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Evolution of the indications for genetic amniocentesis after the introduction of the Prenatal Screening Program by the National Health Insurance in Poland

Zmiana wskazań do amniopunkcji genetycznej po wprowadzeniu Programu badań prenatalnych przez Narodowy Fundusz Zdrowia w Polsce

Katarzyna Ciach, Małgorzata Świątkowska-Freund, Krzysztof Preis

Department of Obstetrics, Medical University of Gdansk, Poland

Abstract

Objective: *In 2008, the Prenatal Screening Program was introduced by the National Health Insurance in the Pomeranian region of Poland. As of then, biochemical and ultrasound screening was offered to women eligible for amniocentesis according to the earlier policy. The aim of the study was to investigate the evolution of the indications for amniocentesis after the introduction of the Program.*

Material and Methods: *In total, 2579 women referred for amniocentesis to the Department of Obstetrics, Medical University of Gdansk, were included in the study. They were divided into two groups: 1705 women referred between 1996 and 2007 (group A) and 874 women referred between 2008 and 2010 (group B). Indications for amniocentesis were compared between the groups.*

Results: *A significant difference in the indications for amniocentesis was found between the groups (Kruskal-Wallis test; $p<0.001$). Maternal age, fetal malformation in the previous pregnancy, and anxiety were less frequent in group B ($p<0.0001$, $p=0.0008$ and $p=0.0156$, respectively). In contrast, a higher frequency of positive biochemical screening and abnormal ultrasound results as indications for amniocentesis was found in group B ($p<0.0001$ and $p=0.0008$, respectively).*

Conclusions: *The introduction of the Prenatal Screening Program by the National Health Insurance shifted the proportion of indications for amniocentesis from maternal age to positive results in biochemical and ultrasound screenings, and increased the number of invasive testing. Further observation of the trend and its influence on the detection rate is imperative to confirm that the proposed Program is adequate and does not require adjustments.*

Key words: **amniocentesis** / **indication** / **maternal age** / **biochemical screening** / / **ultrasound screening** / **foetal malformation** / **chromosomal abnormality** /

Corresponding address:
Katarzyna Ciach
Department of Obstetrics, Medical University of Gdansk
Poland, 80-402 Gdansk, Kliniczna 1a
fax: +48 58 349 3416, ph.:+48 502 115 942
e-mail: kciach@wp.pl

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Streszczenie

Cel: *W 2008 roku Narodowy Fundusz Zdrowia wprowadził Program badań prenatalnych w województwie pomorskim. Od tego momentu badanie biochemiczne i przesiewowe USG genetyczne oferowane było kobietom kwalifikującym się do amniopunkcji według wcześniejszych wskazań. Celem niniejszej pracy było zbadanie ewolucji wskazań do amniopunkcji po wprowadzeniu Programu.*

Materiały i metody: *Materiał kliniczny obejmował 2579 ciężarnych, u których w latach 1996-2010 wykonano amniopunkcję genetyczną w Klinice Położnictwa GUMed. Pacjentki zostały podzielone na 2 grupy: grupa A - 1705 ciężarnych, u których wykonano amniopunkcję w latach 1996-2007, grupa B - 874 ciężarnych, u których wykonano amniopunkcję w latach 2008-2010. Dokonano porównania wskazań do amniopunkcji w obu grupach.*

Wyniki: *Statystycznie znamienne różnice stwierdzono porównując obie grupy (Kruskal-Wallis test; p<0,001). Wiek matki, wady płodu w poprzedniej ciąży, lęk, występowały statystycznie znamiennie rzadziej w grupie B (p<0,0001, p=0,0008 oraz p=0,0156). Nieprawidłowy wynik USG oraz badania biochemicznego był znacząco częstszym wskazaniem do amniopunkcji w grupie B (p<0,0001, p=0,0008).*

Wnioski: *Wprowadzenie Programu badań prenatalnych przez NFZ zmieniło wcześniejsze proporcje wskazań do amniopunkcji ze względu na wiek matki na rzecz nieprawidłowego wyniku testu biochemicznego i USG genetycznego. Dalsza obserwacja tego trendu i jego wpływu na wykrywalność nieprawidłowości jest niezbędna w celu potwierdzenia, że proponowany program jest odpowiedni i nie wymaga zmian.*

Słowa kluczowe: **amniopunkcja** / **wskazania** / **wiek matki** / **skrining biochemiczny** / / **skrining ultrasonograficzny** / **wady płodu** / **aberracje chromosomowe** /

Introduction

In 2007, the Polish National Health Insurance issued new guidelines for prenatal screening. The Pomeranian region was the first one to introduce the guidelines in every-day practice in 2008. On the basis of the National Health Insurance president's directives, general and detailed objectives of the Prenatal Screening Program were prepared. The main purpose of the Program was described as the early identification of the risk of fetal abnormalities via biochemical screening, the early diagnosis of fetal malformations with ultrasound examination, and the increase of the availability of prenatal screening in Poland.

Other aims included the development of a prenatal screening system in Poland, the preparation of an algorithm for non-invasive and invasive prenatal diagnosis, the improvement of prophylaxis in families with a high risk of genetic disorders through molecular diagnosis and genetic counselling.

To be included in the Prenatal Screening Program, the pregnant woman had to meet at least one of criteria listed below:

1. a maternal age of 35 years or more;
2. a chromosomal abnormality in a previous foetus or child;
3. a known structural chromosomal abnormality in the pregnant mother or the father of the baby;
4. a significantly high risk of giving birth to a child with genetic disease conditioned by one known gene or with disease with multifactorial conditioning;
5. a foetal malformation found at the ultrasound examination or a high risk of chromosomal abnormality according to the biochemical screening [1].

Before the introduction of the Prenatal Screening Program, invasive diagnostic procedures were offered to the patients with the aforementioned indications. A very low availability of biochemical and ultrasound screening implied that very few patients referred for amniocentesis, chorionic villus sampling, or foetal blood sampling as a result of an abnormal result in the screening. The majority of women undergoing invasive procedures were referred due to maternal age. The National Health Insurance hoped that a group of patients over 35 years of age with low risk of fetal chromosomal abnormality in the biochemical screening would not ask for an invasive diagnosis and on the other hand, that a group of young women with a high risk will undergo amniocentesis.

The result of these changes should thus increase the detection of chromosomal abnormalities without increasing number of invasive procedures. That effect was observed in Spain, where maternal age is no longer an indication for invasive testing [2]. Tabor even reported a decrease of the number of invasive procedures after the introduction of screening tests [3].

Amniocentesis is one of the most popular and safe methods of invasive prenatal diagnosis offered for pregnant women over 40 years of age [4]. In Poland, it is the method of choice at most of the centres offering prenatal diagnosis, including the Medical University of Gdansk. Chorionic villus sampling is still offered very rarely, and only in chosen cases, and fetal blood sampling is only performed in patients presenting for prenatal diagnosis after 20 weeks of gestation [6].

Aim of the study

The aim of study was to investigate the evolution of the indications for amniocentesis after introduction of the Prenatal Screening Program in 2008.

Material and methods

From 1996 to 2010, 2579 women were referred for amniocentesis to the Medical University of Gdansk. Every woman referred for amniocentesis was first counselled by a geneticist and signed an informed consent. An ultrasound examination was performed before every procedure. Biparietal diameter, femur length, abdomen circumference, the localization of the foetus

and placenta, as well as the amniotic fluid volume were assessed. Amniocentesis was performed using the Yale Spinal 22 Gauge needle under ultrasound guidance. The volume of withdrawn amniotic fluid in ml was equal to the gestational age in weeks, as Hanson proposed. In the case of an ineffective first attempt to obtain amniotic fluid, the second one, with the use of a new needle, was performed. If the second amniocentesis failed and no amniotic fluid was obtained, the patient was scheduled for a repetition of the procedure in a week's time.

After every amniocentesis, the fetal heart rate was confirmed, and bleeding to the amniotic cavity was excluded. In Rh negative women with negative Rh antibodies, 300 μg of human anti-RhD immunoglobulin was administered intramuscularly.

In all cases regardless of the indication for amniocentesis, the patient's age and the gestational age were recorded. If there were two indications, the one suggesting a greater risk of chromosomal aberration was chosen (for example, if the patient was 36 years old, and biochemical screening gave a risk of 1:20, the biochemical screening was recorded as an indication for amniocentesis).

Patients were divided into two groups. Group A consisted of 1705 women who underwent amniocentesis before the introduction of Prenatal Screening Program (1996 to 2007, approximately 142 per year). The patients referred from 2008 to 2010 (874 women, approximately 291 per year), after the introduction of the Program, constituted group B.

The data was recorded in Microsoft Excel 2010 calculation sheet. Statistical software PASW Statistics 18 was used for analysis. Kruskal-Wallis test was used to compare variables and χ^2 test to compare frequencies. The significance level was 0.05.

Results

The median age of the patients was 37 years, and ranged from 15 to 50. 1851 women (71.77%) were older than 34 years of age. Amniocentesis was performed between 10 and 20 weeks of gestation as calculated according to the last menstrual period with a median 14 weeks, and between 12 and 22 weeks with a median 15 weeks according to ultrasound measurements (BPD or CRL).

In the analysed group the most frequent indication for amniocentesis was advanced maternal age – it was the reason of testing in 1729 of the women (67.04%). Less frequent were a high risk of chromosomal abnormality in biochemical screening, a chromosomal abnormality in a previous pregnancy, a foetal abnormality diagnosed in the ultrasound screening, a foetal malformation in a previous pregnancy, a known chromosomal translocation or genetic disorders in family, and anxiety or other not previously mentioned reasons. The data is presented in table 1.

Group A and B were compared next. The patients in the group from 2008-2010 were younger than those from 1996-2007 – the median age was 37 years (17 to 50) in group A and 36 (15 to 46) in group B (Kruskal-Wallis test; $p<0.001$). In group A, 1264 women were 35 years old or more (74.1%) and in group B – 587 women (67.2%), a difference which proved to be statistically significant (χ^2 test; $p<0.001$).

The gestational age at the time of the amniocentesis as calculated by the last menstrual period was lower in group A – the median in group A was 14 (11 to 20) weeks whereas in group B it was 15 (10 to 20) weeks (Kruskal-Wallis test; $p=0.001$).

A detailed analysis of the distribution of the indications for amniocentesis in group A and B was performed. It revealed a significant difference between the groups (Kruskal-Wallis test; $p<0.001$). The frequency calculated for every indication separately for both groups is presented in Table I and Figure 1.

Discussion

A steady increase of prenatal screening and diagnosis demand has been observed for many years. It is caused by the increasing maternal age and awareness of the possibility of giving birth to an anomalous child. Due to the changes of social priorities and lifestyle, more women decide to give birth to their children in their fourth and fifth decades of life, very often as their first pregnancy [5-7]. The proportion of Polish women over 35 at the time of delivery increased by 50% between 1990 and 2000 – from 8.8% to 13.5% [8].

The realization of a greater risk of chromosomal abnormality in advanced maternal age induces questions about the possible

Table I. Indications for amniocentesis in 1996-2007 (group A) and 2008-2010 (group B).

Indication for amniocentesis	All patients N (%)	Group A n (%)	Group B n (%)	χ^2 test p-value
1. Maternal age 35 years or more	1729 (67.04)	1217 (71.38)	513 (58.70)	**<0.0001**
2. Abnormal result of biochemical screening	459 (17.80)	216 (12.67)	243 (27.80)	**<0.0001**
3. Chromosomal abnormality in previous pregnancy	127 (4.92)	94 (5.51)	33 (3.78)	0.0536
4. Fetal abnormality diagnosed in ultrasound screening	106 (4.11)	54 (3.17)	52 (5.95)	**0.0008**
5. Anxiety and other indications	69 (2.68)	55 (3.23)	14 (1.60)	**0.0156**
6. Fetal malformation in previous pregnancy	55 (2.13)	48 (2.82)	7 (0.80)	**0.0008**
7. Genetic disease or chromosomal abnormality in family	33 (1.28)	21 (1.23)	12 (1.37)	0.7624
Total	2579 (100)	1705 (100)	874 (100)	

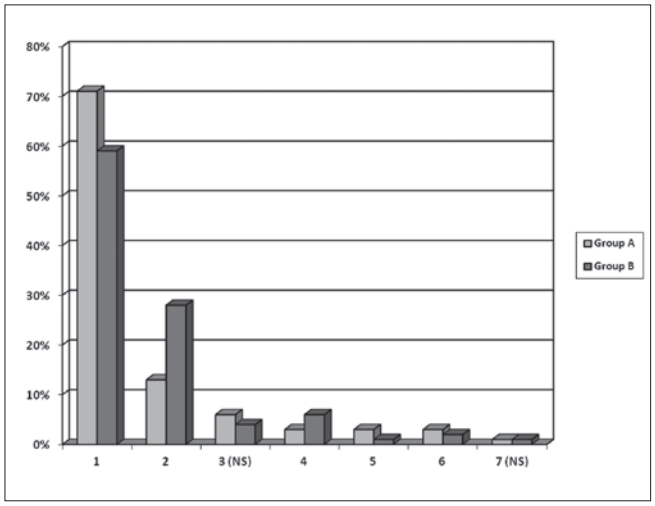

Figure 1. Indications (1-7) for amniocentesis in 1996-2007 (group A) and 2008-2010 (group B).

methods of prenatal diagnosis and trends aimed at improving the proportions of the sensitivity and the risk of complications of the offered procedures. Non-invasive biochemical screening defining the risk of chromosomal abnormality is described by many authors as a way to exclude invasive testing in "older" women with a low risk, and offering it to "younger" ones with a high risk. It is proven to increase the detection rate while maintaining a similar rate of invasive procedures [2, 3, 9].

In the eighties, prenatal invasive diagnosis was mainly offered to patients over 35 years of age. In many reports this regularity is still present [10, 11].

However, the majority of recent publications report a higher incidence of invasive testing due to abnormal ultrasound examination results or a high risk according to biochemical screening [2].

Until the introduction of the Prenatal Screening Program by the National Health Insurance the availability of prenatal screening in Poland was far from ideal. There was no possibility of performing that kind of test without paying for it, and many of the women could not afford it. Even patients who were able to pay for it did not trust a method which was not endorsed by the National Health Insurance. Paradoxically, every pregnant woman over 35 years of age was eligible for amniocentesis according to the National Health Insurance policy. Introducing a Prenatal Screening Program was meant to decrease the proportion of women over 35 years old undergoing an invasive procedure and increase the number of procedures performed due to positive biochemical and ultrasound screening.

The results of our analysis on the indication for amniocentesis revealed that the Program's objective has been fulfilled. The proportion of patients undergoing invasive testing due to maternal age has decreased from 71% to 59%. The increased availability of biochemical and ultrasound screening, and the growing confidence in their results, increased the frequency of amniocentesis due to abnormal results of these tests, from 13% to 28% for biochemical screening and from 3% to 6% for ultrasound examination. The results are similar to those reported by other authors [2, 3, 9-11]

Another trend was also observed in the analysed groups. The improvement in ultrasound detection of foetal malformations and the possibility to assess the risk of chromosomal abnormality via biochemical screening reduced the proportion of women requesting invasive testing due to foetal malformation in a previous pregnancy and anxiety of giving birth to an anomalous child. A low risk of chromosomal abnormality according to biochemical screening and the possibility of excluding foetal malformations by an ultrasound examination have become reliable for pregnant women, and has allowed those who do not require more invasive diagnostic testing to avoid running the risk of pregnancy loss after amniocentesis. There are no reports addressing these indications for invasive testing in the present literature.

An increasing number of invasive procedures observed over the years was also noted in the analysis of our study group. It is consistent with the trends presented by Nicolaides et al. and is caused by the growing anxiety of giving birth to an anomalous child and a decreased risk of pregnancy loss associated with amniocentesis due to a growing experience in invasive procedures [6].

Conclusion

The introduction of the Prenatal Screening Program by the National Health Insurance shifted the proportion of indications for amniocentesis from maternal age to positive results of biochemical and ultrasound screenings, and increased the number of invasive procedures performed. A further observation of the trend and its influence on the detection rate is imperative to confirm that the proposed Program is adequate and does not require modifications.

References

1. http://www.nfz-gdansk.pl/swiadczeniodawcy/konkursy/2007/materialy/2006_z53/z53_20060825_z5.pdf
2. Mademont-Soler I, Morales C, Clusellas N, [et al.]. Group of Cytogenetics from Hospital Clínic de Barcelona. Prenatal cytogenetic diagnosis in Spain: analysis and evaluation of the results obtained from amniotic fluid samples during the last decade. *Eur J Obstet Gynecol Reprod Biol.* 2011, 157, 156-160.
3. Tabor A, Alfirevic Z Update on procedure-related risks for prenatal diagnosis techniques. *Fetal Diagn Ther.* 2010, 27, 1-7.
4. Kowalczyk D, Wiecek J, Guzikowski W, Ośko A. Analysis of the course of pregnancy and labor after genetic amniocenthesis in women after 35 years of age. *Ginekol Pol.* 2011, 82, 738-742.
5. Baird P, Sadovnick A, Yee I. Maternal age and birth defects: a population study. *Lancet.* 1991, 337, 527-530.
6. Nicolaides K. Screening for chromosomal defects. *Ultrasound Obstet Gynecol.* 2003, 21, 313-321.
7. Callaway L, Lust K, McIntyre H. Pregnancy outcomes in women of very advanced maternal age. *Aust N Z J Obstet Gynaecol.* 2005, 45, 12-16.
8. Paszkowski T, Woźniakowska E. Progesteron w profilaktyce porodu przedwczesnego. *Ginekol po Dypl.* 2005,7, 33-38.
9. Nicolaides K, Chervenak F, McCullough L, [et al.]. Evidence-based obstetric ethics and informed decision-making by pregnant women about invasive diagnosis after first-trimester assessment of risk for trisomy 21. *Am J Obstet Gynecol.* 2005, 193, 322–326.
10. Karaoguz M, Bal F, Yakut T, [et al.]. Cytogenetic results of amniocentesis materials: incidence of abnormal karyotypes in the Turkish collaborative study. *Genet Couns.* 2006, 17, 219-230.
11. Tseng J, Chou M, Lo F, [et al.]. Detection of chromosome aberrations in the second trimester using genetic amniocentesis: experience during 1995-2004. *Taiwan J Obstet Gynecol.* 2006, 45, 39-41.