The most memorable explanation of these terms is made with 2 X 2 tables (Table 2).

	GOLDEN STANDARD	
REVIEWED TEST	A-True Positive	B-False Positive
	C-False Negative	D-True Negative

Table 2: *Sensitivity and specificity of the test*

Sensitivity is the ability of a test to correctly classify a person as a case. Sensitivity can be expressed as Sensitivity = A (true positive) / A+C (true positive + false negative) [10].

The test's ability to correctly classify the individual as disease-free is the test's specificity. Specificity can be expressed as Specificity = D (true negative) / B+D (false positive + true negative) [10].

Sensitivity and specificity are opposite concepts. As sensitivity increases, specificity decreases, and vice versa.

PPD is the percentage of people who test positive and have the disease according to the gold test, that is, real patients. It shows to what extent the new test is able to detect cases, how many people who test positive are actually positive. The higher this number, the more reliable the test. PPD can be expressed as PPD = A (true positive) / A+B (true positive + false positive) [10].

NPD is the percentage of those who test negative and who are healthy according to the gold test, that is, true healthy people. It shows how many of the negatives according to the test are true negatives. The higher this number, the closer the test is to the gold standard. NPD can be expressed as NPD = D (true negative) / C+D (false negative + true negative) [10].

PPD and NPD correlate with the prevalence of the disease in the population. Assuming all variables are constant, PPV will increase with prevalence, while NPV will decrease. Sensitivity and specificity have different origins and different purposes than PPD and NPV. All four criteria must be considered important when examining or assessing the adequacy of a test. PPD and NPV are more important than sensitivity and specificity when it comes to screening tests. PPD and NPV values in screening tests should be determined in the light of careful clinical analysis [9, 10].

While calculating the sensitivity, specificity, PPD and NPD values of the tests examined in our study, the test considered as the gold standard was applied to all participants. 2 X 2 tables were created for each of the Nitrazine, Ferning and PAMG-1 tests and sensitivity, specificity, PPD and NPD calculations were made in these tables. When our results are examined, it is seen that the rule of "as the sensitivity increases, the specificity decreases, as the specificity increases, the sensitivity decreases", which is a rule in sensitivity and specificity examinations, is confirmed. Sensitivity is relatively low in Ferning and PAMG-1 tests, where the specificity is calculated as 100%. On the other hand, the sensitivity is higher in the Nitrazine test, where the specificity is calculated as 92.5%.

When the results of a study designed similar to our study were examined, the sensitivity and specificity of PAMG-1 were calculated as 97.33% and 98.67%, respectively. According to the data obtained, while the sensitivity values for the Ferning test were 84.0% and the specificity was 78.6%, these values were calculated as 86.6% and 81.3% for the Nitrazine test, respectively. PPD and NPD values of PAMG-1 were calculated as 98.6% and 97.3%, respectively. These values are 79.7% and 83.1% for Ferning test, 82.2% PPD and 85.9% NPD for Nitrazine test. Our results showed that there was no significant difference between the results of the PAMG-1 test, Ferning and Nitrazine. There is a significant difference between our research and this research in terms of the number of participants. The number of participants in the study is about three times higher than our study. It was considered that the difference in the results of the two studies stemmed from this point [11].

In another study [4], a total of 211 patients were examined. Sensitivity and specificity of PAMG-1 were calculated as 95.7% and 100%, respectively, and PPD and NPD values were calculated as 100% and 100%, respectively. Separate calculations were not made for each of the Ferning and Nitrazine tests, and only one result was given under the title of traditional tests. Accordingly, the sensitivity value is 78.1% and the specificity value is 100%, while the PPD is 100% and the NPV is 36.9%. It is noteworthy that the data obtained in this study are quite different from our study and similar studies. This may be due to the fact that the number of participants in the control group used in the study was quite low compared to the case group. Only 24 of the 211 participants were in the control group. It is possible that the large difference between the case-control numbers may affect the calculations and cause unexpected results [4].

A study was conducted to evaluate the cost-effectiveness of using PAMG-1 for the diagnosis of PROM [13]. The cost-effectiveness of the PAMG-1 test was designed from a third-party payer's perspective, a decision-analytic model was designed, the number of hospital transfers blocked was examined and compared with the Nitrazine and Ferning tests. It has been determined that the PAMG-1 test is a cost-effective test compared to the others. In our study, no data was obtained, since no analysis of cost-effectiveness was performed [13]. The limitation of our study is the small number of samples compared to some of the other studies. In addition, the strength of our study is that it was planned as a prospective case-control study. The reliability of the results obtained from such studies is high.

Conclusion

As a result, the results obtained from our study differed from those obtained from some other studies. It was considered that the difference was due to the number of participants or the difference in practice. It is possible to reach more accurate results with studies to be carried out on larger data sets.

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