

高原藏族儿童过敏性紫癜相关危险因素分析

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【摘要】 目的 分析可能导致高原藏族儿童发生过敏性紫癜(HSP)的危险因素,为高原地区正确识别高危儿童提供参考。方法 选择2015年10月至2018年10月西藏自治区山南市人民医院收治的140例高原藏族HSP儿童为研究对象,另外选择140例高原藏族健康儿童和140例平原地区HSP儿童作为对照。回顾性分析儿童性别、年龄、家族史、过敏史、既往史(风湿性疾病、自身免疫性疾病、哮喘)、临床表型、生化指标(抗体阳性率、血小板计数和血红蛋白)、临床疗效及复发情况,采用单因素和多因素Logistic回归分析筛选影响高原藏族儿童发生HSP的危险因素。结果 单因素分析显示,高原HSP儿童的过敏史、既往史比例较高原健康儿童增多(过敏史:35.7%比11.4%,既往史:21.4%比5.7%,均 $P<0.05$);与平原HSP儿童比较,高原HSP儿童年龄增加(岁:6.5±2.3比5.3±2.2),临床表型更复杂(单纯皮肤和四肢型:37.9%比57.1%,合并腹型:21.4%比14.3%,合并肾型:28.6%比21.4%,合并脑或肺型:7.1%比5.0%,复杂型:5.0%比2.2%),抗体阳性率增加(64.3%比50.0%),血小板计数降低($\times 10^9/L$:116.2±12.3比176.8±35.4),血红蛋白水平升高(g/L :125.6±15.7比113.8±10.9),复发率降低(4.3%比10.7%),差异均有统计学意义(均 $P<0.05$)。Logistic回归分析显示,年龄、过敏史和既往史是影响高原藏族儿童发生HSP的独立危险因素[年龄:优势比(OR)=1.263,95%可信区间($95\%CI$)=1.063~1.968;过敏史: $OR=1.765$, $95\%CI=1.326\sim 2.452$,既往史: $OR=1.421$, $95\%CI=1.102\sim 2.232$;均 $P<0.05$];临床表型和生化指标是影响HSP儿童临床疗效的重要危险因素(非单纯皮肤和四肢型: $OR=2.123$, $95\%CI=1.623\sim 2.869$;抗体阳性: $OR=1.865$, $95\%CI=1.502\sim 2.768$;均 $P<0.05$)。结论 高原藏族儿童HSP的发生与平原地区有一定差异,应注意筛选年龄、过敏史、既往史、临床表型、抗体阳性等高危患儿,给予早期有效干预可提高临床疗效,降低复发率。

【关键词】 高原; 藏族儿童; 过敏性紫癜; 危险因素

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Analysis of relevant risk factors to Henoch-Schönlein purpura in Tibetan children

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【Abstract】 Objective To analyze probable risk factors to Henoch-Schönlein purpura (HSP) in Tibetan children so as to bring evidences for correct identification of high-risk children in plateau areas. **Methods** 140 high-altitude Tibetan children with HSP admitted to Shannan People's Hospital of Tibet Autonomous Region from October 2015 to October 2018 were enrolled, and 140 high-altitude Tibetan healthy children and 140 plain area HSP children were selected as the control. Gender, age, family history, allergy, past history (rheumatic disease, autoimmune disease, asthma), clinical phenotype, biochemical markers (antibody positive rate, platelet count and hemoglobin), clinical efficacy and recurrence were retrospective analyzed. The risk factors of HSP in the high-altitude Tibetan children were analyzed by univariate and multivariate Logistic regression analysis. **Results** It was shown by univariate analysis that the proportion of allergic history and past history of high-altitude HSP children was higher than those of high-altitude healthy children (allergic history: 35.7% vs. 11.4%, past history: 21.4% vs. 5.7%, both $P < 0.05$). Compared with plain area HSP children, the age of high-altitude HSP children was increased (years old: 6.5±2.3 vs. 5.3±2.2), the clinical phenotype was more complex (37.9% vs. 57.1% for simple skin and limb type, 21.4% vs. 14.3% for abdominal type, 28.6% vs. 21.4% for renal type, 7.1% vs. 5.0% for brain or lung type, 5.0% vs. 2.2% for complex type), the positive rate of antibody was increased (64.3% vs. 50.0%), platelet count was decreased ($\times 10^9/L$: 116.2±12.3 vs. 176.8±35.4), hemoglobin level was increased (g/L : 125.6±15.7 vs. 113.8±10.9), recurrence rate was lower (4.3% vs. 10.7%), and the difference was statistically significant (all $P < 0.05$). It was shown by multivariate Logistic regression analysis that age, allergic history

and past history were independent risk factors for HSP in high-altitude Tibetan children [age: odds ratio (OR) = 1.263, 95% confidence interval (95%CI) = 1.063–1.968; allergic history: OR = 1.765, 95%CI = 1.326–2.452, past history: OR = 1.421, 95%CI = 1.102–2.232, all $P < 0.05$]. Clinical phenotypic and biochemical indexes were important risk factors affecting the clinical efficacy of high-altitude Tibetan HSP children (non-simple skin and limb type: OR = 2.123, 95%CI = 1.623–2.869; antibody positive: OR = 1.865, 95%CI = 1.502–2.768; both $P < 0.05$). **Conclusions** It is different of HSP occurrence in Tibetan children from plateau and plain areas. Attention should be paid to screening age, allergy history, past history, clinical phenotype, antibody positive and other high risk children. Early and effective intervention can improve clinical curative effect and reduce recurrence.

【Key words】 Plateau; Tibetan child; Henoch-Schönlein purpura; Risk factor

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过敏性紫癜(HSP)是儿童期最常见的血管炎性疾病,以非血小板减少性紫癜、关节痛、腹痛、胃肠道出血及肾损伤为主要特征,多发生于寒冷季节,合并上呼吸道感染史者约30%~50%,多为病毒或细菌感染^[1]。目前认为HSP可能与感染、疫苗接种、食物、药物及遗传等因素有关^[2];发病机制可能为IgA1分子糖基化异常及清除障碍,沉积于小血管壁引起自身炎症反应和组织损伤^[3];其临床表现各异,早期缺乏特征性体征和诊断指标,易误诊、漏诊,延误病情^[4]。虽然多数HSP患儿临床症状较轻且有自愈性,但严重者可出现胃肠道受损症状(如腹痛、肠出血、肠梗阻、肠穿孔)^[5]、肾脏损伤^[6]及其他器官(脑、肺等血管炎)损伤^[7],危及生命,需要临床医师及时采用适当的诊治方案。由于高原藏族地区平均海拔较平原地区明显升高,故对血液中血红蛋白、红细胞和血小板的数量、形态及功能可造成一定影响^[8]。既往研究多以平原地区HSP患儿的临床特征和主要危险因素为主,缺乏高原藏族儿童HSP的相关资料,对临床诊治缺乏足够的参考。本研究重点分析可能导致高原藏族儿童HSP的危险因素,为高原地区正确识别HSP高危儿童提供参考。

1 对象与方法

1.1 研究对象:选择2015年10月至2018年10月西藏自治区山南市人民医院收治的140例高原藏族HSP儿童为研究对象;另外选择高原藏族健康儿童140例和平原地区HSP儿童140例作为对照。

1.1.1 纳入标准:①年龄1~16岁,高原藏族本地

儿童;②符合HSP诊断标准^[9];③不合并其他类型紫癜(如血小板减少性紫癜)及其他血液系统疾病(如白血病);④临床资料完善。

1.1.2 排除标准:①先天发育异常、肝脾肿大、系统性红斑狼疮;②近期严重全身感染,原发肾脏疾病,如肾小球肾炎;③近期服用过糖皮质激素或其他免疫抑制剂。

1.1.3 伦理学:本研究为回顾性研究,研究方案经医院研究伦理委员会批准(审批号:2019228)。

1.2 研究指标:记录各组儿童一般资料,包括性别、年龄、体重、是否剖宫产、分娩并发症、家族史、过敏史、既往史(风湿性疾病、自身免疫性疾病、哮喘);HSP临床表型、生化指标(抗体阳性率、血小板计数和血红蛋白);定期门诊或电话随访半年的临床疗效(皮肤紫癜、腹痛、肢体肿痛等临床表现消失,尿液检查无异常为有效)及复发情况。

1.3 统计学方法:使用SPSS 20.0软件对数据进行统计。计量资料以均数±标准差($\bar{x} \pm s$)表示,两组间比较用 t 检验,多组间比较用单因素方差分析(ANOVA);计数资料用 χ^2 检验。采用单因素和多因素Logistic回归分析筛选影响高原藏族儿童发生HSP的危险因素。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 各组儿童一般资料比较(表1):与高原健康组比较,高原HSP组儿童过敏史、既往史比例明显增多(均 $P < 0.05$)。与平原HSP组比较,高原HSP组儿童年龄明显增加($P < 0.05$)。

表1 各组儿童一般资料比较

组别	例数 (例)	性别(例)		年龄 (岁, $\bar{x} \pm s$)	体重 (kg, $\bar{x} \pm s$)	剖宫产 [例(%)]	分娩并发症 [例(%)]	家族史 [例(%)]	过敏史 [例(%)]	既往史 [例(%)]
		男性	女性							
平原HSP组	140	55	85	5.3±2.2	20.8±4.6	44(31.4)	17(12.1)	8(5.7)	46(32.9)	27(19.3)
高原健康组	140	70	70	6.4±2.5	21.2±4.8	42(30.0)	15(10.7)	10(7.1)	16(11.4)	8(5.7)
高原HSP组	140	60	80	6.5±2.3 ^a	20.6±4.5	46(32.9)	20(14.3)	13(9.3)	50(35.7) ^b	30(21.4) ^b
χ^2/F 值		3.381		3.352	0.625	0.265	0.834	1.323	25.227	15.544
P 值		0.184		0.025	0.342	0.876	0.659	0.516	0.000	0.000

注: HSP为过敏性紫癜;与平原HSP组比较,^a $P < 0.05$;与高原健康组比较,^b $P < 0.05$

表2 高原与平原 HSP 儿童临床指标比较

组别	例数 (例)	HSP 临床表型 [例(%)]					生化指标			临床有效率 [% (例)]	复发率 [% (例)]
		单纯皮肤 和四肢型	合并 腹型	合并 肾型	合并脑 或肺型	复杂 型	抗体阳性 [例(%)]	血小板计数 ($\times 10^9/L, \bar{x} \pm s$)	血红蛋白 ($g/L, \bar{x} \pm s$)		
平原 HSP 组	140	80(57.1)	20(14.3)	30(21.4)	7(5.0)	3(2.2)	70(50.0)	176.8 \pm 35.4	113.8 \pm 10.9	95.0(133)	10.7(15)
高原 HSP 组	140	53(37.9)	30(21.4)	40(28.6)	10(7.1)	7(5.0)	90(64.3)	116.2 \pm 12.3	125.6 \pm 15.7	92.9(130)	4.3(6)
χ^2/t 值				11.039			5.833	6.493	4.527	0.564	4.170
P 值				0.026			0.016	0.011	0.038	0.453	0.041

注: HSP 为过敏性紫癜

2.2 高原与平原 HSP 儿童 HSP 相关临床资料比较(表2): 与平原 HSP 组比较, 高原 HSP 组患儿临床表型更复杂, 抗体阳性率明显增加, 血小板计数明显降低, 血红蛋白水平明显升高, 复发率明显降低(均 $P < 0.05$)。

2.3 筛选影响高原 HSP 发生和临床疗效的危险因素(表3): Logistic 回归分析显示, 年龄、过敏史和既往史是影响高原藏族儿童发生 HSP 的独立危险因素(均 $P < 0.05$); 临床表型和生化指标是影响 HSP 儿童临床疗效的重要危险因素(均 $P < 0.05$)。

表3 筛选影响高原儿童发生 HSP 和临床疗效危险因素的 Logistic 回归分析

因素	β 值	χ^2 值	P 值	OR 值	95%CI
高原 HSP 发生					
年龄	0.532	3.562	0.033	1.263	1.063 ~ 1.968
过敏史	0.162	4.523	0.017	1.765	1.326 ~ 2.452
既往史	0.342	4.162	0.026	1.421	1.102 ~ 2.232
临床疗效					
非单纯皮肤和四肢型	0.086	4.869	0.009	2.123	1.623 ~ 2.869
抗体阳性	0.146	4.754	0.012	1.865	1.502 ~ 2.768

注: HSP 为过敏性紫癜, OR 为优势比, 95%CI 为 95% 可信区间

3 讨论

HSP 诊断的必需条件为非血小板减少、可触性皮肤紫癜, 而皮疹不是所有患儿的唯一表型, 有 30% ~ 43% 的患儿以关节痛或腹痛为首发症状, 可长达 14 d 无皮疹^[10], 极易误诊, 应引起重视, 诊断疑难时可行皮肤活检。总结误诊原因: ① 患儿首发症状为双下肢或双踝关节肿痛时, 家长多认为是摔伤、扭伤所致, 盲目用药或 X 线检查^[11]; ② 当患儿主诉头痛、头晕(实际是早期紫癜性肾炎性高血压^[12]) 症状时, 家长或医生多认为是“感冒”, 而给予抗菌药物、抗病毒或输液等治疗, 延误治疗患儿会出现抽搐(高血压脑病^[13]) 等症状; ③ HSP 腹型尚未出现皮肤紫癜或已出现而未被发觉与不认知时, 小儿腹痛难以忍受, 误诊收治外科考虑急性阑尾炎等急腹症行剖腹探查, 多数虽切除阑尾, 患儿腹痛症状并不能缓解或进一步加重, 引起一系列的并发症, 增加

后续治疗困难^[14]。

本研究通过对高原藏族 HSP 患儿的临床资料进行回顾性分析, 试图寻找导致疾病发生的高危因素, 结果显示: 高原 HSP 组有过敏史、既往史的比例较高原健康组明显增多; 与平原 HSP 组比较, 高原 HSP 组年龄增加, 临床表型更复杂, 抗体阳性率增加, 血小板计数降低, 血红蛋白水平升高, 复发率降低。无论是高原还是平原 HSP 患儿多伴有过敏史, 与 HSP 的发生机制和自身产生过多的血小板抗体有关^[15]; 高原藏族儿童多有放牧生活史, 与动物毛发接触较多, 更易产生过敏反应^[16]。既往史中风湿性疾病、自身免疫性疾病、哮喘也属于免疫功能紊乱性疾病, 提示机体免疫功能过强, 相关抗体分泌较多^[17]。央珍等^[18]指出, 西藏高原地区儿童 HSP 的发病特点、临床症状、实验室检查等与平原地区有一定差异, 该研究提示, 高原藏族 HSP 患儿的临床表型更复杂, 抗体阳性率增加, 血小板计数降低, 血红蛋白升高。HSP 具有自限性, 单纯皮疹通常无需治疗; 对于合并严重皮疹、急性关节痛、腹痛及肾损伤等, 应控制急性症状, 监测并改善影响预后的因素^[19]。HSP 治疗措施包括支持治疗、对症治疗、免疫抑制治疗及血液净化等, 严格掌握适应证, 最大程度改善临床预后^[20]。HSP 预后主要取决于肾脏损伤程度^[21]。约 1/3 患儿存在肾脏受累, 以血肌酐、尿素氮、血尿及蛋白尿为判断标准, 尿微量蛋白排泄增加可早于尿常规或尿蛋白定量检查, 提示早期隐匿性肾脏损伤^[22]。在三级医疗中心就诊的紫癜性肾炎患儿中, 约 20% 确诊 20 年后可进展为慢性肾脏疾病(CKD), 发生 CKD 的风险与起始临床症状和组织学表现无关^[23]。因此, 对 HSP 患儿须长期随访, 警惕肾损伤的发生。

Logistic 回归分析显示, 年龄、过敏史和既往史是影响高原藏族儿童发生 HSP 的独立危险因素, 临床表型和生化指标是影响 HSP 儿童临床疗效的重要危险因素。表明年龄、过敏史、既往史、临床表型、

抗体阳性与高原藏族儿童 HSP 密切相关。普及健康教育,提高民众对该疾病的认知度;提高医护人员对高原藏族 HSP 的鉴别能力^[24-25],例如:HSP 皮肤型需与药疹或血小板减少性紫癜相鉴别;关节肿痛者与外伤及风湿性关节炎相鉴别;腹痛型与急腹症相鉴别;HSP 肾型与急性肾小球肾炎、狼疮性肾炎相鉴别,从而减少临床误诊,提高诊断准确性,及时诊治,改善 HSP 患儿临床预后。

综上所述,高原藏族儿童 HSP 的发生与平原地区有一定差异,应注意筛选高危患儿,给予早期有效干预可提高临床疗效,降低复发。

利益冲突 所有作者均声明不存在利益冲突

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