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维生素 A、E 水平与儿童反复呼吸道感染的相关性和危险因素研究 *

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摘要 目的:研究维生素 A(VA)、维生素 E(VE)水平与儿童反复呼吸道感染(RRI)的相关性和危险因素。**方法:**选择本院 2017 年 1 月~2019 年 10 月诊治的 318 例 RRI 患儿,同期选择 285 例健康体检儿童作为对照组,比较各组 VA、VE 表达情况,并分析儿童 RRI 发生的危险因素。**结果:**RRI 组 VA 及 VE 水平低于对照组,VA 及 VE 缺乏率高于对照组,差异有统计学意义($P<0.05$)。1~3 岁患儿 VA 及 VE 水平高于 3~6 岁组且高于 >6 岁组($P<0.05$)。对照组和 RRI 组性别、出生时体重比较无统计学差异($P>0.05$);RRI 组自然分娩、母乳喂养率低于对照组,偏食、过敏体质、抗生素滥用、人均居住面积 $<13\text{ m}^2$ 、母亲文化高中及以下率高于对照组($P<0.05$)。多因素 Logistic 回归分析显示,早产、偏食、过敏体质、被动吸烟、抗生素滥用、人均居住面积 $<13\text{ m}^2$ 是 RRI 发生的独立危险因素,VA、VE、自然分娩、母乳喂养、母亲文化程度是 RRI 发生的保护因素。**结论:**RRI 儿童 VA、VE 水平较低,且 RRI 的发生和多种危险因素相关,临床应针对性的进行预防干预。

关键词:儿童反复呼吸道感染;维生素 A;维生素 E;相关性;危险因素

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Correlation and Risk Factors of Vitamin A and E Levels with Recurrent Respiratory Tract Infection in Children*

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ABSTRACT Objective: To study the correlation and risk factors between vitamin A (VA) and vitamin E (VE) levels and recurrent respiratory tract infection (RRI) in children. **Methods:** 318 RRI children diagnosed and treated in our hospital from January 2017 to October 2019 were selected, 285 healthy children were selected as control group at the same time. The expressions of VA and VE in each group were compared and the risk factors of RRI in children were analyzed. **Results:** The VA and VE levels in RRI group were lower than those in the control group, and the VA and VE deficiency rates were higher than those in the control group, the difference was statistically significant ($P<0.05$). VA and VE levels of children aged 1-3 years old were higher than those of 3-6 years old group and higher than those of >6 years old group ($P<0.05$). There was no significant difference in sex and birth weight between control group and RRI group ($P>0.05$). The rates of natural delivery and breast feeding in RRI group were lower than those in the control group, and the rates of partial diet, allergic constitution, antibiotic abuse, per capita living area $<13\text{ m}^2$, mother's cultural high school and below were higher than those in the control group($P<0.05$). Multivariate Logistic regression analysis showed that premature birth, partial diet, allergic constitution, passive smoking, antibiotic abuse and per capita living area $<13\text{ m}^2$ were independent risk factors for RRI, while VA, VE, natural childbirth, breast feeding and mother's educational level were protective factors for RRI. **Conclusion:** The levels of VA and VE in RRI children are relatively low, and the occurrence of RRI is related to various risk factors. Therefore, clinical prevention and intervention should be targeted.

Key words: Recurrent respiratory tract infection in children; Vitamin A; Vitamin E; Relevance; Risk factor

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前言

呼吸道感染为儿童常见疾病之一,其中部分儿童容易发生反复呼吸道感染(RRI),即 1 年内呼吸道感染的次数频繁,超出正常范围^[1,2]。流行病学指出^[3],儿童 RRI 感染持续时间相对较

长,迁延难愈,未经及时治疗可加重病情,另外反复感染能够影响患儿抵抗能力,从而引起恶性循环。儿童 RRI 的病因复杂,由多方面因素所致,相关研究报道^[4],明确 RRTIs 的易感因素对于此类疾病的防控有重要作用。近年来有研究指出,维生素缺乏和 RRI 有一定关系,维生素 A(VA)可促进气道粘膜上皮细胞

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生长,且可调节机体免疫反应,VA 缺乏能够导致粘膜生长受限及损伤,降低呼吸道的抗感染能力^[5]。维生素 E(VE)为机体必要的脂溶性维生素,是良好的抗氧化剂,能够对抗脂质过氧化,改善机体细胞及体液免疫^[6]。本研究就探讨 VA、VE 水平与儿童反复呼吸道感染的相关性和危险因素,为 RRI 的防治提供科学依据。

1 资料与方法

1.1 一般资料

选择本院 2017 年 1 月~2019 年 10 月诊治的 318 例 RRI 患儿,入选标准:符合 RRI 诊断标准^[7]:0~2 岁,上呼吸道感染 ≥ 7 次/年、下呼吸道感染 ≥ 3 次/年,3~5 岁,上呼吸道感染 ≥ 6 次/年、下呼吸道感染 ≥ 2 次/年,6~14 岁,上呼吸道感染 ≥ 5 次/年、下呼吸道感染 ≥ 2 次/年,每次呼吸道感染间隔时间 ≥ 7 d;临床资料完整。排除标准:先天性肺发育不良、风湿性疾病、先天性心脏病等基础疾病;心力衰竭、呼吸衰竭等严重并发症;近期服用过 VA、VE 制剂。318 例 RRI 患儿中男 151 例,女 167 例;年龄 1~14 岁,平均 (5.94 ± 0.69) 岁;感染类型:上呼吸道感染 126 例,其中感冒 61 例、扁桃体炎 32 例、鼻窦炎 19 例、中耳炎 14 例,下呼吸道感染 192 例,其中肺炎 93 例、喘息性支气管炎 57 例、支气管炎 42 例。同期选择 285 例健康体

检儿童作为对照组(1 年之内无呼吸道感染病史),男 131 例,女 154 例;年龄 1~14 岁,平均 (5.85 ± 0.73) 岁。两组性别、年龄比较无统计学差异($P>0.05$)。

1.2 检测方法

所有 RRI 患儿依据相关文献^[7]进行系统、正规治疗,于治疗前及治愈时采集患儿静脉血,用血液分离机按 4000 r/min 离心 10 min,采集上清液,用高效液相色谱仪测定 VA、VE 水平,记录 VA 缺乏(≤ 0.3 mg/L)、VE 缺乏(<4 mg/L)情况。

1.3 问卷调查

自行编制调查问卷,收集所有受试者基本信息、生活及饮食习惯特征和既往病史特点。

1.4 统计学分析

数据处理选用 SPSS18.0 软件包,计量资料用 $(\bar{x} \pm s)$ 表示,选用 t 检验,计数资料用[例(%)]表示,用 χ^2 检验比较,多因素分析采用 Logistic 逐步回归分析, $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 对照组和 RRI 组 VA、VE 水平比较

RRI 组 VA 及 VE 水平低于对照组,VA 及 VE 缺乏率高于对照组,差异有统计学意义($P<0.05$),见表 1。

表 1 对照组和 RRI 组 VA、VE 水平比较 $(\bar{x} \pm s)$ 、(例,%)

Table 1 Comparison of VA and VE levels between control group and RRI group $(\bar{x} \pm s)$ 、(n,%)

Groups	n	VA(mg/L)	VE(mg/L)	VA deficiency rate	VE deficiency rate
Control group	285	0.38 ± 0.04	7.91 ± 0.84	19(6.67)	23(8.07)
RRI group	318	$0.22 \pm 0.03^{\#}$	$6.14 \pm 0.81^{\#}$	38(11.95) [#]	44(13.84) [#]

Note: Compared with control group, [#] $P<0.05$.

2.2 不同年龄段 RRI 患儿 VA、VE 水平比较

($P<0.05$),见表 2。

1~3 岁患儿 VA 及 VE 水平高于 3~6 岁组且高于 >6 岁组

表 2 不同年龄段 RRI 患儿 VA、VE 水平比较 $(\bar{x} \pm s)$

Table 2 Comparison of VA and VE levels in RRI children of different ages $(\bar{x} \pm s)$

Period of time	n	VA(mg/L)	VE(mg/L)
1~3 years old	118	0.27 ± 0.04^b	6.63 ± 0.89^b
3~6 years old	154	0.20 ± 0.02^a	6.01 ± 0.78^a
>6 years old	46	0.16 ± 0.03^{ab}	5.31 ± 0.70^{ab}

Note: Compared with 1 to 3 years old, ^a $P<0.05$; Compared with 3 to 6 years old, ^b $P<0.05$.

2.3 RRI 患儿治疗前后 VA、VE 水平比较

治疗后的 VA、VE 水平高于治疗前($P<0.05$),见表 3。

表 3 RRI 患儿治疗前后 VA、VE 水平比较 $(\bar{x} \pm s)$

Table 3 Comparison of VA and VE levels in RRI children before and after treatment $(\bar{x} \pm s)$

Time	n	VA(mg/L)	VE(mg/L)
Before treatment	318	0.22 ± 0.03	6.14 ± 0.81
After treatment	318	$0.33 \pm 0.04^*$	$7.28 \pm 0.92^*$

Note: Compared with before treatment, ^{*} $P<0.05$.

2.4 对照组和 RRI 组临床资料比较

对照组和 RRI 组性别、出生时体重比较无统计学差异

($P>0.05$);RRI 组自然分娩、母乳喂养率低于对照组,偏食、过敏体质、抗生素滥用、人均居住面积 <13 m²、母亲文化高中及以

下率高于对照组,差异有统计学意义($P<0.05$),见表 4。

表 4 对照组和 RRI 组临床资料比较[($\bar{x} \pm s$), (例, %)]
Table 4 Comparison of clinical data between control group and RRI group[($\bar{x} \pm s$), (n, %)]

Clinical data	Control group(n=285)	RRI group(n=318)	t/χ^2	P
Gender				
Man	131(45.96)	151(47.48)	0.139	0.709
Woman	154(54.04)	167(52.52)		
Age (years)	5.85 $\pm$ 0.73	5.94 $\pm$ 0.69	1.556	0.120
Mode of delivery				
Spontaneous labor	198(69.47)	161(50.63)	22.156	0.000
Cesarean section	87(30.53)	157(49.37)		
Be born prematurely				
Have	17(5.96)	56(17.61)	19.155	0.000
Without	268(94.04)	262(82.39)		
Feeding mode				
Breast feeding	148(51.93)	106(33.33)	26.357	0.000
Artificial feeding	10(3.51)	33(10.38)		
Mixed feeding	127(44.56)	179(56.29)		
Weight at birth				
<2.5 kg	37(12.98)	33(10.38)	0.994	0.319
$\geq$ 2.5 kg	248(87.02)	285(89.62)		
Partial eclipse				
Have	46(16.14)	102(32.08)	20.608	0.000
Without	239(83.86)	216(67.92)		
Allergic constitution				
Be	27(9.47)	69(21.70)	16.779	0.000
No	258(90.53)	249(78.30)		
Antibiotic abuse				
Have	20(7.02)	61(19.18)	19.127	0.000
Without	265(92.98)	257(80.82)		
Passive smoking				
Have	17(5.96)	57(17.92)	19.968	0.000
Without	268(94.04)	261(82.08)		
Per capita living area				
<13 m ²	23(8.07)	69(21.70)	22.067	0.026
$\geq$ 13 m ²	265(92.98)	249(78.30)		
Mother's educational level				
High school and below	164(57.54)	236(74.21)	18.703	0.000
College and above	121(42.46)	82(25.79)		

2.5 RRI 发生的多因素分析

将有无 RRI 发生作为因变量,将 VA、VE 水平、自然分娩、早产、母乳喂养、偏食、过敏体质、被动吸烟、抗生素滥用、人均居住面积 <13 m²、母亲文化程度作为自变量,通过多因素 Lo-

gistic 回归分析显示,早产、偏食、过敏体质、被动吸烟、抗生素滥用、人均居住面积 <13 m² 是 RRI 发生的独立危险因素,VA、VE、自然分娩、母乳喂养、母亲文化程度是 RRI 发生的保护因素,见表 5。

表 5 RRI 发生的多因素分析
Table 5 Multivariate analysis of RRI occurrence

Independent variable	β	S.E	Wald	P	OR	95%CI
Va	-0.581	0.078	1.088	0.000	0.559	0.480~0.651
Ve	-0.347	0.078	19.659	0.000	0.664	0.543~0.811
Spontaneous labor	-0.410	0.103	16.002	0.000	0.707	0.607~0.824
Be born prematurely	0.256	0.098	6.879	0.009	1.292	1.067~1.564
Breast feeding	-0.139	0.061	5.168	0.023	0.870	0.771~0.981
Partial eclipse	1.381	0.495	7.795	0.005	3.979	1.509~10.490
Allergic constitution	0.411	0.207	5.597	0.032	1.142	1.020~1.562
Passive smoking	0.982	0.201	10.840	0.001	2.669	1.810~3.959
Antibiotic abuse	0.846	0.268	6.284	0.012	2.330	1.378~3.940
Per capita living area < 13 m ²	1.152	0.299	14.873	<0.001	3.614	1.762~5.682
Mother's educational level	-0.133	0.021	39.578	<0.001	0.875	0.840~0.912

3 讨论

儿童具有呼吸系统发育不成熟、生理功能不健全等特点,是 RRI 的高发群体^[8,9]。相关研究报道^[10,11],儿童 RRI 治疗不当可能引起哮喘、肾炎及心肌炎等疾病,影响小儿的身体健康及生长发育。

目前多数研究表明 RRI 是多种因素共同作用所致,其中维生素缺乏是其发生的主要因素之一^[12]。VA 为机体必要维生素之一,可参与糖蛋白合成,能够促进免疫蛋白的合成,其作为 T 淋巴细胞增殖分化中的必要营养因子,VA 浓度下降可影响 T 淋巴细胞分化,降低抗体能力^[13]。相关研究表明^[14],外源性补充 VA 能够起到免疫调节作用,并增强免疫细胞吞噬功能,提高机体免疫能力。另外 VA 对呼吸道有局部抗炎作用,VA 水平降低可促进炎症反应,导致局部组织受损。动物模型报道^[15,16],VA 缺乏可破坏呼吸道的免疫屏障,降低呼吸系统清除病原菌的能力,引起呼吸道感染。VE 作为一种脂溶性维生素,能够维持细胞稳定性,保护肺泡细胞,维持呼吸道正常菌群的平衡,降低肺部和呼吸系统感染风险^[17,18]。又有研究表明^[19,20],VE 作为机体的脂溶性抗氧化剂,其浓度下降能够引起自由基反应及炎症反应,进一步增加呼吸道易感性。动物研究报道^[21],VE 能够促进 VA 吸收,又可降低血液循环中 VA 的氧化破坏。本研究结果发现,RRI 组儿童 VA、VE 水平相对较低,进一步分析显示,活动期患儿 VA、VE 水平又低于稳定期,表明感染控制后 VA、VE 水平有所上升,考虑与感染控制后可减少维生素的消耗,加上胃肠功能的恢复,增加维生素摄入及吸收,从而利于 VA 及 VE 的储存。有关研究表明^[22,23],儿童免疫功能不断完善,随着年龄改变,机体对维生素的需求量也相应变化。本研究数据显示,随着年龄增加,RRI 患儿 VA、VE 水平呈下降趋势,Logistic 回归发现,VA 及 VE 是 RRI 发生的保护因素。

Alexandrino AS 等^[24]研究报道,分娩方式和 RRI 发生有一定关联,本研究结果显示,RRI 组自然分娩率相对较低,经多因素 Logistic 回归分析发现自然分娩是 RRI 发生的保护因素。一方面可能与自然分娩的胎儿受到产道的明显挤压,从而促进口

腔及肺内羊水、分泌物的充分排出,利于肺部扩张,从而更好的发育。另一方面子宫及产道剧烈收缩时能够促进免疫球蛋白、肺泡表面活性物的分泌。另外我们发现早产可能增加 RRI 发生风险,早产儿系统器官尚未完全发育,无法有效刺激呼吸中枢,且其肺泡表面活性物质较少,容易发生换气不良,引起组织缺氧,影响肺部发育,增加呼吸道感染疾病发生率^[25]。我们研究发现,母乳喂养是 RRI 发生的保护因素,母乳中的营养成分齐全,富含丰富的免疫因子,可利于婴儿吸收,提高机体抵抗力。偏食和 RRI 的相关性已得到临床证实,偏食可使儿童摄入的能量及营养不平衡,影响儿童的正常生长及发育,本研究也支持此结论^[26]。有关研究认为^[27],过敏体质可能是 RRI 发生的危险因素。本研究显示,RRI 患儿过敏体质率较对照组高,分析原因为过敏体质儿童容易发生过敏性鼻炎,出现上呼吸道感染症状,且多次反复的刺激引起鼻腔解剖结构变化,降低屏障功能,增加上呼吸道感染风险。儿童被动吸烟后的烟雾可刺激并损伤肺功能,降低肺活量,从而影响机体免疫力,本研究中被动吸烟是引起 RRI 发生的危险因素^[28]。有报道指出^[29],抗生素滥用能够引起细菌耐药,导致菌群失调、免疫功能下降,引起呼吸道多次感染,本研究证实抗生素滥用是引起 RRI 的危险因素。本研究也发现,居住面积过小是导致 RRI 的危险因素,居住面积过小容易影响室内空气,促进病原菌的生长,导致呼吸道感染的发生^[30]。此外母亲的文化程度和 RRI 也有一定关系,母亲的个人素质较高能够更加注重儿童生活卫生、均衡饮食及科学护理,降低感染性疾病发生率^[31]。

综上所述,RRI 儿童 VA、VE 水平较低,且 RRI 的发生和多种危险因素相关,临床应针对性的进行预防干预。

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