ISSN: 1813-4890

Analysis of the result of deafness gene screening in 8225 newborns

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Abstract

We analyzed the result of neonatal deafness gene screening in sanshui district of foshan in order to provide reference for prevention and control. In our syudy, a total of 8225 neonates born in Foshan Sanshui District People's Hospital from 2021 to 2023 were screened for deafness gene by PCR combined with diversion hybridization, and the results were analyzed. The result showed that 224 cases were found to carry the deafness gene mutation, with an overall mutation carrying rate of 2.72%. Among them, 120 carriers (1.46%) of GJB2 mutation, 72 carriers (0.88%) of SLC26A4 mutation, 23 carriers (0.28%) of mitochondrial DNA mutation, 7 carriers (0.09%) of GJB3 mutation. In addition, Two kinds of mutations were observed in 2 carriers (0.02%). Therefore, GJB2 and SLC26A4 were the main mutations in neonatal deafness gene in sanshui district of foshan. Aanlysis of deafness gene screening plays a great significance for the genetic counseling and the guidance of marriage and childbearing. It is helpful for early prevention and etiology diagnosis of deafness.

Keywords

Newborn; Deafness; Gene screening; Carrying rate.

1. Introduction

According to the Report on the Prevention and Treatment of Birth Defects in China, deafness has become the second largest birth defect in China. About 35,000 cases of congenital deafness are born every year, of which 50% to 60% are caused by genetic factors, causing a heavy burden to the family and society [1]. By analyzing the genetic screening results of 8225 newborns delivered in Foshan Sanshui District People's Hospital from 2021 to 2023, we studied the carrying rate and distribution of mutation sites of neonatal deafness genes in Sanshui District, which has positive significance for clinical genetic consultation, etiology diagnosis, early prevention and intervention.

2. Research object and method

2.1 Research object A total of 8225 newborns, aged 48-72h, who were born in Foshan Sanshui District People's Hospital from 2021 to 2023 and underwent genetic screening for deafness were selected as the study objects. Among them, there were 4407 males and 3818 females, with a male to female ratio of 1.15:1. This study was approved by the Ethics Committee of the hospital, and all neonatal guardians who participated in this study signed informed consent.

2.2 Method

2.2.1 Specimen collection The heel blood of the newborn was collected within 48-72h after birth, and dropped on the collection filter paper. 3 blood spots were collected, the diameter of which was not less than 8m. And then dried naturally for 3-4h and stored at room temperature.

2.2.2 DNA extraction A blood spot was clipped into a 1.5mL centrifuge tube. 400μL sample dilution and 20μL protease K were added and heated at 56°C for 30min. The liquid was transferred to a nucleic acid extraction plate, and DNA was extracted by magnetic bead method. The DNA was stored at -20°C.

2.2.3 DNA amplification and hybridization

DNA amplification and hybridization of the samples were completed by using the hearing susceptibility gene detection kit. The presence of deafness gene was confirmed by the chromogenic sites of the hybridized membrane strips.

2.3 Detection index Mutation sites of GJB2 gene: c.235del C,c.35del G,c.299del AT,c.155del TCTG,c.176 del16. 3 mutation sites of SLC26A4 gene: c.IVS7-2A>G,c.1229 C>T,c.2168 A>G. Mutation sites of mitochondrial DNA (mtDNA) : 2 mutation sites of 12SrRNA (g.1555 A>G,g.1494 C >T), and 2 mutation sites of tRNA (G.7445 A>G,G.12201 T> C). Mutation site of GJB3 gene: c.538 C>T.

2.4 Statistical analysis SPSS 22.0 software was used for statistical analysis of the data, Excel was used for data entry, and Chi-square test was used for comparison between groups. $P < 0.05$ was considered statistically significant.

3. Result

3.1 Screening results of deafness gene 8371 neonates were born in our hospital between 2021 and 2023, of which 8225 completed screening for deafness gene, with a screening rate of 98.3%. Among 8225 neonates, 224 were found to be carriers of deafness gene, the carrying rate was 2.72%. There were 117 male deafness gene carriers,carrying rate was 2.65% (117/4407) and 107 female deafness gene carriers , carrying rate of 2.8% (107/3818). There was no significant difference between male and female carriers ($\chi 2 = 0.168$, $P > 0.05$).

3.2 Distribution of deafness gene mutation sites Among 224 cases of deafness gene carriers, 120 cases were GJB2 gene mutation and carrying rate was 1.46%. There were 101 cases of c.235delC mutation, and the carrying rate was 1.23%. There were 72 cases with SLC26A4 gene mutation, carrying rate was 0.88%. Carrying rate of mtDNA mutation was 0.28%,23 cases. Carrying rate of GJB3 gene mutation was 0.09%, 7 cases. The remaining 2 cases were complex mutations with a carrying rate of 0.02%. Details are given in Table 1

Table 1 Distribution of deafness gene mutation sites

Genotype	Gene mutation site	Cases	carrying rate （%）	ratio （%）
GJB2		120	1.46	53.57
	c.235del C heterozygous mutation	101	1.23	45.09
	c.299del AT heterozygous mutation	13	0.16	5.80
	c.176del 16 heterozygous mutation	6	0.07	2.68
SLC26A4		72	0.88	32.14
	c.IVS7－2A＞G heterozygous mutation	50	0.61	22.32
	c.1229C＞T heterozygous mutation	16	0.19	7.14
	c.2168A＞G heterozygous mutation	6	0.07	2.68
mtDNA		23	0.28	10.27
	g.1555A＞G homogeneous mutation	10	0.12	4.46
	g.1555A＞G heteromutation	8	0.10	3.57
	G.7445A＞G homogeneous mutation	4	0.05	1.79

	G.7445A＞G heteromutation	1	0.01	0.45
GJB3	c.538C＞T heterozygous mutation	7	0.09	3.13
Complex mutations	c.235del C heterozygous mutation & c.299del AT heterozygous mutation	1	0.01	0.45
	c.299del AT heterozygous mutation & c.IVS7－2A＞G heterozygous mutation	1	0.01	0.45
Total		224	2.72	100.00

4. Discussion

Deafness is a sensory dysfunction disease. With the development of medicine and the popularization of the concept of eugenics, the screening of hereditary deafness has gradually attracted attention in our country[2]. According to reports, the gene carrying rate of neonatal deafness was 3.68% in Guangzhou, 3.63% in Huizhou, 3.85% in eastern Guangdong, and 4.15% in northern Guangdong[3-6]. In this study, 8225 subjects were selected for hereditary deafness gene, and a total of 224 deafness gene carriers were detected, with a carrying rate of 2.72%, which was lower than other areas in Guangdong Province.

GJB2 gene is the earliest discovered deaf-causing gene with autosomal recessive inheritance. The coding protein Cx26 is a member of the gap junction protein family, which is highly expressed in the cochlear gap junction and plays an important role in maintaining the normal physiological function of the inner ear[7]. In China, GJB2 gene is the most common deafness gene, accounting for 55%, and the mutation site is mainly c.235del C[8-9]. A total of 120 cases of GJB2 gene mutation were detected in our study, accounting for 53.57% of the deafness gene carriers. There were 101 cases of c.235 del C mutation, accounting for 45.09% of the carriers. In addition, two mutation types, c.35del G and c.155del TCTG, were not detected.

SLC26A4, also known as the PDS gene, is located in human chromosome 7q31 and encodes the Pendrin protein as a chloride and iodide transporter, which plays an important role in the inner ear and thyroid gland[10]. SLC26A4 gene mutation is mainly manifested as vestibular aqueduct enlargement, sensorineural hearing impairment, and moderate to extremely severe deafness[11]. Our results showed that the carrier rate of SLC26A4 gene mutation was 0.88%, ranking second, and the main mutation site was c.IVS7-2A > G.

The mitochondrial DNA gene is maternal inheritance, in which 12S rRNA belongs to the drug-induced deafness gene, and mutations can lead to hearing loss caused by aminoglycoside antibiotics. In our result, 18 cases of 12S rRNA mutations were all G. 1555A > G site mutations, including 10 homogenous mutations and 8 heterogenous mutations, with a carrying rate of 0.22%. For such patients, aminoglycoside antibiotics should be banned for life once diagnosed. Mitochondrial tRNA mutation is also an important cause of hearing loss in the Chinese population. Five cases of mitochondrial tRNA mutation were detected in Sanshui District, all of which were G.7445A > G, and the carrying rate was 0.06%, which was consistent with the carrying rate of G.7445A > G mutation site in newborns in Foshan[12-13], and no G.12201T> C mutation was detected. GJB3 gene is located on chromosome 1, and the mutation of this gene can lead to high frequency sensorineural deafness[14]. In this study, the carrying rate of GJB3 gene was low, only 0.09%.

There are many types of deafness genes, and the degree of genomic heterogeneity is also high. In the studies of different regions and different nationalities, the data of deafness genes are greatly different[15]. Through more detailed analysis of the genetic data of deafness in Sanshui District, it is helpful to design the screening program of newborn deafness in this district, effectively realize the purpose of early screening and intervention of deafness, and reduce the incidence of deafness.

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