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Chromosomal aberrations in spontaneously aborted products of conception from Ukraine

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Aim: to investigate peculiarities of numerical chromosomal imbalances in spontaneous products of conception from Western region of Ukraine. **Methods:** GTG-banding, interphase mFISH with probe panels for chromosomes 13/21, 14/22, 15, 16, 17, 18, X and Y. **Results:** Cytogenetic and molecular cytogenetic studies on 419 spontaneously aborted fetuses were performed. An abnormal karyotype was detected in 35.80 %. Most often the detected aneuploidies were triploidy (27.3 %), monosomy X (22.7 %), and trisomy 16 (18.7 %), trisomy 21 (6.7 %), trisomy 15 (5.3 %) and trisomy 22 (5.3 %). **Conclusion:** Detection of chromosomal aneuploidies in samples from products of conception plays a key role to find out the reasons of reproductive failure in humans. Our study showed the effectiveness of combining karyotyping and mFISH with the chosen probe set for increasing the detection rate in spontaneous abortions. Most likely while including cases with normal karyotype acc. to GTG-banding in the mFISH approach it would allow detection of low level mosaics of aneuploidies as well. These studies were conducted for the first time in the western Ukrainian region. The obtained results were compared with the similar results from other countries.

Keywords: spontaneous abortion, G-banding cytogenetic, interphase multicolor fluorescence in situ hybridization (mFISH), chromosome abnormalities.

Introduction

Pregnancy loss is one of the most common medical problems in women over 35 years. Approximately 30 % to 50 % of all conceptions and 15–20 % of clinically recognized pregnancies (≥ 6 week of gestation = w.o.g.) fail to result in a live birth; most of those occur in the

first trimester [1–3]. Genetic defects, and predominantly chromosomal abnormalities, are the most common causes of spontaneous miscarriage during the first trimester; indeed, chromosomal abnormalities occur in approximately 45 % of such cases [4]. The most of these abnormalities are numerical ones (86–95 %): about 60 % are trisomies, 20 % are represented by monosomy X and another 15 % by polyploidy, mainly by triploidy, and only a minor part is structural chromosomal aberrations (6 %) or others, including chromosomal mosaicism (8 %) [5–6]. In case of numerical chromosomal aberrations, parental chromosomes are usually normal, thus, cytogenetic analysis of the parents is not indicative. Like numerical changes, structural aberrations of chromosomes can also be the cause of pregnancy loss and infertility. Thus, in the later case and in contrast to the numerical aberrations, parental cytogenetic analyses are to be offered.

In general, chromosomal studies on spontaneous abortions (SAs) provide important information for the recurrence risk of cytogenetic abnormalities in subsequent pregnancies. Following a pregnancy loss with trisomy, an increased recurrence risk for other trisomies in subsequent pregnancies is reported [6]. For the couples who have recurrent miscarriage, aneuploid karyotype of abortion indicates a better chance for a normal live birth in a subsequent pregnancy than if miscarriage is an euploid [7–8]. However, the recurrence risk for spontaneous abortion with trisomy is lower if the fetus has a chromosomal abnormality [8–10] and identification of a chromosomal aberration in the fetus can identify the cause of pregnancy loss.

The aim of the present study was to investigate peculiarities of numerical chromosomal imbalances in spontaneous products of conception from Western region of Ukraine.

Materials and Methods

The specimens from SAs in the period from 4 to 14 w.o.g. were obtained from 419 females aged from 22 to 42 years. The present study was approved by the ethical committee of the

Table 1. **Cytogenetic findings of SAs**

Method of karyotyping	Samples	Euploidy			Abnormal	Trisomy		Polyploidy		Monosomy	
		XX	XY	total	total	total	autosomal	total	triploidy	total	monosomy X
	n / % of total	n/ % of normal	n/ % of normal	n/ % of samples	n/ % of samples	n/ % of abnormal	n/ % of abnormal	n/ % of abnormal	n/% of abnormal	n/% of abnormal	n/% of abnormal
GTG banding	133/31.7	37[a]/41.6	52[a]/58.4	89/66.9	44/33.1	21/47.7	19/43.2	23/52.3	23/52.3	0	0
mFISH	286/66.3	101/56.1	79/43.9	180/62.9	106/37.1	47[b]/44.3	44[b]/41.5	23[b]/21.7	18/17.0	36[b]/34.0	34[b]/32.0
Total number of studies	419	138/51.3	131/48.7	269/64.2	150/35.8	68[b]/45.3	63[b]/42.0	46[b]/30.7	41[b]/27.3	36[b]/24.0	34[b]/22.7

[a] XX and XY at GTG banding mean 46,XX and 46,XY respectively

[b] Mosaic cases were included.

Table 2. **Results of GTG-banding and mFISH of SAs**

Karyotype	GTG-banding (n)	mFISH (n)	GTG- and mFISH (n)
XY	52[a]	79	131
XX	37[a]	101	138
monosomy X	–	33	33
47,XXY	1	1	2
trisomy X	1	1	2
trisomy 3	1	–	1
trisomy 13	–	1	1
trisomy 14	–	2	2
trisomy 15	1	7	8
trisomy 16	6	22	28
trisomy 18	2	1	3
trisomy 20	2	–	2
trisomy 21	5	4	9
trisomy 22	2	5	7
triploidy	23	18	41
tetraploidy	–	3	3
monosomy X[40]/ trisomy X[60]	–	1	1
monosomy X[96]/ disomy X[4]	–	1	1
monosomy 15[61]/ disomy 15[39]	–	1	1
monosomy 15	–	1	1
disomy 21[38]/ trisomy 21[62]	–	1	1
monosomy 22[26]/ disomy 22[23]/ trisomy 22[51]	–	1	1
2n[63]/4n[37]	–	1	1
2n[14]/3n[30]/4n[56]	–	1	1
Total	133	286	419

[a] XX and XY at GTG banding mean 46,XX and 46,XY respectively

Institute of Hereditary Pathology NAMS of Ukraine. Informed consent for cytogenetic studies was obtained from all patients.

Banding cytogenetic processing

For SA-material-processing the cells of chorionic villi were separated from the decidual

Table 3. **Prevalent autosomal trisomy in SAs**

Method of karyotyping	Abnormal Samples		Autosomal trisomy				
		total	trisomy 15	trisomy 16	trisomy 18	trisomy 21	trisomy 22
	n/ % of samples	n/ % of abnormal	n/ % of samples	n/ % of samples	n/ % of samples	n/ % of samples	n/ % of samples
GTG banding	44/33.1	19/43.2	1/2.3	6/13.6	2/4.5	5/11.4	2/4.5
mFISH	106/37.1	44[a]/41.5	7 [a]/6.6	22/20.8	1/0.9	5[a]/4.7	6[a]/5.7
Total number of studies	150/35.8	63[a]/42.0	8 [a]/5.3	28/18.7	3/2.0	10[a]/6.7	8[a]/5.3

[a]Mosaic cases were included.

cells. We used the method of direct chromosome preparation from chorion [11] and analyzed the samples cytogenetically using G-banding technique. Samples were visualized under a light microscope (Zeiss, Axioscope; Jena, Germany). A minimum of 5 metaphases were scored per sample.

Interphase multicolor fluorescence in situ hybridization (mFISH) analysis

Interphase nuclei from cytogenetically prepared cells were used for multicolor fluorescence in situ hybridization (mFISH) if metaphase plates could not be obtained. Hybridization, post-hybridization washes and detection steps were done as it was previously described [12]. Image acquisition was performed by using the Axioplan II microscope (Carl Zeiss Jena GmbH) equipped with filter sets for DAPI, FITC, TR, Cy3 and Cy5 fluorescence channels. Image analysis was done with the Isis DGTSa, BGR-I and DGSoSa software (MetaSystems Hard & Software GmbH, Altlussheim, Germany). Three homemade (Institute of Human Genetics, Jena, Germany) probe sets were used as specified below:

mix 1: centromeric probes for 13p11.1-q11 and 21p11.1-q11.1 (D13/21Z1, labeled in

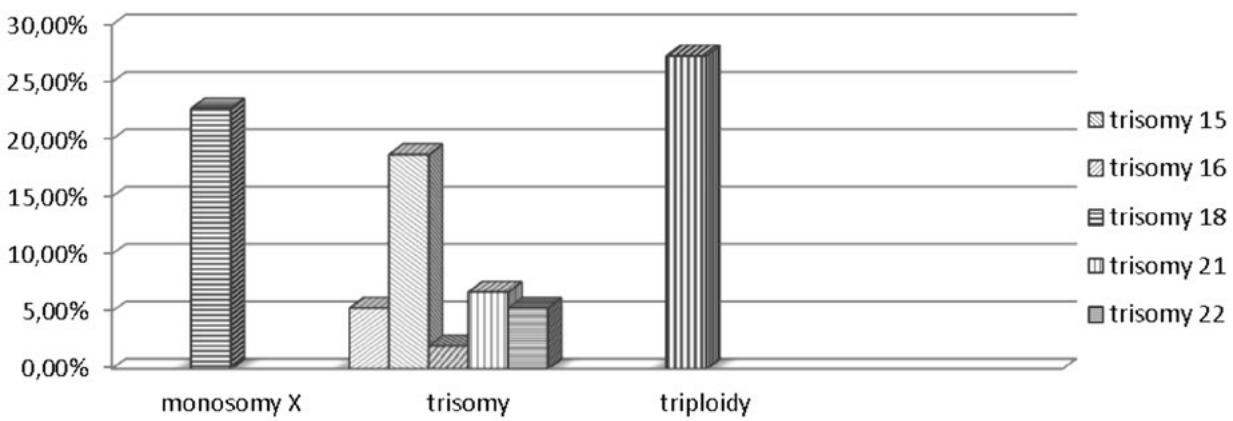

Fig. 1. The most often detected aneuploidies in SA samples

Table 4. **The results of cytogenetic studies using the interphase FISH of the reported series of samples of**

Study	Total number n	Abnormal karyotype (n, % in all cases)	Aneuploidy (monosomy or trisomy),						
			1	9	13	13/21	14	14/22	
Gao *et al,* 2012, China	100	42(42)	*	*	2 (4.8)	*	*	*	
Vorsanova *et al,* 2005, Russian Federation	148	89 (60.1)	1[a] (1.1)	2[a] (2.2)	*	11[a] (12.4)	*	10[a] (11.2)	
Jobanputra *et al,* 2011, USA	153	68 (44.4)	*	*	–	*	*	*	
Russo *et al,* 2016, Italy	855	430 (50.3)	*	*	13 (10)	*	*	*	
Present study, Ukraine	286	106 (37.1)	*	*	1 (0.9)	*	2 (1.9)	*	

* – CEP label not used, [a] – mosaicism is included, [b] – monosomy X.

Spectrum Green = SG), 15q11 (D15Z3 labelled in Texas-red = TR), and 18p11.1-q11.1 (D18Z1 labeled in – Diethylaminocoumarin = DEAC);

mix 2: centromeric probes for 14p11.1-q11.1 and 22p11.1-q11.1 (D14/22Z1 labeled in SG) and 16p11.1-q11.1 (D16Z2 labeled in TR);

mix 3: centromeric probes for 17p11.1-q11.1 (D17Z1 labeled in Spectrum Orange = SO) andXp11.1-q11.1 (DXZ1 labeled in DEAC), together with a probe for Yq12 (DYZ1 labeled in SG).

In cases where we detect the 5th signal of 13/21 we applied the fourth mFISH set consisting of three bacterial artificial (BAC) probes:

– RP11-2P5 in 13q14.11 labeled with SG;
– RP11-89H21 in 21q11.2 labeled with TR; and
– RP11-973L24 in 21q21.1 labeled with DEAC.

In cases where we detect the 5th signal of 14/22 we performed interphase FISH using a probe for 22p11.2 (D22Z4), labeled with SG.

All probe sets were preliminarily tested separately on human metaphase spreads prior to use them in the probe mixes to evaluate quality and to exclude contamination. The region specific probes were mapped cytogenetically based on the inverted DAPI banding pattern of chromosomes. At least 100 interphase nuclei per sample were analyzed.

Results

We performed GTG-banding and/or molecular cytogenetics on 419 chorionic villus samples (CVS) received from women with echographically diagnosed missed abortions or blighted ovum (from 4 to 14 w.o.g.). Banding cytogenetic results were received from 133 of the remainder 419 cases. For the analysis of SAs where banding analysis was not possible due to the absence of metaphases, interphase mFISH analysis was performed. Interphase mFISH with the probe panel for chromosomes 13/21, 14/22, 15, 16, 17, 18 X and Y was performed on 286 uncultured cell suspensions from spontaneous abortions samples. Additional probe sets to distinguish tri-

the spontaneous abortions received in different countries and Western regions of Ukraine

n (% of abnormalities)							Sex chromosome polysomy	Polyploidy		Double anomaly
15	16	17	18	21	22	X		3n	4n	
*	16 (38.1)	*	1 (2.4)	10 (23.8)	10 (23.8)	4 (9.5)	–	4 (9.5)	–	–
1 (1.1)	11[a] (12.4)	*	3[a] (3.4)	*	*	12[a] (13.5)	10[a] (11.2)	12[a] (13.5)	9[a] (10.1)	7 (7.9)
8 (11.8)	9 (13.2)	*	5 (7.4)	12 (17.6)	4 (5.9)	14 (20.6)	3 (4.4)	10 (14.7)	1 (1.5)	2 (2.9)
36[a] (8.4)	61 (14.2)	*	14 (3.2)	52[a] (12.1)	87 (20.2)	60[a] (13.9)	5 (1.2)	91[a] (21.2)	9[a] (2.1)	2 (0.5)
9[a] (8.5)	22 (20.8)	–	1 (0.9)	5[a] (4.7)	6[a] (5.7)	35[a] (33.0)	2 (1.9)	18[a] (17.0)	5[a] (4.7)	–

somy 13 from trisomy 21 and identify trisomy 22 were applied when indicated (Table 1, Table 2).

In our study mFISH detected more abnormalities than karyotyping (37.1 % versus 33.1 %). Less than half of the numerical aberrations were trisomy (47.7 % versus 44.3 %). Monosomy, especially monosomy X, was detected only by mFISH. The percentage of polyploidy was higher among the samples analyzed by karyotyping – 52.3 % (23/44) compared to 21.7 % (23/106). Mosaicism could be detected exclusively in the samples analyzed by means of interphase mFISH, i.e. in 4.7 % of the cases.

In 150/419 cases (35.80 %) an abnormal karyotype was detected. None of the chromosomal abnormalities were identified to be gender-specific (male/female 205/214). The most often detected aneuploidies, as shown in Table 3 and Figure 1 were: triploidy (27.3 %), monosomy X (22.7 %), trisomy 16 (18.7 %), trisomy 21 (6.7 %), trisomy 15 (5.3 %) and trisomy 22 (5.3 %).

Mosaicism was detected in 7(4.7 %) samples: gonosomal mosaicism – monosomy X[96]/disomy X[4] and monosomy X[40]/ trisomy X[60]; autosomal mosaicism – monosomy 15,XX[61]/disomy 15,XX[39], disomy 21,XY[38]/ trisomy 21,XY[62] and monosomy 22,XX[26]/disomy 22,XX[23]/trisomy 22,XX[51]; mosaic form of polyploidy – 2nXY[63]/4nXXYY[37] and 2nXX[14]/ 3nXXX[30]/4nXXXX[56].

Discussion

Karyotyping of SAs has limitations such as the absence of cell growth, bacterial/fungal contamination or insufficient metaphase quality. The success rate of karyotyping in miscarriages tissue is dependent on experience of the performing lab, ranging from 46 to 89 %, but in general ~ 70 % [7–9, 13–22]. The effectiveness of karyotyping in directly prepared, not cultivated CVS cells is even lower because of the absence of metaphases or their low quality. In our study, the later method was successful in only 133 (31.7 %) of 419 cases. The frequency of numerical chro-

mosomal abnormalities was 33.1 % and is similar to the data of other authors [13, 14, 16, 17, 20, 23, 24]. The most frequent were triploidies (52.3 %) and trisomies (47.7 %) whereas monosomies were not detected. Our results do not coincide with the data of other studies [7–9, 13–24] in which trisomies (59–68 %), polyploidies (6–19 %) and monosomy X (4–14 %) prevail in descending order. We assume that this is a feature of our region. Predominated autosomal trisomies are observed for chromosomes 16, 21, and 22 [18, 22, 24–27]. Although double or triple aberrations were found by other investigators at the early pregnancy losses [13, 18, 20, 25–28], they were not found in our study.

The molecular cytogenetic techniques such as interphase FISH allow diagnosis of uncultured cells, but they are also limited to a certain spectrum of cytogenetic abnormalities detectable and effectiveness of mFISH within 25–68.9 % [19, 24, 28–31]. The chromosomal abnormalities were detected in 37.1 % of SAs studied by mFISH compared with 33.1 % by conventional karyotyping. The underlying aberrations were autosomal trisomies in 41.5 %, monosomy X in 32.0 % and triploidy in 17.0 % of the cases, that is in concordance with other studies [24, 25, 28–31].

In Table 4, the results of our study are compared with the results of investigations [24, 25, 28, 30, 31] carried out in other countries. Such analysis revealed some peculiarities of the SA found in the population of the Western regions of Ukraine comparing with China, Russian Federation, USA and Italy. Particularly, we did not detect double and triple aberrations, whereas the ratio of the gonosomal monosomy was much higher in the Western Ukraine compared to the above listed countries.

In contrast to the cases analyzed by karyotyping, it was found 7 samples (4.7 %) with mosaicism. This difference can be explained by the fact that significantly more nuclei were studied (minimum 100 per mix) compared to the number of metaphases (5–15) in each sample. Double and triple aberrations were not observed that could be related to limitations of number of chromosomes analyzed by the mFISH set. The frequency of autosomal trisomy of chromosomes 15, 16, 18, 21 and 22 is different from conventional karyotyping: 15 – 6.6 % vs. 2.3 %, 16 – 20.8 % vs. 13.6 % 18 – 0.9 % versus 5 % 21 – 4.7 % vs 11.5 22 % and – 5.7 % vs. 4.5 %. However, overall they are comparable to the data of other researchers [24, 25, 28, 29, 31].

It should be emphasized that 53 cases (35.3 %) of anomalies, namely, monosomy X, trisomy 13, 18, 21, X and XXY, are among live births. However, it is well known that certain percentages of these imbalances are lethal before birth.

Overall, the combination of GTG-banding and mFISH data enabled detection of the reasons for SAs in significantly more cases. Among 419 analyzable cases the diagnoses could be given to 150 cases. After GTG-banding alone only 44 cases could be solved; i.e. the rate of cases with identified SA-causative chromosomal imbalance could be enhanced by 340% with the application of described approach.

Conclusion

1. Our study showed the effectiveness of combining karyotyping and mFISH with the chosen probe set for increasing the detection rate in SAs.

2. Cytogenetic and molecular-cytogenetic investigations of SA material identified karyotype anomalies in 35.8 % of cases with prevalence of autosomal trisomy – 42.0 %, triploidy – 27.3 % and monosomy X – 22.7. Mosaicism was detected only by iFISH in 4.7 %.

REFERENCES

1. *Edmonds DK, Lindsay KS, Miller JF, Williamson E, Wood PJ.* Early embryonic mortality in women. *Fertil Steril.* 1982;**38**(4):447–53.
2. *Steer C, Campbell S, Davies M, Mason B, Collins W.* Spontaneous abortion rates after natural and assisted conception. *BMJ.* 1989;**299**(6711):1317–8.
3. *Zinaman MJ, Clegg ED, Brown CC, O'Connor J, Selevan SG.* Estimates of human fertility and pregnancy loss. *Fertil Steril.* 1996;**65**(3):503–9.
4. *van den Berg MM, van Maarle MC, van Wely M, Goddijn M.* Genetics of early miscarriage. *Biochim Biophys Acta.* 2012;**1822**(12):1951–9.
5. *Goddijn M, Leschot NJ.* Genetic aspects of miscarriage. *Baillieres Best Pract Res Clin Obstet Gynaecol.* 2000;**14**(5):855–65.
6. *Warburton D, Dallaire L, Thangavelu M, Ross L, Levin B, Kline J.* Trisomy recurrence: a reconsideration based on North American data. *Am J Hum Genet.* 2004;**75**(3):376–85.
7. *Ogasawara M, Aoki K, Okada S, Suzumori K.* Embryonic karyotype of abortuses in relation to the number of previous miscarriages. *Fertil Steril.* 2000;**73**(2):300–4.
8. *Carp H, Toder V, Aviram A, Daniely M, Mashiach S, Barkai G.* Karyotype of the abortus in recurrent miscarriage. *Fertil Steril.* 2001;**75**(4):678–82.
9. *Stephenson M, Kutteh W.* Evaluation and management of recurrent early pregnancy loss. *Clin Obstet Gynecol.* 2007;**50**(1):132–45. Review.
10. *Warburton D, Kline J, Stein Z, Hutzler M, Chin A, Hassold T.* Does the karyotype of a spontaneous abortion predict the karyotype of a subsequent abortion? Evidence from 273 women with two karyotyped spontaneous abortions. *Am J Hum Genet.* 1987;**41**(3):465–83.
11. *Baranov VS.* [A method of shaking-blotting--a simple and reliable means for obtaining direct chromosomal preparations from chorionic biopsies]. *Tsitologiia.* 1989;**31**(2):251–3.
12. *Liehr T, Pellestor F.* Molecular cytogenetics: the standard FISH and PRINS procedure In: Ed. Liehr T. Fluorescence In Situ Hybridization (FISH) – Application Guide. *Springer, Berlin, Heidelberg*. 2009; 23–34.
13. *Diego-Alvarez D, Ramos-Corrales C, Garcia-Hoyos M, Bustamante-Aragones A, Cantalapiedra D, Diaz-Recasens J, Vallespin-Garcia E, Ayuso C, Lorda-Sanchez I.* Double trisomy in spontaneous miscarriages: cytogenetic and molecular approach. *Hum Reprod.* 2006;**21**(4):958–66.
14. *Diego-Alvarez D, Rodriguez de Alba M, Cardero-Merlo R, Diaz-Recasens J, Ayuso C, Ramos C, Lorda-Sanchez I.* MLPA as a screening method of aneuploidy and unbalanced chromosomal rearrangements in spontaneous miscarriages. *Prenat Diagn.* 2007;**27**(8):765–71.
15. *Menten B, Swerts K, Delle Chiaie B, Janssens S, Buysse K, Philippé J, Speleman F.* Array comparative genomic hybridization and flow cytometry analysis of spontaneous abortions and mors in utero samples. *BMC Med Genet.* 2009;**10**:89.
16. *Robberecht C, Schuddinck V, Fryns JP, Vermeesch JR.* Diagnosis of miscarriages by molecular karyotyping: benefits and pitfalls. *Genet Med.* 2009;**11**(9): 646–54.
17. *Zhang YX, Zhang YP, Gu Y, Guan FJ, Li SL, Xie JS, Shen Y, Wu BL, Ju W, Jenkins EC, Brown WT, Zhong N.* Genetic analysis of first-trimester miscarriages with a combination of cytogenetic karyotyping, microsatellite genotyping and arrayCGH. *Clin Genet.* 2009;**75**(2):133–40.
18. *Dória S, Carvalho F, Ramalho C, Lima V, Francisco T, Machado AP, Brandão O, Sousa M, Matias A, Barros A.* An efficient protocol for the detection of chromosomal abnormalities in spontaneous miscarriages or foetal deaths. *Eur J Obstet Gynecol Reprod Biol.* 2009;**147**(2):144–50.
19. *Shearer BM, Thorland EC, Carlson AW, Jalal SM, Ketterling RP.* Reflex fluorescent in situ hybridization testing for unsuccessful product of conception

cultures: a retrospective analysis of 5555 samples attempted by conventional cytogenetics and fluorescent in situ hybridization. *Genet Med.* 2011;**13**(6): 545–52.
20. *Sullivan AE, Silver RM, LaCoursiere DY, Porter TF, Branch DW.* Recurrent fetal aneuploidy and recurrent miscarriage. *Obstet Gynecol.* 2004;**104**(4):784–8.
21. *Halder A, Fauzdar A.* Skewed sex ratio and low aneuploidy in recurrent early missed abortion. *Indian J Med Res.* 2006;**124**(1):41–50.
22. *Wang BT, Chong TP, Boyar FZ, Kopita KA, Ross LP, El-Naggar MM, Sahoo T, Wang JC, Hemmat M, Haddadin MH, Owen R, Anguiano AL.* Abnormalities in spontaneous abortions detected by G-banding and chromosomal microarray analysis (CMA) at a national reference laboratory. *Mol Cytogenet.* 2014;**7**:33.
23. *Kooper AJA, Faas BHW, Feenstra I, de Leeuw N and Smeets DFCM.* Best diagnostic approach for the genetic evaluation of fetuses after intrauterine death in first, second or third trimester: QF-PCR, karyotyping and/or genome wide SNP array analysis. *Mol Cytogen.* 2014; **7**:6. doi: 10.1186/1755-8166-7-6.
24. *Gao J, Liu C, Yao F, Hao N, Zhou J, Zhou Q, Zhang L, Liu X, Bian X, Liu J.* Array-based comparative genomic hybridization is more informative than conventional karyotyping and fluorescence in situ hybridization in the analysis of first-trimester spontaneous abortion. *Mol Cytogenet.* 2012;**5**(1):33.
25. *Jobanputra V, Sobrino A, Kinney A, Kline J, Warburton D.* Multiplex interphase FISH as a screen for common aneuploidies in spontaneous abortions. *Hum Reprod.* 2002;**17**(5):1166–70.
26. *Morales C, Sánchez A, Bruguera J, Margarit E, Borrell A, Borobio V, Soler A.* Cytogenetic study of spontaneous abortions using semi-direct analysis of chorionic villi samples detects the broadest spectrum of chromosome abnormalities. *Am J Med Genet A.* 2008;**146A**(1):66–70.
27. *Eiben B, Bartels I, Bähr-Porsch S, Borgmann S, Gatz G, Gellert G, Goebel R, Hammans W, Hentemann M, Osmers R.* Cytogenetic analysis of 750 spontaneous abortions with the direct-preparation method of chorionic villi and its implications for studying genetic causes of pregnancy wastage. *Am J Hum Genet.* 1990;**47**(4):656–63.
28. *Jobanputra V, Esteves C, Sobrino A, Brown S, Kline J, Warburton D.* Using FISH to increase the yield and accuracy of karyotypes from spontaneous abortion specimens. *Prenat Diagn.* 2011;**31**(8):755–9.
29. *Lebedev IN, Ostroverkhova NV, Nikitina TV, Sukhanova NN, Nazarenko SA.* Features of chromosomal abnormalities in spontaneous abortion cell culture failures detected by interphase FISH analysis. *Eur J Hum Genet.* 2004;**12**(7):513–20.
30. *Vorsanova SG, Kolotii AD, Iourov IY, Monakhov VV, Kirillova EA, Soloviev IV, Yurov YB.* Evidence for high frequency of chromosomal mosaicism in spontaneous abortions revealed by interphase FISH analysis. *J Histochem Cytochem.* 2005;**53**(3):375–80.
31. *Russo R, Sessa AM, Fumo R, Gaeta S.* Chromosomal anomalies in early spontaneous abortions: interphase FISH analysis on 855 FFPE first trimester abortions. *Prenat Diagn.* 2016;**36**(2):186–91.

Хромосомні аберації у матеріалі мимовільно втрачених вагітностей з України

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Мета: дослідити особливості чисельних хромосомних аномалій у матеріалі мимовільно втрачених вагітностей із Західного регіону України. **Методи:** стандартний цитогенетичний метод, інтерфазний mFISH метод з центромерними зондами до хромосом 13/21, 14/22, 15, 16, 17, 18, X та Y. **Результати:** Виконано цитогенетичні та молекулярно цитогенетичні дослідження 419 зразків ворсин хоріона ранніх мимовільно втрачених вагітностей. У 35,80 % виявлено чисельні зміни каріотипу. Найчастіше зустрічались наступні анеуплоідії: триплоідія (27,3 %), моносомія X (22,7 %), трисомія 16 (18,7 %), трисомія 21 (6,7 %), трисомія 15 (5,3 %) та трисомія 22 (5,3 %)**. Висновки:** Діагностика анеуплоїдій у зразках мимовільно втрачених вагітностей відіграє ключову роль при з'ясуванні причини репродуктивної невдачі. Показана висока ефективність комбінування GTG каріотипування та mFISH з вибраним набором міток. Застосування mFISH дозволило виявити низькодозовий мозаїцизм у випадках нормального GTG-каріотипу. Такі дослідження по західноукраїн-

ському регіону проведені вперше, отримані результати співставлені з результатами по інших країнах.

Ключові слова: мимовільно втрачені вагітності, GTG-каріотип, інтерфазний FISH, хромосомні аномалії.

Хромосомные аберрации у материале самопроизвольных выкидышей с Украины

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Цель: исследовать особенности количественных хромосомных аномалий в образцах самопроизвольных выкидышей из Западного региона Украины. **Методы:** стандартный цитогенетический метод, интерфазный mFISH метод с центромерными зондами к хромосомам 13/21, 14/22, 15, 16, 17, 18, X и Y. **Результаты:** Выполнены цитогенетические и молекулярно-цитогенетические исследования 419 образцов ворсин хориона ранних самопроизвольных выкидышей. В 35,80 % выявлено изменения кариотипа. Наиболее часто встречались следующие анеуплоидии: триплоидия (27,3 %), моносомия X (22,7 %), трисомия 16 (18,7 %), трисомия 21 (6,7 %), трисомия 15 (5,3 %) и трисомия 22 (5,3 %). **Выводы:** Диагностика анеуплоидий в образцах самопроизвольных выкидышей играет ключевую роль при выяснении причины репродуктивной неудачи. Показано высокую эффективность комбинированного применения GTG кариотипирования и метода mFISH с предложенным набором меток. Применение mFISH позволило выявить низкодозовый мозаицизм в случаях нормального GTG-кариотипа. Такие исследования по западноукраинскому региону проведены впервые, а полученные результаты сопоставили с результатами других стран.

Ключевые слова: самопроизвольные выкидыши, GTG-кариотип, интерфазный FISH, хромосомные аномалии.

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