Experimental
&
Clinical Article

Comparison of Triple and Qadrupple Test in Second Trimester Down Syndrome Screening

R. Sinan KARADENİZ, M. Metin ALTAY, Yetkin KARASU, Orhan GELİŞEN, Ali HABERAL

Ankara, Turkey

OBJECTIVE: To compare the Down syndrome detection ratio of triple test and qaudruple test in the second trimester of pregnancy.

STUDY DESIGN: 148 patients whose were admitted to our clinic in the second trimester of their pregnancy were included in this study. All the patients were screened for trisomy 21, trisomy 18 and neural tube defects (NTD) with both triple and quadruple tests. Each patient gave one blood sample and both triple and quadruple tests were studied within the same sample. Any sign of down syndrome, trisomy 18 and NTD was not detected by ultrasound examination. Treshold value for down syndrome is 1/300, for trisomy 18 is 1/300 and for NTD is 1/1000. Amniocentesis was performed to the patients with high test results for trisomy 21 and 18.

RESULTS: There were 6 patients (4.05%) in triple test and 5 patients (3.37%) in quadruple test with high risk results for Down syndrome. In three patient both triple and quadruple tests were reported as high risk. There were 12 patients (8.1%) in high risk group due to maternal age. These patiens were evaluated with amniocentesis and there were no difference between the triple test and quadruple test for detection rates of Down syndrome.

CONCLUSION: In our study we did not find statistical difference between the detection and false positive rates of triple and quadruple tests for trizomi 21 and trizomi 18.

Key Words: Down syndrome, Second pregnancy trimester, Alpha inhibin-92, Pregnancy tests, Pregnancy-Associated plasma protein-A

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Screening test are used to find out people who carries high risk for a known disease in a certain population. So screening test should be easy to perform, with high sensitivity and with low coast. Screening tests in pregnancy aim to find fetuses that have congenital anomalies and inform parents as soon as posibble. In whole world screening tests used in down syndrome are nuchal translucency (NT), double test (free-βhCG+PAPP-A), combined test (NT+free-βhCG+PAPP-A), triple test (AFP+hCG+uE3), quadruple test (AFP+hCG +uE3+inhibin), intagrated test (NT+PAPP-A+AFP+hCG +uE3+inhibin),and combine test (PAPP-A+AFP+hCG +uE3+ inhibin).[1]

Triple test in the second trimester is stil the most commonly used screening test. In down syndrome free βhCG levels rises but estriol and AFP levels are decrease.[2] But in trisomy 18 all these biochemical markers are decrease. Sensitivity and false positive rates of second trimester triple test for down syndrome are shown in table I

Tablo I: Different treshold values and detection rate % and false positive rates % for down syndrome

Treshold values	Detection rate %	False positive rate %
1/200	57	4.3
1/250	61	5.6
1/300	64	6.8
1/350	67	8.1
1/400	69	9.3

To increase the sensitivity of screening tests, other biochemical markers are combined. Most commonly used one is combining Inhibin-A with triple test. Blood level of inhibin-A in Down sendrome is decreased.[3] In quadruple test, detection rate for down syndrome with 5% false positivity is 76%. This is 69% for triple test,[4] (Table II).

The objective of our study was to compare the detection rates and false positive rates of triple and quadruple tests in second trimester of pregnancy.

Etlik Zübeyde Hanım Maternity and Women's Health Academic and Research Hospital, Ankara

Address of Correspondence: *Rahmi Sinan Karadeniz*
Çukurambar Mah. 44. Cad. 457. Sok.
4 / 1 Balgat Çukurambar
Ankara
sinankaradeniz@gmail.com

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Table II: Comparison of screening tests

	Second trimester (14-22 weeks)			First trimester (10-13 weeks)	First and second trimester
	Double test	Triple test	Quadruple test	Combined test	Integrated test
	Detection rate (%)				
False Positive Rate					
1%	35	46	54	72	85
3%	50	62	69	81	92
5%	59	69	76	85	94
7%	65	74	81	88	96
	False positive rate (%)				
Detection Rates					
60%	5,4	2,7	1,6	0,2	0,03
70%	9,4	5,2	3,2	0,8	0,12
80%	16,5	10,2	6,6	2,6	0,45
90%	30,5	21,5	15,2	9,9	2,10

Material and Method

The local Education Committee at Etlik Zübeyde Hanım Maternity And Women's Health Academic and Research Hospital approved the study protocol and informed patient consent was obtained. One hundred-forty-eight patients were included in the study. This study was planned as a prospective trial. None of the patients had a risk factor for a congenital anomaly and a known disease. Each patients were tested for down syndrome, trisomy 18 and NTD with both triple and quadrupple test in the second trimester of their pregnancy. Each patient gave a blood sample and both triple and quadruple tests were studied with the same sample. After that according to the treshold values amniocentesis was performed and results of the screening tests were compared. Before amniocentesis an ultrasound examination was performed for each patient. There were no risk factor for down syndrome, trisomy 18 or NTD in ultrasound examinations. Median of gestational age was 17.79±1.10 (16-20) weeks. MoM values for AFP, uE3, hCG were 1.05, 1.25, 1.13 reciprocally. Median value for inhibin-A was 0.96. Treshold value for down syndrome was 1/300, for trisomy 18 was 1/300 and for NTD was 1/1000. Results of the study was analysed with SPSS 10.0, chi square test.

Results

148 patients were included in the study. Median age was 26.74±5.12 (18-42). None of the patient had a risk factor for down syndrome and trisomy 18 except maternal age. Triple and quadruple test was performed to each patient in second trimester of her pregnancy. Treshold value for NTD was 1/1000. There were 13 patients (8.78%) who had increased risk for NTD. AFP, uE3, hCG and inhibin-A levels of of these 13 patients are shown in Table III.

Table III: AFP, uE3, hCG, and Inhibin-A levels of patients with high NTD risk

1	AFP (MoM)	uE3 (MoM)	hCG (MoM)	İnhibin-A
2	2.81	2.79	0.88	1.19
3	2.75	3.06	2.48	0.95
4	2.1	3.27	0.97	0.92
5	2.64	1.0	2.13	1.52
6	1.64	1.37	2.07	0.93
7	1.64	0.63	2.97	0.76
8	7.83	1.27	0.42	0.42
9	4.25	2.91	2.13	0.83
10	2.31	2.39	1.12	0.82
11	3.46	8.81	1.00	1.24
12	2.14	1.41	2.2	0.99
13	3.37	2.30	1.27	1.33
14	1.82	1.53	2.05	0.67

Triple and quadruple test results are compared for down syndrome. Results above 1/300 accepted as high risk. There were 6 (4.05%) patients in triple test and 5 (3.37%) patients in quadruple test with high risk (table IV-V).

Table IV: AFP, uE3, hCG levels of patients with high Down syndrome risk in triple test

	AFP (MoM)	uE3 (MoM)	hCG (MoM)
1	1.19	0.69	2.30
2	0.64	0.90	0.58
3	0.58	0.50	1.19
4	0.72	0.61	0.94
5	0.54	0.94	0.63
6	0.63	0.89	2.75

Tablo V: AFP, uE3, hCG, and inhibin-A levels of patients with high Down syndrome risk in quadruple test

AFP	(MoM)	uE3 (MoM)	hCG (MoM)	Inhibin-A
1	0.64	0.90	3.55	1.78
2	0.45	0.84	1.67	1.6
3	0.58	0.50	1.19	1.14
4	0.72	0.61	1.7	1.79
5	0.57	0.88	0.77	2.09

According to the maternal age there were 12 (8.10%) patients with high risk. The treshold value for trisomy 18 was 1/300. There were one (0.67%) patient with high risk test result in triple test (table VI).

Tablo VI: AFP, uE3 and hCG blood levels of the patient with high risk for trisomy 18 in triple test

	AFP (MoM)	uE3 (MoM)	hCG (MoM)
1	0.83	0.55	0.29

There were only 3 (2.02%) patients in both triple and quadruple tests with high risk results. There was 1 (8.3%) patient among advanced maternal age group

who had high risk in triple test. In the other hand there was no patient with high risk in quadruple test who had a high risk for maternal age. There were 2 patients above 35 years old with high risk for NTD. There was no patient who had high risk for Down syndrome either in triple test or in quadruple test with high risk for NTD. According to the amniocentesis results there was no abnormal karyotype.

Discussion

Biochemical screening tests for Down syndrome has been done from 1984 when Merkatz reported low AFP levels first in Down syndrome.[5] After that βhCG and unconjugated estriol had been in use. In complicated pregnancies βhCG level is high and unconjugated estriol level is low.[2] In trisomy 18 all these three markers are low. In 1992 Haddow reported a study of 25207 patients. In that study detection rate of triple test for Down syndrome reported as 60%. In another study of Cheng of 7718 patients the detection rate was 91%.[6] There are many studies with similar results. In literature accepted level is approximately 70%.[7] Detection rate of quadruple test is higher, appoximately 76%. In down syndrome Inhibin-A level is high. From 1984 different methods have been tried to increse sensitivity of screening tests for Down syndrome diagnosis. Ultrasonographic parameters are also in use. Nuchal translucency (NT) and nuchal bone measurement in first trimester are the most commonly used ones. Another parameter used in the first trimester is pregnancy associated plasma protein-A (PAPP-A). The level of PAPP-A is low in Down syndrome.[8]

Our patients are screened for Down syndrome with triple and quadruple tests. According to statistical analyisis of this study there was no difference between these tests. FASTER study which was run between 1999-2002 reported 69% detection rate for triple test and 81% detection rate for quadruple test. Major limitations of our study may be the small sample size and absence of any down syndrome case after amniocentesis. In our study the false positive rates of triple and quadruple tests were 4.05% and 3.37 reciprocally. There was not statistically significant difference between false positive rates. In our hospital there were 985 patients tested with amniocentesis. In 25 (2.53%) of these patients there were chromosomal anomaly. Nine of them was Down syndrome.

As a result according to the results of our study there is no statistical difference between triple and quadruple tests in Down syndrome screening but other studies with larger sample size are necessary.

İkinci Trimester Down Sendromu Taramasında Üçlü ve Dörtlü Testin Etkinliklerinin Karşılaştırılması

AMAÇ: Gebeliğin ikinci trimesterinde down sendromunun tespit edilme oranının triple test (üçlü test) ve quadruple test (dörtlü test) ile karşılaştırılması.

GEREÇ VE YÖNTEM: Kliniğimize gebeliklerinin ikinci trimesterinde başvuran 148 hasta bu çalışmaya dahil edildi. Tüm hastalar down sendromu, trizomi 18 ve nöral tüp defekti (NTD) açısından üçlü ve dörtlü testle tarandı. Tüm hastalar kan örneği verdi ve her iki tarama testi üçlü ve dörtlü test aynı kan örneğinde çalışıldı. Ultrasonografik incelemede olgularda trizomi 21, trizomi 18 ve nöral tüp defekti açısından risk faktörü yoktu. Sınır değerler, down sendromu için 1/300, trizomi 18 için 1/300 ve NTD için 1/1000 alındı. Trizomi 18 ve trizomi 21 için yüksek test sonucu olan hastalara amniosentez uygulandı.

BULGULAR: Üçlü test ve dörtlü testle değerlendirilen 148 hastanın üçlü testte 6 (%4.05), dörtlü testte 5 (%3,37) tanesinde trizomi 21 riski yüksek bulundu. Üçlü ve dörtlü test ile değerlendirilen hastaların sadece 3 tanesinde her iki testte de risk yüksek olarak rapor edildi. Anne yaşına göre yüksek riskli olarak değerlendirilen hasta sayısı 12 (%8.1) idi. Amniosentez sonuçları ile değerlendirilen hastalarda down sendromu açısından üçlü ve dörtlü testin etkinlikleri ve yanlış pozitiflikleri arasında fark saptanmadı.

SONUÇ: Bizim çalışmamıza göre üçlü ve dörtlü testin trizomi 21 ve trizomi 18 için tarama etkinlikleri ve yanlış pozitiflik oranları arasında istatistiksel fark bulunamamıştır.

Anahtar Kelimeler: Down sendromu, İkinci trimester gebelik, Alfa inhibin, Gebelik testleri, Gebelikle ilişkili, protein-A

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