



中国西部某三甲医院藏族与汉族唇腭裂患者ABO血型及Rh血型分布研究*

段世均¹, 郑谦¹, 石冰¹, 冯帆^{2△}

1. 口腔疾病防治全国重点实验室 国家口腔医学中心 国家口腔疾病临床医学研究中心 四川大学华西口腔医院(成都 610041);
2. 成都医学院人事处(成都 610041)

【摘要】 目的 研究中国西部藏族与汉族唇腭裂患者ABO血型和Rh血型分布的关系。方法 统计2016年1月-2023年9月就诊于四川大学华西口腔医院的藏族及汉族先天性唇腭裂患者的A、B、O、AB血型及Rh血型,与正常人群的A、B、O、AB血型及Rh血型进行比较。分别统计A、B、O、AB血型患者中单纯唇裂、单纯腭裂及唇裂伴腭裂表型发病人数,采用卡方检验进行统计学分析。结果 共收集藏族唇腭裂患者1227例,汉族唇腭裂患者4064例,对照组人群5360例。藏族唇腭裂患者ABO血型分布特征为O>B>A>AB, Rh阳性血型为100%, O型占41.15%, B型占30.64%。汉族唇腭裂患者ABO血型分布特征为O>A>B>AB, Rh阳性血型为99.58%, O型占35.78%, A型占30.54%。藏、汉族唇腭裂患者之间ABO血型表现出明显差异($P<0.005$), Rh血型无明显差异;藏族唇腭裂患者与对照组人群ABO血型分布显示出明显的差异,而汉族唇腭裂患者与对照组人群ABO血型分布并未显示出明显的差异;在对亚型的分析中发现,藏族患者单纯唇裂、单纯腭裂以及唇裂伴腭裂各亚型血型分布均为O>B>A>AB,汉族唇腭裂患者各亚型血型分布均为O>A>B>AB,单纯唇裂及唇裂伴腭裂亚型中藏族与汉族血型分布存在差异($P<0.001$),而在腭裂亚型分组中血型分布无差异;藏族唇腭裂患者中O型血的比例明显高于汉族唇腭裂患者。四川省、西藏自治区及青海省藏族唇腭裂患者血型分布均为O>B>A>AB,其中甘孜州石渠县、白玉县及昌都市察雅县以B型血为主,其余均以O型血为主。结论 中国西部藏族与汉族唇腭裂患者ABO血型分布均表现出明显差异,唇腭裂患者中O型血的分布高于正常人群,且在不同表型中均表现出同样的趋势,但仅在单纯唇裂与唇裂伴腭裂表型中表现出藏族与汉族间ABO血型分布的差异,O型血藏族唇腭裂患者较汉族患者更容易出现唇裂畸形。

【关键词】 唇裂 腭裂 藏族 ABO血型系统 Rh血型系统

Distribution of ABO and Rh Blood Groups in Tibetan and Han Populations With Cleft Lip and Palate in a Tertiary Hospital in Western China DUAN Shijun¹, ZHENG Qian¹, SHI Bing¹, FENG Fan^{2△}. 1. State Key Laboratory of Oral Diseases, National Center for Stomatology, National Clinical Research Center for Oral Diseases, West China Hospital of Stomatology, Sichuan University, Chengdu 610041, China; 2. Department of Human Resources, Chengdu Medical College, Chengdu 610041, China

△ Corresponding author, E-mail: fengfan13@126.com

【Abstract】 Objective Congenital cleft lip and palate is a common birth defect that seriously affects the lives of the afflicted children and their families. Previously, no research has been done to investigate the pathogenic characteristics of cleft lip and palate among ethnic minorities, for example, Tibetans, a minority ethnic group with a large population in China. This study aims to investigate the relationship between the occurrence of cleft lip and palate in Tibetans and Han Chinese in western China and the distribution of ABO blood groups and Rh blood groups to provide a theoretical basis for the precise prevention and treatment of cleft lip and palate. **Methods** In this study, statistics on Tibetan patients with cleft lip and palate, some Han patients with cleft lip and palate, and normal controls from western China were retrospectively collected. All participants were patients from West China Stomatology Hospital, Sichuan University. All patients with cleft lip and palate received treatment at the hospital between January 2016 and September 2023. The normal controls were outpatients or inpatients who did not have cleft lip and palate, and who received treatment at the hospital between January 2020 and October 2023. Information on the A, B, O, and AB blood groups and Rh positive and negative blood groups of the patients was collected and compared with that of the normal controls. The incidence of different phenotypes, including cleft lip alone, cleft palate alone, and cleft lip with cleft palate, in patients of blood groups A, B, O and AB were statistically analyzed by Chi-square test. **Results** A total of 1227 Tibetan patients with cleft lip and palate, 4064 Han patients with cleft lip and palate, and 5360 normal controls were included in the study. Among all the patients with cleft lip and palate, 1863 had cleft lip alone, 1425 had cleft palate alone, and 2003 had cleft lip with cleft palate. The ABO blood group distribution of Tibetan patients with cleft lip and palate was characterized as O>B>A>AB, with Rh positive

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△ 通信作者, E-mail: fengfan13@126.com

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blood group accounting for 100%, blood type O accounting for 41.15%, and blood type B accounting for 30.64%. The blood group distribution of the Han patients with cleft lip and palate was characterized as O>A>B>AB, with Rh positive blood group accounting for 99.58%, blood type O accounting for 35.78%, and type A accounting for 30.54%. There was a significant difference in ABO blood groups between Tibetan and Han patients with cleft lip and palate ($P<0.005$), but no significant difference in Rh blood groups. The ABO blood group distribution of the Tibetan patients with cleft lip and palate showed an obvious difference from that of the control group, while those of the Han patients with cleft lip and cleft palate and the control group did not show obvious differences. In the analysis of the subtypes, it was found that the blood group distribution in the subtypes of cleft lip alone, cleft palate alone, and cleft lip with cleft palate in the Tibetan population was O>B>A>AB, while that in the Han Chinese population was O>A>B>AB. There were differences in blood group distribution between Tibetans and Hans of the subtypes of cleft lip alone and cleft lip with cleft palate ($P<0.001$), but there was no difference in blood group distribution in the population of cleft palate-only subtype. The proportion of blood type O in Tibetan patients with cleft lip and palate was significantly higher than that in the Han patients with cleft lip and palate. The blood group distribution of Tibetan patients with cleft lip and palate in Sichuan Province, Xizang Autonomous Region, and Qinghai Province was always O>B>A>AB. Tibetan patients from Shiqu County and Baiyu County, Ganzi Tibetan Autonomous Prefecture and Chaya County, Qamdo City were predominantly of blood type B, and those from other regions were mainly of blood type O. **Conclusion** There were significant differences in the phenotype composition and ABO blood group distribution between the Tibetan and Han populations with cleft lip and palate in western China. The distribution of blood group O in the population with cleft lip and palate was higher than that in the normal population, and the same trend was observed for different phenotypes. However, differences between Tibetan and Han populations in ABO blood group distribution were only found in the phenotypes of cleft lip only and cleft lip with palate. Tibetans with blood type O are more prone to cleft lip deformity than Han people, and the effect in the phenotype of cleft lip with palate is less pronounced than that in the phenotype of cleft lip only.

【Key words】 Cleft lip Cleft palate Tibetans ABO blood-group system Rhesus blood group system

血型是人类血液的主要特征之一,其中ABO及Rh血型是血液系统中最重要的两个血型系统,自发现红细胞血型以来,血液抗原所表达的各种遗传性状在遗传学、临床医学及法医学等领域都发挥了重要的作用^[1]。随着现代生物学技术的发展,科学家已经揭示了ABO血型系统的分子基础,ABO基因位于人类第9号染色体9q34.1~9q34.2区域,由7个外显子和6个内含子组成,其中第6和第7外显子编码了大部分的糖基转移酶催化活性区域,而该编码产物糖基转移酶则是决定ABO血型的重要功能部分^[1]。随着学者对血型研究的进一步深入,越来越多的研究表明ABO血型与疾病有密切关系,作为重要的风险因素参与了多种疾病的发生、发展^[2-3],但其确切的参与机制还未完整阐明。

先天性唇腭裂作为口腔颌面部最常见的一种出生缺陷,多年以来一直是我国新生儿主要出生缺陷疾病之一,严重影响我国出生人口素质^[4]。综合国内外研究报道,唇腭裂世界平均发生率约1/700,但在亚洲及拉丁美洲人群中唇腭裂的发生率明显高于其他地区,可达到1/500^[5],其中中国属于唇腭裂高发病率国家,其发生率约1.38%~1.67%,而西部地区的发生率甚至高达1.97%~2.19%^[6-7]。唇腭裂的病因复杂,涉及基因、环境以及二者之间的相互作用,随着唇腭裂遗传学研究的不断深入,越来越多的候

选基因或染色体区域被发现与唇腭裂的发生相关^[5,8]。ABO血型的遗传稳定性高,既往已有研究认为ABO血型与唇腭裂的发生有一定的相关性^[9-11],为探寻唇腭裂的遗传特征提供了线索。中国地域辽阔,民族多样,其中藏族人群主要分布于西部地区,且聚居地基本处于高海拔地区,其生存环境以及种族来源与汉族均存在明显差异^[12],因此有必要分析藏族与汉族唇腭裂发生与ABO血型的关系以及二者之间的不同,为开展藏族与汉族唇腭裂精准防控提供依据。

1 资料与方法

1.1 研究对象

以2016年1月-2023年9月就诊于四川大学华西口腔医院的藏族及汉族先天性唇腭裂患者作为研究对象,同一患者多次入院只统计一次。病例组纳入标准:①患者临床诊断为先天性唇腭裂,包括唇裂、腭裂以及唇裂伴腭裂;②患者身份证登记民族为藏族及汉族。排除标准:①患者不符合先天性唇腭裂诊断;②患者入院后因各种原因退院导致信息不全。对照组病例来自本院2020年1月-2023年10月门诊就诊和非唇腭裂疾病入院患者。对照组纳入标准:①患者身份证登记民族为汉族;②以非唇腭裂为主诉就诊;③体格检查无唇腭裂畸形。

1.2 研究内容

所有唇腭裂患者入院时均签署知情同意书(未成年患者由监护人签署),该研究通过四川大学华西口腔医院伦理委员会批准,批准号WCHSIRB-D-2016-281R1。所有研究对象由四川大学华西口腔医院唇腭裂外科专科医师对其进行病史采集及体格检查,调查及记录内容包括患者姓名、性别、居住地址及诊断等。患者就诊或入院后,由护士抽血送医院检验科检测ABO及Rh血型。

1.3 唇腭裂类型分类

唇腭裂畸形依据裂隙累及的解剖部位,可将其分为单纯唇裂(cleft lip only, CLO)、单纯腭裂(cleft palate only, CPO)以及唇裂伴腭裂(cleft lip with palate, CLP)。其中单纯唇裂仅累及唇部解剖结构,可表现出左侧、右侧以及双侧;单纯腭裂累及腭部解剖结构,依据其严重程度可以表现出从切牙孔至悬雍垂不同程度的裂开;唇裂伴腭裂则累及唇部和腭部,部分完全性腭裂与唇裂同时发生,裂隙在前颌骨部分,斜向侧方,与同侧牙槽突裂和唇裂相接。

1.4 统计学方法

所有统计分析采用SPSS 22.0软件进行,组间比较采用 χ^2 检验, Bonferroni多重校正的 $P=0.05/4=0.0125$, $P<0.0125$ 为差异有统计学意义。

2 结果

2.1 藏族与汉族唇腭裂患者表型分布

本研究共纳入5291例唇腭裂患者,其中藏族患者1227例(23.19%),汉族患者4064例(76.81%),藏族唇腭裂构成比低于汉族($P<0.001$);单纯唇裂1863例,单纯腭裂1425例,唇裂伴腭裂2003例,各表型分布见表1。结果显示不同性别藏族与汉族患者单纯唇裂、单纯腭裂及唇裂伴腭裂的构成比的差异有统计学意义($P<0.001$),说明藏族唇

表 1 藏族与汉族唇腭裂患者表型分布

Table 1 Distribution of cleft lip and palate patients of Tibetan and Han ethnicities

Race	Sex	CLO	CPO	CLP	Total	χ^2	P
Tibetan	Male	239	57	366	662	149.987	<0.001*
	Female	235	111	219	565	495.405	<0.001 [△]
Han	Male	782	449	970	2201	53.791	<0.001 [#]
	Female	607	808	448	1863	108.786	<0.001 [▲]
Total		1863	1425	2003	5291		

CLO: cleft lip only; CPO: cleft palate only; CLP: cleft lip with palate.
* Overall comparison of the distribution of phenotypes between Tibetan and Han patients. [△] Comparison of the distribution of phenotypes between male and female groups in Tibetan and Han patients. [#] Comparison of the distribution of phenotypes between Tibetan and Han males. [▲] Comparison of the distribution of phenotypes between Tibetan and Han females.

腭裂患者各表型构成与汉族唇腭裂患者有明显不同。

2.2 藏族与汉族唇腭裂患者ABO血型分布

对藏族与汉族唇腭裂患者ABO血型分布进行比较,藏族唇腭裂患者血型频率特征为O>B>A>AB,而汉族唇腭裂患者血型频率特征为O>A>B>AB,藏族唇腭裂患者中O型占41.15%,B型占30.64%,汉族唇腭裂患者中O型占35.78%,A型占30.54%,藏族与汉族唇腭裂患者ABO血型分布差异有统计学意义($P<0.001$),提示藏族唇腭裂患者与汉族唇腭裂患者血型分布存在不同;按照性别分组进行对比,不管是相同人群男女性别之间,还是藏族与汉族相同性别之间的差异均有统计学意义($P<0.005$),进一步证明藏族与汉族唇腭裂患者间的差异在男性与女性均存在。见表2。

表 2 藏族与汉族唇腭裂患者ABO血型统计结果

Table 2 Statistical findings for ABO blood groups in Tibetan and Han people with cleft lip and palate

Race	Sex	n	A	B	AB	O	χ^2	P
Tibetan	Male	662	130	212	46	274	46.997	<0.001*
	Female	565	135	164	35	231	43.250	<0.001 [△]
Han	Male	2210	682	558	172	789	36.245	<0.001 [#]
	Female	1863	559	474	165	665	14.678	0.003 [▲]

* Overall comparison of ABO blood group distribution between Tibetan and Han patients. [△] Comparison of ABO blood group distribution between male and female groups in Tibetan and Han patients. [#] Comparison of ABO blood group distribution between Tibetan and Han male patients. [▲] Comparison of ABO blood group distribution between Tibetan and Han female patients.

2.3 藏族唇腭裂患者与正常对照组ABO血型分布

本研究共收集5360例汉族非唇腭裂畸形患者作为正常对照组。将藏族唇腭裂患者与正常对照组进行比较,发现正常对照组血型分布为O>A>B>AB,藏族唇腭裂患者与正常对照组ABO血型分布差异有统计学意义($P<0.001$)。进一步将所有藏族患者按照性别分组进行分析,藏族唇腭裂患者与正常对照组男女性别之间的ABO血型分布差异仍有统计学意义($P<0.001$),但Cramer's $V=0.062$,提示血型与性别之间的相关性较弱;藏族唇腭裂男、女性患者的血型分布均为O>B>A>AB,而正常对照组男、女性血型分布均为O>A>B>AB,在相同性别人群中藏族唇腭裂患者与正常对照组间ABO血型分布差异均有统计学意义($P<0.001$)。见表3。

2.4 汉族唇腭裂患者与正常对照组ABO血型分布

将汉族唇腭裂患者与正常对照组进行比较,发现两组对象血型分布均为O>A>B>AB,汉族唇腭裂患者中O型占35.78%,正常对照组中O型占34.03%,两组ABO血型分

表3 藏族唇腭裂患者与正常对照组ABO血型统计结果

Table 3 Statistical findings for ABO blood groups of Tibetan patients with cleft lip and palate and the Han control group

Group	Sex	n	A	B	AB	O	χ^2	P
Tibetan patients	Male	662	130	212	46	274	75.055	<0.001 [△]
	Female	565	135	164	35	231	69.139	<0.001 [*]
Han control	Male	2544	836	621	223	864	52.440	<0.001 [#]
	Female	2816	873	718	265	960	21.872	<0.001 [▲]

[△] Comparison of ABO blood group distribution between male and female groups in Tibetan patients and Han control group, Cramer's V=0.062.

^{*} Overall comparison of ABO blood group distribution between Tibetan patients and Han control group. [#] Comparison of ABO blood group distribution between Tibetan male patients and Han male control group.

[▲] Comparison of ABO blood group distribution between Tibetan female patients and Han female control group.

布差异无统计学意义。将所有汉族唇腭裂患者按照性别分组进行分析,汉族唇腭裂患者与正常对照组男女性别之间的ABO血型分布存在差异($P=0.004$),但Cramer's $V=0.030$,提示血型与性别之间的相关性较弱,不管是男性还是女性,汉族唇腭裂患者与正常对照组ABO血型分布均无明显差异($P>0.05$)。见表4。

表4 汉族唇腭裂患者与正常对照组ABO血型分布结果

Table 4 The distribution of ABO blood groups in the Han cleft lip and palate patients and the Han control group

Group	Sex	n	A	B	AB	O	χ^2	P
Han patients	Male	2201	682	558	172	789	24.360	0.004 [△]
	Female	1863	559	474	165	665	5.269	0.156 [*]
Han normal control	Male	2544	836	621	223	864	4.205	0.240 [#]
	Female	2816	873	718	265	960	1.570	0.666 [▲]

[△] Comparison of ABO blood group distribution between male and female groups in Han patients and Han control group, Cramer's V=0.030.

Overall comparison of ABO blood group distribution between Han patients and Han control group. [#] Comparison of ABO blood group distribution between Han male patients and Han male control group.

[▲] Comparison of ABO blood group distribution between Han female patients and Han female control group.

2.5 唇腭裂患者与正常对照组Rh血型分布

本研究所收集的藏族唇腭裂患者Rh阳性占比为100%,而汉族唇腭裂患者Rh阳性占比为99.58%,Rh阴性占比为0.42%,正常对照组Rh阳性占比为99.74%,Rh阴性占比为0.26%。汉族唇腭裂患者Rh阴性排序为O⁻>A⁻>B⁻>AB⁻,而正常对照组Rh阴性排序为A⁻>O⁻>B⁻>AB⁻,但两组人群Rh血型分布差异无统计学意义。见表5。

2.6 唇腭裂各亚型ABO血型分布

按照唇腭裂不同亚型进行分组比较,发现藏族患者单纯唇裂、单纯腭裂以及唇裂伴腭裂各亚型血型分布均为O>B>A>AB,而汉族唇腭裂患者各亚型血型分布均为

表5 唇腭裂患者与正常对照组Rh血型分布结果

Table 5 The distribution of Rh blood groups in the cleft lip and palate patients and the Han normal control group

Group	n	Rh ⁺	A ⁻	B ⁻	AB ⁻	O ⁻	χ^2	P
Tibetan patients	1227	1227	0	0	0	0	1.74	0.206 [*]
Han patients	4064	4047	3	2	1	11		
Han control	5360	5346	8	1	0	5		

^{*} Han cleft lip and palate patients vs. Han control group.

O>A>B>AB;按照亚型进行比较,发现在单纯唇裂及唇裂伴腭裂亚型中藏族与汉族血型分布存在差异($P<0.001$),而在单纯腭裂亚型分组中血型分布无明显差异($P=0.557$),见表6。藏族与汉族唇腭裂患者均为以O型血为主,本研究进一步将A型血、B型血、AB型血统一为非O型血,发现在单纯唇裂亚型中,藏族单纯唇裂患者中O型血的比例高于汉族单纯唇裂患者($P=0.006$),而在单纯腭裂以及唇裂伴腭裂亚型中,藏族与汉族患者均无明显差异($P=1.000, P=0.015$),见表7。

表6 唇腭裂各亚型ABO血型分布结果

Table 6 The distribution of ABO blood groups among patients of subtypes of cleft lip and palate

Group	n	A	B	AB	O	χ^2	P
Tibetan CLO	474	100	150	25	199	30.146	<0.001
Han CLO	1389	432	345	128	484		
Tibetan CPO	168	46	49	12	61	2.077	0.557
Han CPO	1257	392	307	99	459		
Tibetan CLP	585	119	177	44	245	18.797	<0.001
Han CLP	1418	417	380	110	511		

The abbreviations are explained in the note to Table 1.

表7 唇腭裂各亚型O型血与非O型血分布结果

Table 7 Distribution of patients with type O blood and non-type-O blood in each subtype of cleft lip and palate

Group	n	Non-O	O	χ^2	P
Tibetan CLO	474	275	199	7.754	0.006
Han CLO	1389	905	484		
Tibetan CPO	168	107	61	0.003	1.000
Han CPO	1257	798	459		
Tibetan CLP	585	340	245	6.019	0.015
Han CLP	1418	907	511		

The abbreviations are explained in the note to Table 1.

2.7 研究纳入藏族唇腭裂患者ABO血型地区分布情况

按照1227例藏族唇腭裂患者入院登记地区来源统计,地区分布前三位的分别是四川省677例(55.18%),西藏自治区431例(35.13%),青海省100例(占8.15%),其血型分布均为O>B>A>AB,3组间血型分布差异无统计学意

义,另外还有来自甘肃省患者(17例),新疆维吾尔自治区及云南省各1例;进一步对四川省内唇腭裂来源主要县域进行分析,来源于甘孜州石渠县及白玉县以B型血为主,其余均以O型血为主;对西藏自治区唇腭裂来源主要县域进行分析,来源于昌都市察雅县以B型血为主,其余均以O型血为主,见图1。

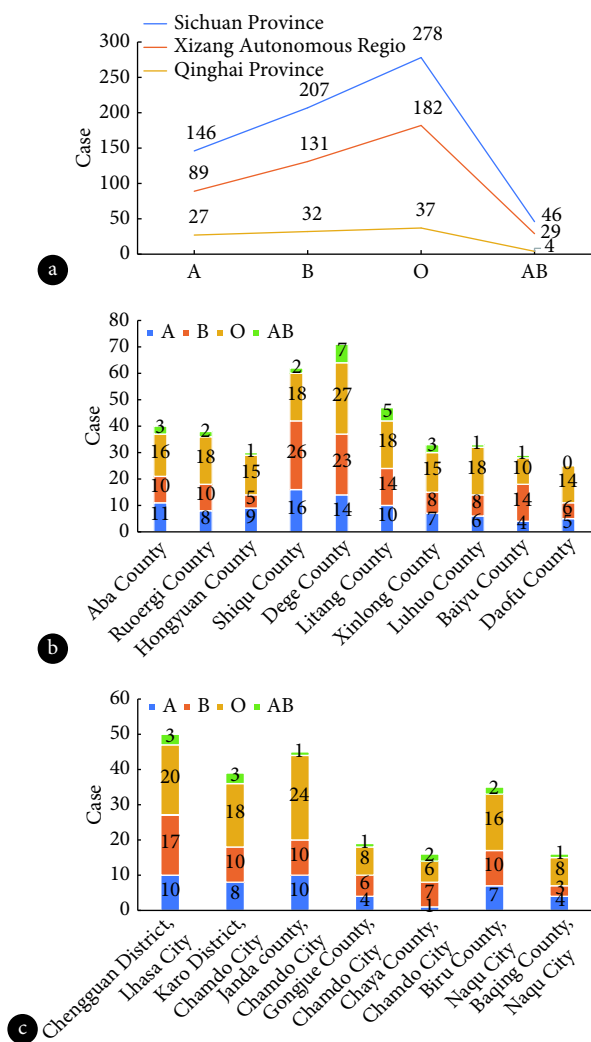


图1 某三甲口腔医院2016-2023年藏族先天性唇腭裂患者ABO血型地区分布

Fig 1 Regional distribution of ABO blood group in Tibetan patients with congenital cleft lip and palate in 2016-2023 from a tertiary stomatology hospital

a, Overall distribution map in Sichuan Province ($n=677$), Xizang Autonomous Region ($n=431$) and Qinghai Province ($n=100$); b, ABO blood group distribution map in major counties of Sichuan Province; c, ABO blood group distribution map in major counties of Xizang Autonomous Region.

3 讨论

先天性唇腭裂是口腔颌面部最常见的一种出生缺陷,是由于胚胎在发育早期因各种因素导致面突融合障碍所致^[5]。依据出生缺陷监测中心数据以及各地区文献

报道,唇腭裂一直是我国主要出生缺陷之一^[4,13-14];研究显示唇腭裂的发生存在明显的种族、地域差异^[5,8],而我国民族众多、地域广阔且东西部经济差异较大,导致东西部的唇腭裂发生率也存在不同^[7,15],基于我国少数民族的唇腭裂发生率仍未见报道,藏族作为我国较大人群的少数民族,长期生活在高海拔地区,不管是遗传性状还是生活习惯与汉族人群均存在差异^[12,16],因此有必要开展针对藏族人群的唇腭裂相关研究,希望获得更多唇腭裂病因学线索,为藏族人群制定唇腭裂预防策略提供更多依据。

ABO血型是人类最早发现以及最重要的血型分类,在亲代及子代间保持着稳定的遗传特征^[17],目前已有大量文献报道不同ABO血型与疾病发生相关,如A型血与胃癌、B型血与新生儿罹患B组链球菌导致的疾病、A型血与胰腺癌、AB型血与子痫前期等^[1-3,18-19]。既往研究也有报道ABO血型与中国不同地区唇腭裂的相关性,李小丹等^[10]报道湖北唇腭裂人群中A型血较正常人群低,O型血较正常人群高;史春玲等^[11]报道在东北地区腭裂患者与对照组血型分布无明显差异,腭裂的发生与ABO血型无关;杨威等^[20]报道在河北地区唇腭裂人群中B型血患者明显高于其他血型。

本研究针对就诊于四川大学华西口腔医院的藏族及汉族唇腭裂患者进行了分类研究,发现藏族唇腭裂患者血型频率特征为O>B>A>AB,而汉族唇腭裂患者血型频率特征均为O>A>B>AB,藏族与汉族唇腭裂患者均以O型血为主,这与湖北唇腭裂人群类似,而与河北唇腭裂人群不同,但藏族与汉族唇腭裂的血型总体分布以及男性、女性间均存在明显差异,进一步明确了藏族与汉族人群遗传背景的不同,分析发现藏族唇腭裂患者中B型血的比例明显高于汉族唇腭裂患者,而汉族唇腭裂患者中的A型血比例又明显高于藏族唇腭裂患者,这可能是藏汉唇腭裂人群的差异所在。通过与汉族正常对照进行比较,藏族唇腭裂患者与汉族正常对照间ABO血型分布、藏族唇腭裂患者与汉族正常对照男女性别之间的ABO血型分布均存在明显差异,而汉族唇腭裂患者与汉族正常对照间ABO血型分布差异无统计学意义,但按照性别分组进行分析,汉族唇腭裂患者与汉族正常对照男女性别之间的ABO血型分布存在明显差异,由此可见种族差异所带来的遗传异质性起了不可忽视的作用,因此针对遗传性疾病防控措施的制定与实施应当考虑地域、种族等因素。另外本研究所纳入的藏族唇腭裂患者均为Rh⁺血型,而汉族唇腭裂患者中Rh⁻型血比例为0.42%,汉族正常对照Rh⁻型血比例为0.26%,汉族唇腭裂患者与汉族正常对照之间无明显差异;周云^[21]报道藏族人群中RhD⁻型频率为

0.6%, 明显高于本研究纳入藏族唇腭裂患者, 一方面可能与地区差异性相关, 另一方面可能与本研究未进行Rh阴性确诊试验, 可能遗漏弱抗原所导致的阳性结果。

唇腭裂包含多种表型, 随着研究的不断深入, 学者发现唇裂、腭裂与唇裂伴腭裂这3种亚型存在着较明显的遗传差异^[8, 22], 而针对复杂性疾病, 表型的精确诊断在确定疾病的遗传机制中起了重要作用^[23]。本研究将所有唇腭裂患者按照不同亚型进行分析, 发现唇裂及唇裂伴腭裂亚型藏族与汉族患者间血型分布存在差异, 差异也主要表现在A型血与B型血分布的差异, 而腭裂患者间无明显差异。本研究所纳入的唇腭裂患者均以O型血比例最多, 为进一步探究O型血与各表型中是否存在相关性, 将A、B及AB型血统一为非O型血进行比较, 发现在单纯唇裂亚型中藏族与汉族患者间O型血的比例有明显差异, 说明O型血藏族人群更容易出现唇裂畸形; 而在单纯腭裂以及唇裂伴腭裂亚型中, 藏族与汉族患者间均无明显差异, 说明O型血在腭裂和唇裂伴腭裂表型中的作用较唇裂表型弱。

唇腭裂致病机制复杂, 其中综合征型唇腭裂中绝大多数病例符合孟德尔单基因遗传病模式, 而非综合征型唇腭裂被认为是一种多基因易感疾病, 已报道的与唇腭裂发生相关的染色体区域包括1p22、1p36、1q32、2p21、8q24、9q22~q34、10q25、13q31、17q22、15q22等^[5, 8, 24], 目前已有多项研究报道位于9q22-q34染色体区域的PTCH1、TGFBRI、FOXE1、KLF4等基因在唇腭裂发生中发挥作用^[25-27]。ABO血型基因位于人类第9号染色体9q34.1~9q34.2区域, 且ABO血型表现为显性遗传, 推测9q22~q34染色体区域可能存在与ABO血型基因相关联的唇腭裂易感基因, 但仍需更严谨的分子生物学实验对其进行验证。本研究是基于单中心数据开展的回顾性研究, 同时受限于医院地域, 研究对象主要局限于西部唇腭裂患者, 且对照组中未包含藏族正常对照, 因此仅初步探索ABO血型与西部藏汉族唇腭裂发生的关系, 其ABO血型及Rh血型分布的差异可能来源于人群, 仍需加大样本量进一步探索; 另外, 本研究也未开展针对血型对应基因的分子生物学检测, 其确切的分子机制尚待进一步研究。

综上所述, 中国西部藏族与汉族唇腭裂患者不管是表型构成, 还是ABO血型分布均表现出明显差异, 藏族与汉族唇腭裂患者中O型血的分布明显高于汉族正常对照, 可能与唇腭裂的发生存在相关性, 且在不同性别中均表现出同样的趋势; 在对不同亚型的比较中发现, 仅在单纯唇裂与唇裂伴腭裂表型中表现出ABO血型分布的差

异, O型血藏族人群更容易出现唇裂畸形, 且在腭裂及唇裂伴腭裂表型中的作用较唇裂表型弱。

* * *

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