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湖南省9所医院早产儿卡介苗及乙肝疫苗接种情况及未接种原因分析*

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摘要 目的:了解湖南省9所医院早产儿卡介苗及乙肝疫苗接种现状,并分析未接种的原因。**方法:**收集2014年11月至2015年10月期间参与研究的湖南省9所医院产科分娩的早产儿相关临床资料及卡介苗和第一剂乙肝疫苗的接种资料,分析各医院的接种原则以及未接种的原因。**结果:**各医院间早产儿的出生体重及出生胎龄比较差异均有统计学意义($P<0.05$);9所医院遵循的卡介苗和第一次乙肝疫苗接种原则不尽相同;出院时卡介苗未接种率为45.0%,明显高于第一剂乙肝疫苗未接种率的16.7%($P<0.05$);卡介苗因低体重、疾病、IVIG、家长拒绝而未接种的比例分别为82.5%、12.9%、4.3%、0.3%,第一剂乙肝疫苗因疾病、低体重、IVIG、家长拒绝而未接种的比例分别为53.1%、41.6%、4.0%、1.3%。**结论:**湖南省9所医院早产儿卡介苗及乙肝疫苗接种率较低,疾病和低体重位居出院时未接种原因的前两位,应规范早产儿疫苗接种,避免遗漏或不恰当推迟疫苗接种。

关键词:湖南;早产儿;卡介苗;乙肝疫苗;接种原则;原因

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Analysis of Bacillus Calmette-Guerin and Hepatitis B Vaccine Inoculation in Preterm Infants and the Reasons for Uninoculated in 9 Hospitals of Hunan Province*

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ABSTRACT Objective: To understand the current status of Bacillus Calmette-Guerin and hepatitis B vaccine inoculation in preterm infants in 9 hospitals of Hunan Province, and analyze the reasons for uninoculated. **Methods:** The clinical data of obstetric delivery preterm infants in 9 hospitals of Hunan province from November 2014 to October 2015 and the inoculation data of Bacillus Calmette-Guerin and the first dose of hepatitis B vaccine were collected, and the inoculation principles and the reasons for the uninoculated were analyzed. **Results:** There were significant differences in birth weight and gestational age of preterm infants in different hospitals ($P<0.05$). The principles of Bacillus Calmette-Guerin and the first hepatitis B vaccine inoculation were not the same in 9 hospitals. The uninoculated rate of Bacillus Calmette-Guerin was 45.0% at discharge, significantly higher than 16.7% of the first dose of hepatitis B vaccine ($P<0.05$). The uninoculated rate of Bacillus Calmette-Guerin for low weight, disease, IVIG and parental rejection were 82.5%, 12.9%, 4.3% and 0.3% respectively. The uninoculated rate of the first dose of hepatitis B vaccine for disease, low weight, IVIG and parental rejection were 53.1%, 41.6%, 4.0%, 1.3% respectively. **Conclusion:** The inoculated rate of Bacillus Calmette-Guerin and hepatitis B vaccine in preterm infants is lower in 9 hospitals of Hunan Province. The disease and low weight are the top two uninoculated

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reasons at discharge. Vaccination for preterm infants should be standardized to avoid missing or inappropriate vaccination.

Key words: Hunan; Preterm infant; Bacillus Calmette-Guerin; Hepatitis B vaccine; Principle of inoculation; Reason

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前言

早产儿,尤其是极早早产儿,由于其免疫功能低下的特点,在新生儿期以及婴幼儿期,均是感染发生的易感人群,胎龄及出生体重越小,感染发生率越高^[1-3],疫苗接种可预防感染,改善早产儿长期预后^[4,5]。由于早产儿出生后并发症发生率明显高于足月儿,按时接种疫苗往往不如足月儿,可能影响其免疫保护效果^[6,7]。我国计划免疫程序规定在新生儿期接种卡介苗和乙肝疫苗^[8],这对于预防结核病和乙型肝炎具有重要意义。湖南省规定由新生儿出生的医院负责卡介苗和乙肝疫苗的接种,并将相关接种信息上传到儿童疫苗接种系统^[9],但是对于早产儿这一特殊群体无特殊规定,由各家医院确定接种原则,在临床实践中存在潜在风险。本研究拟通过多中心调查,收集不同级别医院出生的早产儿接种乙肝疫苗和卡介苗的信息,了解早产儿出生后早期疫苗接种的现状,分析影响早产儿卡介苗及乙肝疫苗接种的相关因素。

1 对象与方法

1.1 研究对象

选择湖南省9所医院自2014年11月至2015年10月期间产科分娩的早产儿作为研究对象,纳入标准:(1)均符合第4版《实用新生儿学》^[10]中关于早产儿的诊断标准;(2)出生胎龄<37周;(3)早产儿家长对本研究知情同意并签署知情同意书。排除标准为出生后短期内家长放弃治疗而死亡的早产儿。

1.2 研究方法

收集参与研究的9所医院早产儿的临床调查资料,包括参与研究医院的基本信息(医院级别、早产儿例数、接种科室、出生体重、出生胎龄)、早产儿卡介苗和第一剂乙肝疫苗的接种所遵循原则、疫苗接种时间、影响接种的因素,建立数据库,进行分析。所有纳入研究的早产儿随访至生后两年,在此期间完成相关疫苗接种终止随访。

1.3 统计学方法

采用SPSS19.0软件进行统计处理,计数资料以频数分布或率描述,两组间比较采用卡方检验,计量资料以 $(\bar{x} \pm s)$ 描述,两组间比较为成组t检验,多组间比较采用单因素方差分析。检验标准为 $\alpha=0.05$ 。

2 结果

2.1 一般资料

参与研究的9所医院包括三级综合性医院4所,三级妇幼专科医院1所,二级综合性医院3所,二级妇幼专科医院1所。纳入研究的早产儿共1925例,各医院间早产儿的出生体重及出生胎龄比较差异均有统计学意义($F=17.397, 11.324$, 均 $P<0.001$)。在9所医院中,6所医院由产科负责接种早产儿卡介苗和乙肝疫苗,2所医院由新生儿科负责接种早产儿卡介苗和乙肝疫苗,1所医院由儿童保健科负责接种早产儿卡介苗和乙肝疫苗,见表1。

表1 各医院早产儿的一般资料

Table 1 General information of preterm infants in each hospital

Hospitals	Hospital level	n	Vaccination department	Birth weight (g)	Birth gestational age (weeks)
A	Three level synthesis	589	Newborn pediatrics	2 160.1± 561.2	33.8± 2.1
B	Three level maternity and child specialist	582	Newborn pediatrics	2 403.3± 525.5	34.5± 1.8
C	Two level synthesis	345	Obstetrics department	2 340.0± 570.2	34.2± 2.0
D	Three level synthesis	242	Obstetrics department	2 028.4± 530.2	33.5± 2.3
E	Three level synthesis	50	Obstetrics department	2 620.5± 601.5	35.1± 1.2
F	Two level synthesis	33	Obstetrics department	2 581.2± 464.1	35.5± 1.1
G	Two level maternity and child specialist	30	Child healthcare department	2 550.2± 490.6	35.0± 1.1
H	Two level synthesis	29	Obstetrics department	2 180.5± 380.1	34.5± 1.6
L	Two level synthesis	25	Obstetrics department	2 498.1± 445.3	35.3± 1.3

Note: A: Xiangya No.2 Hospital of Central South University; B: Changsha maternal and child health care hospital; C: Xinhua People's Hospital; D: First Hospital Affiliated to Nanhua University; E: Affiliated Hospital of Yongzhou Vocational Technical College; F: Guidong County People's Hospital; G: Zhangjiajie Yongding District Maternal and child health care hospital; H: Cili People's Hospital; L: Xiangxi Tujia and Miao Autonomous Prefecture national traditional Chinese medicine hospital.

2.2 各医院卡介苗与第一剂乙肝疫苗注射原则比较

9所医院均遵循体重超过2.5 kg出院时或出院后随访时注射卡介苗,患有严重急慢性疾病或治疗中应用静脉丙种球蛋白

(IVIG)1个月内则暂缓接种。永州职业技术学院附属医院规定在新生儿科住院超过7天者需行结核菌素试验,阴性者接种,其余各医院均为出生后超过3个月未接种卡介苗者行结核

菌素试验,阴性者接种。

对于乙肝病毒表面抗原阳性母亲所分娩的早产儿均在出生后 24 小时内注射第一次乙肝疫苗和乙肝高效价免疫球蛋白。对于 HBsAg 阴性母亲所分娩的早产儿,3 所医院(长沙市妇幼保健院、新化县人民医院和南华大学附属第一医院)遵循体重超过 2.0 kg 注射第一次乙肝疫苗,其余 6 所医院注射第一次乙肝疫苗时对体重无限制规定,但其中 3 所医院(桂东县人民医院、张家界市永定区妇幼保健院和湘西土家族苗族自治州民族中医院)具体操作中与卡介苗同时接种。南华大学附属第一医院规定在治疗中应用 IVIG 后 1 个月内暂缓接种,在其他医院 IVIG 应用与乙肝疫苗接种无关。

2.3 卡介苗和乙肝疫苗未接种原因分析

出院时第一剂乙肝疫苗未接种率为 16.7%(322/1925),卡

介苗未接种率为 45.0%(866/1925),出院时卡介苗未接种率明显高于第一剂乙肝疫苗未接种率($\chi^2=360.181, P<0.001$);各医院间第一剂乙肝疫苗和卡介苗未接种率比较差异具有统计学意义($\chi^2=606.239, 41.080, P<0.001$)。9 所医院中卡介苗因低体重、疾病、IVIG、家长拒绝而未接种的比例分别为 82.5%(714/866)、12.9%(112/866)、4.3%(37/866)、0.3%(3/866),第一剂乙肝疫苗因疾病、低体重、IVIG、家长拒绝而未接种的比例分别为 53.1%(171/322)、41.6%(134/322)、4.0%(13/322)、1.3%(4/322)。见表 2。所有接种疫苗的早产儿仅 1 名在接种乙肝疫苗和卡介苗后有发热现象。

随访 2 年,有 3 例在注射卡介苗前行结核菌素试验,结果为阳性,诊断结核感染,给予抗结核治疗。在随访结束时,仍有 2 例因患有先天性心脏病尚未治愈而未接种卡介苗。

表 2 早产儿出院时未接种乙肝疫苗和卡介苗原因分析

Table 2 Analysis of uninoculated reasons for hepatitis B vaccine and Bacillus Calmette-Guerin in preterm infants at discharge

Hospitals	The first dose of hepatitis B vaccine					Bacillus Calmette-Guerin				
	Uninoculated	Low weight	Disease	IVIG	Parental rejection	Uninoculated	Low weight	Disease	IVIG	Parental rejection
A	12	0	12	0	0	245	189	38	18	0
B	34	21	13	0	0	268	255	13	0	0
C	181	61	116	0	4	180	153	27	0	3
D	58	17	28	13	0	102	61	28	13	0
E	1	1	0	0	0	25	15	4	6	0
F	7	7	0	0	0	7	7	0	0	0
G	21	21	0	0	0	21	21	0	0	0
H	0	0	0	0	0	10	10	0	0	0
L	8	6	2	0	0	8	6	2	0	0
Total	322	134	171	13	4	866	714	112	37	3

Note: A: Xiangya No.2 Hospital of Central South University; B: Changsha maternal and child health care hospital; C: Xinhua People's Hospital; D: First Hospital Affiliated to Nanhua University; E: Affiliated Hospital of Yongzhou Vocational Technical College; F: Guidong County People's Hospital; G: Zhangjiajie Yongding District Maternal and child health care hospital; H: Cili People's Hospital; L: Xiangxi Tujia and Miao Autonomous Prefecture national traditional Chinese medicine hospital.

3 讨论

在全球范围新出生的婴儿中,早产儿的比例不断上升,占活产新生儿的比例为 10%左右,这意味着每年大约有 1500 万的早产儿出生,而早产在 5 岁以下儿童患病率和死亡率的原因位列前三,感染则是导致早产儿患病死亡的主要原因之一^[11-13],这其中有很多感染性疾病通过疫苗接种获得免疫力可以预防,比如呼吸道合胞病毒肺炎、肺炎链球菌肺炎、轮状病毒肠炎等^[14-16]。我国计划免疫规定新生儿期接种卡介苗和乙肝疫苗,正常足月新生儿多于生后 1-3 天接种,而在早产儿疫苗接种国内多参照美国 Committee on Infectious Diseases 的推荐^[17,18]。在本研究中参与的 9 所医院,既包括综合性医院,也有专科医院,而且有不同等级医院参与,这些医院所执行的疫苗接种标准各不相同,导致卡介苗和第一剂乙肝疫苗接种缺乏一致性,而且负责接种的科室主要为产科,由新生儿科或儿童保健科负责接种的医院仅有 3 所,产科医护人员非专业儿科医生,这就可能存在早产儿情况判断的差异而影响疫苗接种时机的选择^[19,20]。

本研究结果显示早产儿出院时乙肝疫苗未接种率达 16.7%,而卡介苗未接种率则高达 45.0%,这些早产儿出院后何时接种疫苗更多的取决于家长的依从性,这将明显影响疫苗的及时接种。在不同级别的医院之间,出院时疫苗未接种率有显著性差异,这与不同级别的医院所接诊的早产儿的早产程度和因早产而致疾病的严重程度不同有关,三级医院的早产儿中,出生低体重儿的比例高,而疾病严重程度也往往高于二级医院,导致三级医院出院时疫苗未接种率高于二级医院,但是有个别医院因自身习惯,导致早产儿出院时疫苗未接种率增高^[21,22]。在导致出院时未接种疫苗的原因中,疾病因素和体重因素位居前两位,这是由早产儿自身特点所决定的^[23,24]。由于卡介苗接种基本上都遵循体重达到 2.5kg 以上的原则,而各家医院乙肝疫苗的接种对体重的要求不严格,是导致卡介苗未接种率明显高于乙肝疫苗的主要原因^[25-27]。在未接种疫苗早产儿中,有 7 例为家长拒绝,这就需要普及疫苗接种知识,取得家长配合,及时接种疫苗。

在接种疫苗的早产儿中,仅有 1 例有发热现象,提示早产

儿生后早期接种卡介苗和乙肝疫苗是安全的,但对于疫苗免疫效果需要进一步随访。而在未接种卡介苗的早产儿中,有3例在注射卡介苗前行结核菌素试验,结果为阳性,诊断结核感染,而在随访2年结束,仍有早产儿因为疾病因素未接种卡介苗,这提示未接种卡介苗的早产儿要做好保护性隔离,同时做好随访,督促家长及时接种疫苗,避免人为地拖延或遗漏接种疫苗^[28-30]。

综上所述,湖南省9所医院早产儿生后早期疫苗接种原则存在差异,疾病因素和体重因素位居出院时未接种疫苗的原因的前两位,需要出台全国性的早产儿预防接种指南,最大程度使早产儿出生后早期疫苗接种规范化,避免遗漏或不恰当地推迟疫苗接种。

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