TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2018) 48: 150-156
© TÜBİTAK
doi:10.3906/sag-1704-1

Translocation breakpoints of chromosome 3 in male carriers: a report of twelve cases and a review of the literature

Hongguo ZHANG, Ruixue WANG, Linlin LI, Haibo ZHU, Hao ZHANG, Ruizhi LIU*
Center for Reproductive Medicine and Center for Prenatal Diagnosis, First Hospital, Jilin University, Changchun, P.R. China

Received: 01.04.2017 • **Accepted/Published Online:** 10.12.2017 • **Final Version:** 23.02.2018

Background/aim: This study aimed to explore the breakpoints in chromosome 3 translocation and the clinical features present in male carriers to enable informed genetic counseling of these patients.

Materials and methods: A total of 5235 men who were infertile or receiving counseling for infertility were recruited. Cytogenetic analyses were performed using G-banding. A search for translocations on chromosome 3 involved in male infertility was performed using PubMed, Google Scholar, and CNKI. The relationships of translocation breakpoints with male infertility and recurrent pregnancy loss were also analyzed.

Results: Among the 82 patients with balanced reciprocal translocations among 5235 male patients, 12 patients were carriers of chromosome 3 translocation: two presented with pregestational infertility, while 10 presented with gestational infertility. The breakpoint at 3p13 was related to pregestational infertility, whereas those at 3p23, 3q10, 3q12, 3q21, 3q25, and 3q29 were related to gestational infertility. By an analysis combining data from the literature, 63 carriers of chromosome 3 translocation were reviewed and all breakpoints at chromosome 3 were correlated with gestational infertility.

Conclusion: All breakpoints at chromosome 3 were correlated with gestational infertility. The breakpoints at 3q12 and 3q29 were the most common. Carriers of chromosome 3 translocation should thus be counseled on the need for other chromosomal breakpoints and preimplantation genetic diagnosis or prenatal testing.

Key words: Male infertility, chromosome 3, balanced translocation, breakpoint, genetic counseling

1. Introduction

Male factor is responsible for 30%–50% of all infertility, and genetic abnormalities are thought to account for 15%–30% of male factor infertility (1,2). Chromosomal aberrations play a major role in infertile men because findings have shown that sperm concentration is strongly correlated with the presence of chromosomal abnormalities (3,4). Since structural chromosomal aberrations are up to 10 times more common in infertile men than in fertile controls, karyotypes are important in the work-up of infertile men (5). Structural chromosomal abnormalities in men can lead to abnormal sperm concentrations while leading to male infertility or increasing miscarriages (6,7). Reciprocal translocations are mainly structural chromosomal abnormalities, the carriers of which can be phenotypically normal but may experience reduced fertility and spontaneous abortions (8). These effects are dependent on the specific chromosomes and breakpoints involved in the translocation (8,9). Some translocation breakpoints can interrupt an important gene structure, causing male infertility (10).

Previous reports have indicated the involvement of chromosome 3 translocations in male infertility and recurrent pregnancy loss (11–13). Sperm chromosome complements were studied in men heterozygous for the carriers of reciprocal chromosome 3 translocation. The frequency of spermatozoa carrying an abnormal chromosome constitution was found to be significantly higher than the frequency in control semen specimens (14). However, Martin (15) reported that there was no evidence for an interchromosomal effect because the frequencies of numerical and structural abnormalities (unrelated to the translocation) were within the normal range of the control group. Additionally, the WD repeat-containing protein 10 gene (*WDR 10*) is located on chromosome 3q21 and highly expressed in testes (16). The centrosomal protein 19-KD gene (*CEP19*), mapped on chromosome 3 at 3q29, may be associated with spermatogenic failure (17).

* Correspondence: lrz410@126.com

The present study was performed to determine the correlation between the clinical characteristics of male infertility and the carriers of translocation breakpoints in chromosome 3. This paper also highlights the importance of genetic counseling for infertile patients.

2. Materials and methods

2.1. Study subjects

Between July 2010 and December 2015, 5235 men who were infertile or receiving counseling for infertility were recruited from among outpatients of the Center for Reproductive Medicine, First Hospital of Jilin University, Changchun, China. All patients underwent a thorough physical examination and a semen analysis and were required to complete a detailed questionnaire pertaining to their smoking, drinking, marital status, childbearing histories, spontaneous abortion status, medical history, and working conditions. Oligozoospermia was defined as per our previous definition (10). The study protocol was approved by the Ethics Committee of First Hospital of Jilin University and written informed consent was obtained from all participants.

2.2. Cytogenetic analysis

All patients were subjected to a cytogenetic analysis. Peripheral blood (0.5 mL) was collected in sterile tubes containing 30 U/mL heparin. Lymphocytes were cultured in appropriate culture medium (Yishengjun; Guangzhou Baidi Biotech, Guangzhou, China) for 72 h and subsequently treated with 20 μg/mL colcemid for 1 h. G-banding of metaphase chromosomes and karyotype analysis were performed using our previously reported methods (18).

2.3. Analysis of translocation breakpoints reported

A search for translocations in chromosome 3 involved in male infertility was performed using PubMed, Google Scholar, and CNKI. The keywords were "chromosome / translocation / sperm" and "chromosome / translocation / abortion" for the PubMed search. Available papers were included from 1986 to 2017. We excluded those translocations involving chromosome 3 but with no reported breakpoint. The relationships of translocation breakpoints with male infertility and recurrent pregnancy loss were analyzed.

3. Results

A total of 82 translocation carriers were detected among 5235 male patients in this study. Of these carriers, 12 patients (12/82; 14.6%) were carriers of a chromosome 3 translocation. Two of these patients exhibited pregestational infertility (clinical manifestation: oligozoospermia), while the remaining ten patients exhibited gestational infertility (patients' partners were able to conceive but tended to miscarry). The results of a karyotype analysis of the 12 patients with chromosome 3 translocation are summarized in Table 1.

Breakpoints at 3q12 and 3q21 were observed in three patients each. The breakpoint at 3p13 was related to pregestational infertility, while the breakpoints at 3p23, 3q10, 3q12, 3q21, 3q25, and 3q29 were related to gestational infertility (Table 2).

From an analysis of the literature, 63 carriers of chromosome 3 translocations were reviewed. The breakpoints at 3q12 and 3q29 were the most common. All breakpoints were related to gestational infertility. The karyotypes of and breakpoints in chromosome 3 and their related clinical symptoms are summarized in Table 3.

Table 1. Karyotypes of chromosome 3 translocation carriers and their clinical features.

Infertility causes	Clinical findings	Karyotype
Pregestational infertility	Oligozoospermia	46,XY,t(1;3)(p22;p13) 46,XY,t(3;15)(p13;q22)
Gestational infertility	Normal sperm density; a history of miscarriage	46,XY,t(3;6)(q10;q10) 46,XY,t(3;6)(q12;q27) 46,XY,t(3;6)(q21;q25) 46,XY,t(3;7)(p23;q21.2) 46,XY,t(3;9)(q21;q22) 46,XY,t(3;15)(q21;q22) 46,XY,t(3;17)(q29;q23) 46,XY,t(3;17)(q25;q23) 46,XY,t(3;19)(q12;q13) 46,XY,t(3;20)(q12;q13)

Table 2. Incidence of breakpoints on chromosome 3.

Breakpoints	Number of patients with pregestational infertility	Number of patients with gestational infertility	Total (%)
p23		1	1 (8.3%)
p13	2		2 (16.7%)
q10		1	1 (8.3%)
q12		3	3 (25%)
q21		3	3 (25%)
q25		1	1 (8.3%)
q29		1	1 (8.3%)

Table 3. Breakpoints in chromosome 3 translocation carriers and clinical features reported in previous literature.

Karyotype	Breakpoints	Clinical findings	Reference
t(1;3)	1p32.1; 3q29	Primary infertility, 1 IVF-ET abortion	Vozdova et al. (26)
t(1;3)	1p22; 3q29	Miscarriage	Li et al. (27)
t(1;3)	1q24; 3q28	ICSI	Gekas et al. (51)
t(1;3)	1q21; 3q25	Repeated miscarriage	Goddijn et al. (49)
t(1;3)	1q42.1; 3q21	Infertility	Matsuda et al. (40)
t(2;3)	2p13; 3p25	Normozoospermia	Haapaniemi Kouru et al. (38)
t(2;3)	2p12; 3q26	Oligospermia	Antonelli et al. (48)
t(2;3)	2q21; 3p21	Recurrent spontaneous abortion	Tunç et al. (13)
t(2;3)	2p13; 3q27	Recurrent spontaneous abortion	Ocak et al. (46)
t(3;4)	3p25; 4q21.3	Infertility	Matsuda et al. (40)
t(3;4)	3q12; 4p15.2	Miscarriage	Escudero et al. (35)
t(3; 4)	3q29; 4q26	Recurrent pregnancy loss	Kochhar et al. (24)
t(3;4)	3p25.2; 4q25	Primary infertility 18 months	Vozdova et al. (26)
t(3;5)	3q27; 5p15	A boy 46,XY,t(3;5)pat	Vozdova et al. (26)
t(3;5)	3q13; 5q35	Repeated abortion	Venkateshwari et al. (28)
t(3;5)	3q26.2; 5p15.1	Miscarriage	Sugiura-Ogasawara et al. (54)
t(3;5)	3q28; 5p13	Recurrent spontaneous pregnancy loss	Gada Saxena et al. (11)
t(3;5)	3q29; 5q13	Multiple abortions	Castle et al. (44)
t(3;6)	3q12; 6q27	2 spontaneous abortions	Zhang et al. (21)
t(3;6)	3q13; 6p25	5 fetal losses	Adamoli et al. (45)
t(3;6)	3q21; 6q23	Reproductive failures	Mokánszki et al. (29)
t(3;6)	3q25.3; 6q11.2	Recurrent fetal wastage	Fryns et al. (23)
t(3;6)	3q28; 6q13	Infertility	Mierla et al. (12)
t(3;6)	3q28; 6q21	Repeated miscarriages	Iyer et al. (53)
t(3; 6)	3q29; 6q21	Recurrent pregnancy loss	Kochhar et al. (24)
t(3;7)	3p25; 7q32	Term birth, defects in children	Zhang et al. (41)

Table 3. (Continued).

Karyotype	Breakpoints	Clinical findings	Reference
t(3;7)	3p23; 7q21.2	Recurrent spontaneous abortion	Zhang et al. (21)
t(3;7)	3p23; 7p13	Oligoasthenozoospermia	Haapaniemi Kouru et al. (38)
t(3;7)	3q25; 7q22	Severe oligozoospermia	Dong et al. (30)
t(3;7)	3q25.3; 7q21.1	Miscarriage	Sugiura-Ogasawara et al. (54)
t(3;7)	3q25.3; 7p22.1	PGD	Pundir et al. (58)
t(3; 8)	3p25; 8p11	Recurrent abortion	Gaboon et al. (31)
t(3; 8)	3p13; 8p21	Spontaneous abortion	Jenderny (62)
t(3; 8)	3q22; 8q23	Infertility	Perrin et al. (36)
t(3;11)	3p14; 11p15	Recurrent abortion	Portnoï et al. (55)
t(3;11)	3q25.3; 11q25	Unbalanced pregnancies	Martin et al. (61)
t(3;11)	3q27.3; 11q24.3	7 early miscarriages	Martini et al. (14)
t(3; 12)	3p14; 12p11	OAT	Peschka et al. (60)
t(3; 12)	3p24; 12p12	Severe A	Peschka et al. (60)
t(3; 12)	3q13.3; 12p13.3	Recurrent pregnancy loss	Kochhar et al. (24)
t(3; 12)	3q23; 12q21	Normozoospermia	Haapaniemi Kouru et al. (38)
t(3;12)	3q25.2; 12p12	Recurrent fetal wastage	Celep et al. (32)
t(3;12)	3q28; 12q12	PGD	Gianaroli et al. (52)
t(3;13)	3p21; 13p11.2	Infertility	Mierla et al. (12)
t(3;13)	3p13; 13q14	Recurrent fetal wastage	Fryns et al. (23)
t(3;13)	3q27; 13q11	Oligospermia	Perrin et al. (36)
t(3;14)	3p12; 14q12–13	Recurrent miscarriages	Dutta et al. (33)
t(3;14)	3q23; 14q32.2	Spontaneous abortion	Kyu Lim et al. (42)
t(3;14)	3q27; 14q11	Infertility	Matsuda et al. (40)
t(3;15)	3p22; 15q26.2	Miscarriage	Sugiura-Ogasawara et al. (54)
t(3;15)	3q24; 15q21	Recurrent fetal loss	Meza-Espinoza et al. (57)
t(3;15)	3q24; 15q25	PGD	Ko et al., (43)
t(3;15)	3q26.2; 15q26.1	Did not start a family	Estop et al. (50)
t(3;16)	3q12;16q23	Miscarriage	Dul et al. (34)
t(3;16)	3p23; 16q24	Not applicable	Brandriff et al. (47)
t(3;17)	3p12; 17q12	Infertility	Gada Saxena et al.(11)
t(3;17)	3q23; 17q21	Primary infertility	Machev et al.(56)
t(3;18)	3p27.3; 18q21.1	Asthenozoospermia	Vegetti et al. (59)
t(3;18)	3q13.2; 18p11.32	PGD	Pundir et al. (58)
t(3;18)	3q29; 18q21.3	Recurrent fetal wastage	Fryns et al. (23)
t(3;19)	3p21; 19p13.3	Infertility	Oliver-Bonet et al. (37)
t(3;20)	3p14.1; 20p13	Recurrent spontaneous abortion	Ocak et al. (46)
t(3;22)	3q21; 22q11.2	Infertility	Rouen et al. (38)

4. Discussion

Karyotype analysis remains a powerful and cheap technology and continues to have wide applications in the field of genetics (19). This technology can detect chromosomal translocations or deletions and is a valuable tool in genetic counseling for infertility (20). Cytogenetic evaluation of men with abnormal sperm parameters reveals balanced translocations and abnormal karyotypes in up to 13% of them, significantly more frequently than in fertile controls (5). Structural chromosomal abnormalities are associated with male factor infertility (7). In the previous literature, it was reported that the presence of translocations alters the process of spermatogenesis (21). Chromosome 3 translocations are also often known to be involved in male infertility and recurrent pregnancy loss (11–13,22).

Male factor infertility is divided into two types of reproductive failure: pregestational and gestational infertility (23). In this study, chromosome 3 translocation was found to be associated with two cases of pregestational and 10 cases of gestational infertility. The breakpoint at 3p13 was related to pregestational infertility, while the breakpoints at 3p23, 3q10, 3q12, 3q21, 3q25, and 3q29 were related to gestational infertility. To investigate the relationship of the breakpoints at chromosome 3 and male infertility, an analysis of related literature published in recent years revealed a close association between breakpoints in chromosome 3 translocation carriers and male infertility and reproductive failure. Table 3 shows that all breakpoints were associated with recurrent pregnancy loss or recurrent miscarriages (11,13,24,25). These cases indicated that these breakpoints are not responsible for these conditions, suggesting that another breakpoint of translocation is responsible for pregestational infertility. Although *WDR 10*, located on chromosome 3q21, expressed in testes, and *CEP19*, mapped on chromosome 3q29, may be associated with spermatogenic failure (16,17), the details of their functions are unclear. Hence, carriers of chromosome 3 translocations should receive appropriate counseling to appraise them of suitable reproductive options. Patients with gestational infertility should be counseled regarding preimplantation genetic diagnosis or prenatal testing, as these patients are at an increased risk of recurrent fetal wastage (26).

In conclusion, all breakpoints at chromosome 3 were correlated with gestational infertility. The breakpoints at 3q12 and 3q29 were the most common and were associated with gestational infertility. Carriers of chromosome 3 translocation should thus be counseled on the need for other chromosomal breakpoints and preimplantation genetic diagnosis or prenatal testing.

Acknowledgment

This research was supported by the National Natural Science Fund of China (No. 81471515).

References

1. Song SH, Chiba K, Ramasamy R, Lamb DJ. Recent advances in the genetics of testicular failure. Asian J Androl 2016; 18: 350-355.
2. Al-Turki HA. A 5-year analysis of semen parameters in Saudi Arabian men attending infertility clinics. J Int Med Res 2016; 44: 656-661.
3. Dul EC, Groen H, van Ravenswaaij-Arts CM, Dijkhuizen T, van Echten-Arends J, Land JA. The prevalence of chromosomal abnormalities in subgroups of infertile men. Hum Reprod 2012; 27: 36-43.
4. Gao M, Pang H, Zhao YH, Hua J, Tong D, Zhao H, Liu Y, Zhao Y, Zhang M, Yan XJ et al. Karyotype analysis in large sample cases from Shenyang Women's and Children's hospital: a study of 16,294 male infertility patients. Andrologia 2017; 49: 12649.
5. Hotaling J, Carrell DT. Clinical genetic testing for male factor infertility: current applications and future directions. Andrology 2014; 2: 339-350.
6. Pastuszek E, Kiewisz J, Kulwikowska PM, Lukaszuk M, Lukaszuk K. Sperm parameters and DNA fragmentation of balanced chromosomal rearrangements carriers. Folia Histochem Cytobiol 2015; 53: 314-321.
7. Suganya J, Kujur SB, Selvaraj K, Suruli MS, Haripriya G, Samuel CR. Chromosomal Abnormalities in Infertile Men from Southern India. J Clin Diagn Res 2015; 9: GC05-10.
8. Harton GL, Tempest HG. Chromosomal disorders and male infertility. Asian J Androl 2012; 14: 32-39.
9. Godo A, Blanco J, Vidal F, Anton E. Accumulation of numerical and structural chromosome imbalances in spermatozoa from reciprocal translocation carriers. Hum Reprod 2013; 28: 840-849.
10. Zhang HG, Wang RX, Li LL, Sun WT, Zhang HY, Liu RZ. Male carriers of balanced reciprocal translocations in Northeast China: sperm count, reproductive performance, and genetic counseling. Genet Mol Res 2015; 14: 18792-18798.
11. Gada Saxena S, Desai K, Shewale L, Ranjan P, Saranath D. Chromosomal aberrations in 2000 couples of Indian ethnicity with reproductive failure. Reprod Biomed Online 2012; 25: 209-218.
12. Mierla D, Jardan D, Stoian V. Chromosomal abnormality in men with impaired spermatogenesis. Int J Fertil Steril 2014; 8: 35-42.

13. Tunç E, Tanrıverdi N, Demirhan O, Süleymanova D, Çetinel N. Chromosomal analyses of 1510 couples who have experienced recurrent spontaneous abortions. Reprod Biomed Online 2016; 32: 414-419.

14. Martini E, von Bergh AR, Coonen E, de Die-Smulders CE, Hopman AH, Ramaekers FC, Geraedts JP. Detection of structural abnormalities in spermatozoa of a translocation carrier t(3;11)(q27.3;q24.3) by triple FISH. Hum Genet 1998; 102: 157-165.

15. Martin RH. Sperm chromosome complements in a man heterozygous for a reciprocal translocation t(2;3)(q24;p26). Hum Reprod 1994; 9: 1512-1515.

16. Gross C, De Baere E, Lo A, Chang W, Messiaen L. Cloning and characterization of human *WDR10*, a novel gene located at 3q21 encoding a WD-repeat protein that is highly expressed in pituitary and testis. DNA Cell Biol 2001; 20: 41-52.

17. Shalata A, Ramirez MC, Desnick RJ, Priedigkeit N, Buettner C, Lindtner C, Mahroum M, Abdul-Ghani M, Dong F, Arar N et al. Morbid obesity resulting from inactivation of the ciliary protein CEP19 in humans and mice. Am J Hum Genet 2013; 93: 1061-1071.

18. Zhang HG, Liu XY, Hou Y, Chen S, Deng S, Liu RZ. Reproductive outcome of a case with familial balanced translocation t(3;6): implications for genetic counseling. Genet Mol Res 2015; 14: 2809-2815.

19. Pasquier L, Fradin M, Chérot E, Martin-Coignard D, Colin E, Journel H, Demurger F, Akloul L, Quélin C, Jauffret V et al. Karyotype is not dead (yet)! Eur J Med Genet 2016; 59: 11-15.

20. Poli MN, Miranda LA, Gil ED, Zanier GJ, Iriarte PF, Zanier JH, Coco R. Male cytogenetic evaluation prior to assisted reproduction procedures performed in Mar del Plata, Argentina. JBRA Assist Reprod 2016; 20: 62-65.

21. Stouffs K, Seneca S, Lissens W. Genetic causes of male infertility. Ann Endocrinol (Paris) 2014; 75: 109-111.

22. Zhang M, Fan HT, Zhang QS, Wang XY, Yang X, Tian WJ, Li RW. Genetic screening and evaluation for chromosomal abnormalities of infertile males in Jilin Province, China. Genet Mol Res 2015; 14: 16178-16184.

23. Li D, Zhang H, Wang R, Zhu H, Li L, Liu R. Chromosomal abnormalities in men with pregestational and gestational infertility in northeast China. J Assist Reprod Genet 2012; 29: 829-836.

24. Fryns JP, Van Buggenhout G. Structural chromosome rearrangements in couples with recurrent fetal wastage. Eur J Obstet Gynecol Reprod Biol 1998; 81: 171-176.

25. Kochhar PK, Ghosh P. Reproductive outcome of couples with recurrent miscarriage and balanced chromosomal abnormalities. J Obstet Gynaecol Res 2013; 39: 113-120.

26. Vozdova M, Oracova E, Kasikova K, Prinosilova P, Rybar R, Horinova V, Gaillyova R, Rubes J. Balanced chromosomal translocations in men: relationships among semen parameters, chromatin integrity, sperm meiotic segregation and aneuploidy. J Assist Reprod Genet 2013; 30: 391-405.

27. Li LL, Dong Y, Wang RX, An N, Yun X, Liu RZ. Sperm aneuploidy and implications for genetic counseling in a pedigree of three t(1;3) balanced translocation carriers. Genet Mol Res 2015; 14: 5003-5009.

28. Venkateshwari A, Srilekha A, Begum A, Sujatha M, Sunitha T, Nallari P, Jyothy A. De novo chromosomal translocation t(3;5)(q13;q35) in an infertile man. Andrologia 2011; 43: 428-430.

29. Mokánszki A, Ujfalusi A, Balogh E, Sümegi A, Antal-Szalmás P, Bazsáné ZK, Molnár Z, Varga A, Sápy T, Jakab A et al. Meiotic segregation study of a novel t(3;6)(q21;q23) in an infertile man using fluorescence in situ hybridization (FISH). Syst Biol Reprod Med 2012; 58: 160-164.

30. Dong Y, Du RC, Jiang YT, Wu J, Li LL, Liu RZ. Impact of chromosomal translocations on male infertility, semen quality, testicular volume and reproductive hormone levels. J Int Med Res 2012; 40: 2274-2283.

31. Gaboon NE, Mohamed AR, Elsayed SM, Zaki OK, Elsayed MA. Structural chromosomal abnormalities in couples with recurrent abortion in Egypt. Turk J Med Sci 2015; 45: 208-213.

32. Celep F, Karagüzel A, Ozeren M, Bozkaya H. The frequency of chromosomal abnormalities in patients with reproductive failure. Eur J Obstet Gynecol Reprod Biol 2006; 127: 106-109.

33. Dutta UR, Rajitha P, Pidugu VK, Dalal AB. Cytogenetic abnormalities in 1162 couples with recurrent miscarriages in southern region of India: report and review. J Assist Reprod Genet 2011; 28: 145-149.

34. Dul EC, van Echten-Arends J, Groen H, Dijkhuizen T, Land JA, van Ravenswaaij-Arts CM. Chromosomal abnormalities in azoospermic and non-azoospermic infertile men: numbers needed to be screened to prevent adverse pregnancy outcomes. Hum Reprod 2012; 27: 2850-2856.

35. Escudero T, Abdelhadi I, Sandalinas M, Munné S. Predictive value of sperm fluorescence in situ hybridization analysis on the outcome of preimplantation genetic diagnosis for translocations. Fertil Steril 2003; 79 (Suppl. 3): 1528-1534.

36. Perrin A, Caer E, Oliver-Bonet M, Navarro J, Benet J, Amice V, De Braekeleer M, Morel F. DNA fragmentation and meiotic segregation in sperm of carriers of a chromosomal structural abnormality. Fertil Steril 2009; 92: 583-589.

37. Oliver-Bonet M, Navarro J, Carrera M, Egozcue J, Benet J. Aneuploid and unbalanced sperm in two translocation carriers: evaluation of the genetic risk. Mol Hum Reprod 2002; 8: 958-963.

38. Haapaniemi Kouru K, Malmgren H, White I, Rodriguez Sanchez A, Syk Lundberg E. Meiotic segregation analyses of reciprocal translocations in spermatozoa and embryos: no support for predictive value regarding PGD outcome. Reprod Biomed Online 2017; 34: 645-652.

39. Rouen A, Carlier L, Heide S, Egloff M, Marzin P, Ader F, Schwartz M, Rogers E, Joyé N, Balet R et al. Potential selection of genetically balanced spermatozoa based on the hypo-osmotic swelling test in chromosomal rearrangement carriers. Reprod Biomed Online 2017; 35: 372-378.

40. Matsuda T, Horii Y, Ogura K, Nonomura M, Okada K, Yoshida O. Chromosomal survey of 1001 subfertile males: incidence and clinical features of males with chromosomal anomalies. Hinyokika Kiyo 1992; 38: 803-809.

41. Zhang YP, Xu JZ, Yin M, Chen MF, Ren DL. Pregnancy outcomes of 194 couples with balanced translocations. Zhonghua Fu Chan Ke Za Zhi 2006; 41: 592-596.

42. Kyu Lim C, Hyun Jun J, Mi Min D, Lee HS, Young Kim J, Koong MK, Kang IS. Efficacy and clinical outcome of preimplantation genetic diagnosis using FISH for couples of reciprocal and Robertsonian translocations: the Korean experience. Prenat Diagn 2004; 24: 556-561.

43. Ko DS, Cho JW, Park SY, Kim JY, Koong MK, Song IO, Kang IS, Lim CK. Clinical outcomes of preimplantation genetic diagnosis (PGD) and analysis of meiotic segregation modes in reciprocal translocation carriers. Am J Med Genet A 2010; 152A: 1428-1433.

44. Castle D, Bernstein R. Cytogenetic analysis of 688 couples experiencing multiple spontaneous abortions. Am J Med Genet 1988; 29: 549-556.

45. Adamoli A, Bernardi F, Chiaffoni G, Fraccaro M, Giardino D, Romitti L, Simoni G. Reproductive failure and parental chromosome abnormalities. Hum Reprod 1986; 1: 99-102.

46. Ocak Z, Özlü T, Ozyurt O. Association of recurrent pregnancy loss with chromosomal abnormalities and hereditary thrombophilias. Afr Health Sci 2013; 13: 447-452.

47. Brandriff B, Gordon L, Ashworth LK, Littman V, Watchmaker G, Carrano AV. Cytogenetics of human sperm: meiotic segregation in two translocation carriers. Am J Hum Genet 1986; 38: 197-208.

48. Antonelli A, Gandini L, Petrinelli P, Marcucci L, Elli R, Lombardo F, Dondero F, Lenzi A. Chromosomal alterations and male infertility. J Endocrinol Invest 2000; 23: 677-683.

49. Goddijn M, Joosten JH, Knegt AC, van der Veen F, Franssen MT, Bonsel GJ, Leschot NJ. Clinical relevance of diagnosing structural chromosome abnormalities in couples with repeated miscarriage. Hum Reprod 2004; 19: 1013-1017.

50. Estop AM, Van Kirk V, Cieply K. Segregation analysis of four translocations, t(2;18), t(3;15), t(5;7), and t(10;12), by sperm chromosome studies and a review of the literature. Cytogenet Cell Genet 1995; 70: 80-87.

51. Gekas J, Thepot F, Turleau C, Siffroi JP, Dadoune JP, Briault S, Rio M, Bourouillou G, Carré-Pigeon F, Wasels R et al. Chromosomal factors of infertility in candidate couples for ICSI: an equal risk of constitutional aberrations in women and men. Hum Reprod 2001; 16: 82-90.

52. Gianaroli L, Magli MC, Ferraretti AP, Munné S, Balicchia B, Escudero T, Crippa A. Possible interchromosomal effect in embryos generated by gametes from translocation carriers. Hum Reprod 2002; 17: 3201-3207.

53. Iyer P, Wani L, Joshi S, Lakshmi J, Dalvi R, Chavan D, Das BR, Mandava S. Cytogenetic investigations in couples with repeated miscarriages and malformed children: report of a novel insertion. Reprod Biomed Online 2007; 14: 314-321.

54. Sugiura-Ogasawara M, Aoki K, Fujii T, Fujita T, Kawaguchi R, Maruyama T, Ozawa N, Sugi T, Takeshita T, Saito S. Subsequent pregnancy outcomes in recurrent miscarriage patients with a paternal or maternal carrier of a structural chromosome rearrangement. J Hum Genet 2008; 53: 622-628.

55. Portnoï MF, Joye N, van den Akker J, Morlier G, Taillemite JL. Karyotypes of 1142 couples with recurrent abortion. Obstet Gynecol 1988; 72: 31-34.

56. Machev N, Gosset P, Warter S, Treger M, Schillinger M, Viville S. Fluorescence in situ hybridization sperm analysis of six translocation carriers provides evidence of an interchromosomal effect. Fertil Steril 2005; 84: 365-373.

57. Meza-Espinoza JP, Anguiano LO, Rivera H. Chromosomal abnormalities in couples with reproductive disorders. Gynecol Obstet Invest 2008; 66: 237-240.

58. Pundir J, Magdalani L, El-Toukhy T. Outcome of preimplantation genetic diagnosis using FISH analysis for recurrent miscarriage in low-risk reciprocal translocation carriers. Eur J Obstet Gynecol Reprod Biol 2016; 203: 214-219.

59. Vegetti W, Van Assche E, Frias A, Verheyen G, Bianchi MM, Bonduelle M, Liebaers I, Van Steirteghem A. Correlation between semen parameters and sperm aneuploidy rates investigated by fluorescence in-situ hybridization in infertile men. Hum Reprod 2000; 15: 351-365.

60. Peschka B, Leygraaf J, Van der Ven K, Montag M, Schartmann B, Schubert R, van der Ven H, Schwanitz G. Type and frequency of chromosome aberrations in 781 couples undergoing intracytoplasmic sperm injection. Hum Reprod 1999; 14: 2257-2263.

61. Martin RH, Hultén M. Chromosome complements in 695 sperm from three men heterozygous for reciprocal translocations, and a review of the literature. Hereditas 1993; 118: 165-175.

62. Jenderny J. Sperm chromosome analysis of two males heterozygous for a t(2;17)(q35;p13) and t(3;8)(p13;p21) reciprocal translocation. Hum Genet 1992; 90: 171-173.