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Analysis Of Seven-Year Second Trimester Genetic Amniocentesis Results Of Our Clinic

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Abstract

Objective: To evaluate the second trimester amniocentesis procedures in last seven years performed in our clinic.

Methods: Indications of 594 amniocentesis procedures are high risk in triple test (38%), advanced maternal age (24.9%), high risk in first trimester screening test (14.8%), advanced maternal age together with high risk in triple test (10.9%), major anomaly (3.7%), minor anomaly (3%), previous fetus with Down syndrome (2%), history of trisomy in the family (0.5%), maternal anxiety (2.2%). There were trisomy 21 in 18 patients, trisomy 13 in two patients, trisomy 18 in two patients, other aneuploidies in 12 patients. The frequency of major chromosomal anomalies was 3.7%. This resulted in an abortion rate of 1.18% in the first two weeks following the procedure. Additionally, there occurred four other fetal deaths in the coming next two weeks. Totally, the fetal loss rate follow-ing the second-trimester amniocentesis in the first four weeks was calculated to be 1.9%. To obtain one chromosome anomaly, the least number of amniocentesis was performed by the indication of high risk in first trimester test .

Results: Indications of amniocentesis, karyotype anomalies, fetal loss ratios between the years of 2001-2008 have been reviewed retrospectively.

Conclusion: In last seven years , amniocentesis was performed mostly by the indication of high risk in triple test. The frequency of major chromosomal anomalies and fetal loss rate was compatible with the litreture. To obtain one chromosome anomaly, the least number of amniocentesis was performed by the indication of high risk in first trimester test . As first trimester screening test is more commonly used, the number of procedures to obtain one chromosome anomaly will decrease.

Keywords: Amniocentesis, chromosomal anomaly, fetal loss.

Yedi yıllık ikinci trimester genetik amniyosentez sonuçlarımız

Amaç: Kliniğimizde son yedi yılda yapılan ikinci trimester amniyosentez işlemlerini değerlendirmek.

Yöntem: 2001-2008 yılları arasında yapılan amniyosentez işlemlerinin endikasyonları, saptanan karyotip anomalileri, karyotip anomalisi saptanan olguların özellikleri, ve işleme bağlı fetal kayıp oranları retrospektif olarak değerlendirildi.

Bulgular: 594 amniyosentez işleminin endikasyonları, üçlü testte yüksek risk (%38), ileri anne yaşı (%24,9), birinci trimester taramada yüksek risk (%14,8), ileri anne yaşı ve üçlü testte yüksek risk (%10,9), major anomali (%3,7), minor anomali (%3), Down sendromlu bebek doğurma öyküsü (%2), ailede trizomi öyküsü (%0,5), maternal anksiyete (%2,2) idi. Toplam 18 hastada trizomi 21, iki hastada trizomi 13, iki hastada trizomi 18, 12 hastada diğer anöploidiler tespit edilmiş olup, major kromozom anomalisi sıklığı %3,7 olarak tespit edildi. İşlemi takip eden 15 gün içinde, toplam abortus oranı %1,18 olarak hesaplandı. Ayrıca işlemi takip eden bir ila dört hafta içinde dört olguda in utero fetal ölüm saptandı. İşlemi takip eden bir ila dört hafta içinde toplam fetal kayıp oranı % 1,9 olarak bulundu. Bir anomali saptamak için en az işlemin ikili testte yüksek risk grubunda yapıldığı saptandı.

Sonuç: Amniosentez işlemi, son yedi yılda kliniğimizde en sık üçlü testte yüksek risk endikasyonu ile yapılmış olup, major kromozom anomali sıklığı ve fetal kayıp oranı literatürle uyumlu bulunmuştur. Bir anomali saptamak için en az işlemin birinci trimester tarama testinde yüksek risk grubunda olması nedeniyle, birinci trimester tarama testinin yaygınlaşması ile kromozom anomalisi saptayabilmek için yapılan işlem sayısı azalacaktır.

Anahtar Sözcükler: Amniyosentez, kromozom anomalisi, fetal kayıp

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Introduction

First amniocentesis had been performed in 1881 for the treatment of polyhydramnios. Steele and Breg defined cell culture and chromosome analysis in 1966, after that amniocentesis performed for prenatal diagnosis.[1,2]

As prenatal diagnostic procedures progress, the diagnosis of numeric and structural chromosomal anomalies, single gene disorders, hemoglobinopathies, enzyme deficiencies, congenital infections become possible. Chromosomal anomalies are responsible for 50% of early pregnancy loss, 6-11% of all fetal death and neonatal death.[3,4] Invasive antenatal procedures are performed more common due to widespread use of biochemical screening tests and development of ultrasonographic technology. Whereupon, amniocentesis is the most common invasive prenatal diagnostic procedure.[5] The aim of this retrospective study is to evaluate the second trimester amniocentesis procedures performed in last seven years of our clinic.

Methods

732 amniocentesis procedures were performed between the years of 2001-2008 with the indications of high risk in first trimester screening test and triple test (>1/300), advanced maternal age (>35), advanced maternal age together with high risk in triple test, major anomaly, minor anomaly (hyperechogenic bowel, echogenic intracardiac focus, single umblical artery, coroid plexus cyst, pyelectasis), previous fetus with Down syndrome, history of trisomy in the family, maternal anxiety.

Informed consent were signed by the patient and her husband. Fetal heart activity and biometry was evaluated before the procedure and the procedure was performed between 16-20 gestational weeks. All procedures were performed by 20 Gauge spinal needle, from a point as far as possible from placenta and fetal face and body via abdominal route with the aid of Logiq 200 Pro Series ultrasonography. First 1-2 ml of amniotic fluid was discarded and 1 ml sample for each gestational week was taken. Cytogenetic analysis of amniotic fluid was performed by a special genetic laboratory via Giemsa band technique. Mean duration for cell culture was 14-20 days. After amniocentesis, the patients were followed in perinatology clinic. 594 patients with full records and followed up to delivery were included to the study. The indications of amniocentesis, results of the chromosome analysis, complications of procedure and results of the pregnancy were studied.

Results

732 amniocentesis procedures were performed in our clinic in last seven years. 138 patients with incomplete records were excluded from the study. 594 patients were studied retrospectively. When we look at demographic characteristics of the patients, the mean age was found to be 32.2 (17-47).

The most common indication was high risk in triple test (%38, n=226). Other indications were advanced maternal age (% 24.9, n=147), high risk in first trimester screening test (%14.8, n=88), advanced maternal age together with high risk in triple test (%10.9, n=65), major anomaly (%3.7, n=22), minor anomaly (%3, n=18), previous fetus with Down syndrome (%2, n=12), history of trisomy in the family (%0.5, n=3), family anxiety (%2.2, n=13) (Table 1).

We obtained Trisomy 21 in 18 patients, trisomy 13 in two patients, trisomy 18 in two patients, other aneuploidies in 12 patients and the frequency of major chromosome anomaly was calculated as %3.7 (Table 2).

When we evaluate the rate of chromosomal anomaly according to the indications high risk in first trimester screening test was in the first term (5.6%), advanced maternal age together with high risk in triple test was in the second term (4.6%), high risk in triple test was in the third term (3.5%). When the indication was only advanced maternal age, chromosomal anomaly was obtained 2.7% of the cases.

There were no amnion cell culture failure reported.

We suggested termination to 25 patients with major aneuploidies, all preferred termination despite one (Table 3). Complications that occurred in 15 days after the procedure were spontaneous abortion in four patients, amniorexis in three patients and total rate of abortion was 1.18%. Furthermore, intrauterine fetal death occurred one to four weeks after the procedure in four patients, after four weeks in three patients. Total fetal loss ratio that occurred one to four weeks after the procedure was 1.9%. Twenty patients (3.5%) delivered between 30-34 weeks.

Number of procedures to obtain one anomaly is calculated according to the indications. The least number of procedures to obtain one anomaly is in high risk in first trimester screening test group and the most number of procedures is in advanced maternal age group (Table 2).

Discussion

There has been no significant decrease in the number of invasive procedures performed for prenatal diagnosis although developments in ultrasonographic technology and variability in serum biochemical screening tests. Due to widespread use of rapid genetic assessment methods like polimerase chain reaction (PCR) and flouresance insitu hybridization (FISH), invasive procedures like amniocentesis are more frequently performed. Advanced maternal age, high risk in first trimester screening test and triple test, fetal anomaly, parental reciprocal translocation, habituel abortion and history of previous fetus with chromosomal anomaly are classical indications for amniocentesis.[6]

Table 1. The distribution of indications for amniocentesis.

Indication	%	n
High risk in triple test	38	226
Advanced maternal age	24,7	147
First-trimester screening high-risk	14,8	88
Advanced maternal age + High risk in triple test	10,9	65
Major anomaly	3,7	22
Minor anomaly	3	18
History of trisomy	2	12
A family history of trisomy	2	12
Maternal anxiety	2,2	13
Total	100	594

Table 2. Amniocentesis is the distribution of businesses detected karyotype anomalies

Indication	n (%)	Normal	Trizomi 21	Trizomi 18	Trizomi 13	Other Aneuploidy	Aneuploidy, the number of transactions required to determine
Advanced maternal age	147 (24,7)	140	3	-	1	3	37
Advanced maternal age+ High risk in triple test	65 (10,9)	61	3	-	-	1	21
High risk in triple test	226 (38)	215	7	-	-	4	32
First-trimester screening high-risk	88 (14,8)	82	4	1	-	1	17

Table 3. The results of amniocentesis karyotype anomaly.

Karyotype	Age	Indication	Ultrasound findings	Week on	Prognoz
46, XX, 15p	39	Advanced maternal age	No	37	normal phenotype
46, XY, inv (9) (p1q1)	43	Advanced maternal age + Triple test-High risk	No	39	normal phenotype
46, XX, inv dup (9)	25	Triple test-High risk	No	39	Normal phenotype (mother carrier)
46, XY, t (1;3) dengeli	42	Advanced maternal age	No	39	Normal phenotype (father carrier)
46, --, t (3;12) (q12;p13)	27	Major anomaly	Dandy-Walker malformasyon	-	Ended
46,--,t (2;7) (p11.1;q22.1)	28	Binary test-high risk	No	38	normal phenotype
46,--,t (11;12) (p11;q11)	34	Triple test-High risk	No	38	normal phenotype
46,--, 1qh+,1qh+	30	Triple test-High risk	No	39	normal phenotype
45,--,der(18)(21qter-21q11:18p11.1-18qter)	26	Triple test-High risk	Increased nuchal pilisi	39	normal phenotype
47,--,idic(15;15) (q12;p12)	41	Advanced maternal age + Triple test-High risk	No	39	normal phenotype
69,--	26	Triple test-High risk	Symmetrical IUGR + syndactyly	-	Ended
47, XX+9	32	Major anomaly	Dandy-Walker malformation + micrognathia + VSD + double-outlet right ventricle +symmetrical IUGR	-	Ended
47, XX+13	40	Major anomaly	omphalocele	-	Ended
47, XX+13	25	Major anomaly	Dandy-Walker malf + hyperechoic bowel + Polydactyly	-	Ended
47,--,+18	30	Major anomaly	Omfolosel + bilateral. Choroid plexus cyst + single umbilical artery + hyperechoic bowel	-	Ended
47,--,+18	33	Binary test-high risk	Early symmetrical IUGR	-	Ended
47, XX+21	35,43	Advanced maternal age	No	-	Ended
47, XX+21	22	Binary test-high risk	duodenal atresia	-	Ended
47, XX+21	36	Binary test-high risk	No	-	Ended
47, XX+21	36	Binary test-high risk	Large cisterna magna + thickened nuchal pilisi + hypertelorism + hyperechoic focus cardiogenic	-	Ended
47, XX+21	41	Advanced maternal age + Triple test-High risk	Nonimmun hydrops fetalis	-	Ended
47, XY+21	37,40	Advanced maternal age + Triple test-High risk	No	-	Ended
47, XX+21	19,23, 29,29	Triple test-High risk	No	-	Ended
47, XY+21	38	Binary test-high risk	Thickened nuchal pilisi + VSD	-	Ended
47, XY+21	23	Minor anomaly	bilateral pyelectasis	-	Ended
47, XX+21	24,28	Triple test-High risk	hyperechoic bowel	-	Ended
47, XX+21	38	Advanced maternal age	hyperechoic bowel	-	Ended
47, XY+21	23	Triple test-High risk	No	-	Did not accept termination

In this study as we look at the indications for amniocentesis, high risk in triple test is in the first term and advanced maternal age is in the second term. Other indications are as follows high risk in first trimester screening test, advanced maternal age together with high risk in triple test, pathological findings in ultrasonography. Since we did not have the facilites of genetic laboratory for karyotype analysis from chorion villus sampling (CVS), our patients mainly preferred amniocentesis as the invasive test of choice. In the literature there are different ratios by years in the studies that evaluate indications of amniocentesis. Especially, in previous years the most common indication was advanced maternal age. In one study the most common indication is advanced maternal age (%86.3).[7] In the study of Şener et al. the most common indication is high risk in triple test the same as our study.[8]

When we evaluate amniocentesis results numerical chromosomal anomalies were obtained in 3.9% of cases, minor structural chromosomal anomalies were obtained in 1.9% of cases. According to the literature the rate of catching chromosomal anomaly by amniocentesis is between 2.3%- 4.5%. For example, this ratio is found to be 2.3% by Şener et. al, 3.6% by Yayla et. al., 3.5% by Başaran et. al., 4.5% by Cengizoğlu et. al.[8-11]

The ratio of catching chromosomal anomaly of our clinic is similar to that of various clinics in Turkey.

Although widespreadly used in practice, advanced maternal age as an indication of invasive prenatal diagnostic test is contraversial. Although once used widespread, the use of advanced maternal age as an indication for invasive test has been controversial. With the extended use of first trimester Down syndrome screening during the last 10 years, advanced maternal age is no more accepted as an indication for amniocentesis. However,in this study, advanced maternal age was the second most common indication of amniocentesis. The main reasons for this were women with advanced age who could not make use of Down syndrome screening tests, maternal anxiety due to age factor and referral of advanced age pregnant women due to unawareness of the clinicians about the knowledge of exclusion of these women for amniocentesis. We caught chromosomal anomaly in 2.7% of 147 cases with maternal age more than 35 which is found to be 3% by Cruikshank et. al, 3.7% by Hassold et al. Sjögren et al. found that ratio as 2.2% when maternal age was more than 35 and 5.3% when maternal age was more than 40.[12-14] In the literature of our country, chromosomal anomaly ratio was found to be 4% by Yayla et al., 6.1% by Cengizoğlu et al., 13.3% by Bal et al. among similar cases.[9,11,15] In the study of Dommerguez et al. it is reported that amniocentesis should not be suggested as a routine procedure in advanced maternal age (>38) but as a result of noninvasive screening tests selectively.[16] In their study, no woman in 359 patients between the ages of 38-47 delivered baby with chromosomal anomaly when nuchal translucency in first trimester was less than 3 mm and second trimester ultrasonography was normal although down synrome risk in triple test was less than 1/250. Thus first trimester screening test, triple/quater screening tests and detailed ultrasonography in second trimester have higher rates of catching anomaly it seems to be logical to avoid invasive tests performed only by advanced maternal age.

In this study when we analyse the number of procedures to obtain one chromosomal anomaly, the least number of procedures performed

with the indication of high risk in first trimester screening (17 procedures) and the most number of procedures performed by the indication of only advanced maternal age (37 procedures). In the study of Güven et al. no karyotype anomaly was obtained in 49 amniocentesis procedures although Kutlu Dilek et al. obtained five karyotype anomaly in 341 procedures performed by the indication of only advanced maternal age.[17,18] In our series, 27 procedures performed to obtain one chromosomal anomaly in terms of all indications. When it is compared with the literature, this number was reported as 25 by Önderoğlu et al., 63 by Bal et al., 49 by Kutlu Dilek et al.[19,15,18]

The most important complication of amniocentesis is fetal loss. The definition of fetal loss related to the procedure and complications in which period can be included to this definion is contraversial in the literature. When we analyse spontaneous abortion and fetal death rates together, total fetal loss rate was calculated as 1.9% in one month after the procedure. In the literature, the risk of fetal loss related to the procedure is reported between 0.2-2.1% in broad series.[5] The fetal loss rate in our series is compatible with the literature.

Conclusion

Consequently, amniocentesis was performed mostly by the indication of high risk in triple test in last seven years of our clinic. The frequency of major chromosomal anomalies and fetal loss rate was compatible with the litreture. Thus, the least number of procedures performed in the group of high risk in first trimester screening test, as first trimester screening test is more commonly used, the number of procedures to obtain one chromosome anomaly will decrease.

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