doi: 10.13241/j.cnki.pmb.2017.26.028

脂联素、胰岛素生长因子-Ⅰ、前清蛋白与早产儿宫外发育缓慢的相关性

晋芙莉[1] 宋红霞[2] 宋文萍[1] 张 丽[1] 包晓玲[1△]

(1 陕西省渭南市妇幼保健院新生儿科 陕西 渭南 714000;2 西安交通大学医学院第一附属医院新生儿科 陕西 西安 710000)

摘要 目的:探究早产儿血清脂联素、胰岛素生长因子-Ⅰ(IGF-Ⅰ)、前清蛋白(PA)水平,并分析其与早产儿宫外发育缓慢(EUGR)的相关性。**方法:**选择2014年1月~2016年1月于我院产科出生并在24 h内转入新生儿科的321例早产儿,将321例早产儿分为EUGR组和非EUGR组。比较两组新生儿生长发育情况及血清脂联素、IGF-Ⅰ、PA水平。**结果:**321例早产儿中EUGR发生率为55.76%(179/321);EUGR组新生儿在出生后第42 d及三个月时体重与非EUGR组比较明显较低,且差异具有统计学意义(P<0.05)。两组早产新生儿出生后第42 d及三个月时体重与我国9市儿童体格发育数值表相比,体重标准差(SDS)均为负值,且EUGR组新生儿的体重标准差(SDS)显著低于非EUGR组(p<0.05)。出生后第7天,EUGR组与非EUGR组新生儿血清脂联素、IGF-Ⅰ、PA水平均显著低于对照组,且EUGR组的PA水平显著低于非EUGR组(p<0.05)。出生后第14天,EUGR组血清脂联素、PA水平与第7天相比差异无统计学意义(p>0.05),非EUGR组的血清脂联素、PA水平明显增加,显著高于EUGR组(p<0.05),EUGR组和非EUGR组新生儿血清IGF-Ⅰ水平均无明显改善(p>0.05)。**结论:**较低水平的血清脂联素、IGF-Ⅰ、PA与早产儿宫外发育缓慢密切相关,可作为临床上早期判断宫外发育迟缓的辅助参考指标。

关键词:宫外发育缓慢;早产儿;脂联素;胰岛素生长因子-Ⅰ;前清蛋白

中图分类号:R722 **文献标识码:**A **文章编号:**1673-6273(2017)26-5128-03

Correlation of the Serum Levels of Adiponectin, IGF- I, PA with EUGR in Preterm Infants

JIN Fu-li[1], SONG Hong-xia[2], SONG Wen-ping[1], ZHANG Li[1], BAO Xiao-ling[1△]

(1 Department of Neonatology, Weinan Maternity and Child Health Care Hospital, Weinan, Shaanxi, 714000, China;

2 Department of Neonatology, The First Affiliated Hospital of Xi'an JiaoTong University, Xi'an, Shaanxi, 710000, China)

ABSTRACT Objective: To explore the levels of serum adiponectin, insulin growth factor I (IGF- I) and prealbumin in preterm infants, and analyze their correlation with preterm EUGR infant. **Methods:** 321 cases of preterm infants who were born in our hospital and transferred to neonatal department in 24 hours from January, 2014 to January, 2016 were enrolled in the present study. According to the weight at discharge, they were divided into the EUGR group and the non EUGR group, the growth and development as well as the levels of serum adiponectin, IGF- I and PA in the two groups were compared. **Results:** The occurrence rate of EUGR was 55.76% (179/321) in the 321 cases of preterm infants; the weight of EUGR group was significantly lower than that of the non EUGR group at 42 th days and three months after birth(p<0.05). The SDS of both groups were all negative, and that of EUGR group was significantly lower than non EUGR group (p<0.05). The levels of serum adiponectin, IGF- I and PA of both groups were significantly lower than the control group at seventh days of birth, and the PA level of EUGR group was significantly lower than non EUGR group (p<0.05). There was no significant difference in the serum adiponectin and PA levels between 7 days and 14 days in EUGR group (P > 0.05), however, the serum adiponectin and PA levels in the non EUGR group was obviously increased and significantly higher than that of the EUGR group (p< 0.05). The level of IGF- I in both groups keep unchanged during two weeks (P>0.05). **Conclusion:** The lower levels of serum adiponectin, IGF- I and PA were closely related to the EUGR of preterm infants, which could be used as biochemical indexes to early diagnosis of EUGR.

Key words: EUGR; Preterm infants; Adiponectin; IGF-Ⅰ; PA

Chinese Library Classification(CLC): R722 Document code: A

Article ID: 1673-6273(2017)26-5128-03

前言

宫外发育缓慢(EUGR)是指新生儿出院时生长发育指标小于对应宫内生长速率期望水平的10%,新生儿出生后由于营养

作者简介:晋芙莉(1977-),女,本科,主治医师,研究方向:新生儿呼吸支持,电话:13992370221,

E-mail: jinfuli_1977@medarticleonline.com

△ 通讯作者:包晓玲(1973-),女,本科,副主任医师,研究方向:新生儿危重症,电话:15129333553,

E-mail: baoxiaoling_1973-11@medicinepaper.com.cn

(收稿日期:2016-11-14 接受日期:2016-12-09)

或疾病等因素使生长发育受限，不仅提示近期体格发育落后，而且对远期健康造成不良影响[1,2]。早产儿宫外发育迟缓发生率显著高于足月儿，国外研究报道胎龄不足 37 周的早产儿的体重及头围的相应宫外发育迟缓率分别为 28.0%及 16.1%，我国相应的调查结果分别为 49.7%和 23.1%[3]，表明我国早产儿宫外发育缓慢的情况更为严峻。另有研究表明对宫外发育迟缓的早产儿行早期干预(营养支持，智能锻炼)可明显改善早产儿生存质量，使其在生长速度，智力发育等方面接近正常足月新生儿，对降低早产儿宫外发育迟缓的发生率有着重要的意义[4,5]。然而，目前临床上较为缺乏用于早期判断宫外发育迟缓的生化指标，对早期干预方案的实施带来一定困扰。因此，本研究测定了 2014 年 1 月～2016 年 1 月于我院收治的 321 例早产儿体格发育指标、血清脂联素、IGF-Ⅰ、PA 水平，并分析其相关性。

1 资料与方法

1.1 一般资料

研究对象：2014 年 1 月 ~2016 年 1 月于我院产科出生并在 24 h 内转入新生儿科的 321 例早产儿。按照出院时体重，将 321 例早产儿分为 EUGR 组和非 EUGR 组。两组早产儿的胎龄，性别等基线资料如表 1 所示。纳入标准：① 所有入组新生儿均符合早产适于胎龄儿；② 将所有入组新生儿出院时体重与中国 15 城市不同胎龄新生儿体重百分数标准[6]对比进行分组；③ 所有家属签署知情同意书，该研究获得我院伦理委员会批准。排除标准：① 合并先天代谢性疾病；② 合并先天性染色体疾病；③ 先天性胃肠道畸形，体表畸形；④ 先天性心脏病。另外选择 20 名同期入院，且年龄、性别相匹配的足月新生儿为对照组。

1.2 方法

将 321 例新生儿分为 EUGR 组和非 EUGR 组，EUGR 定义为：体重低于相应胎龄第十个百分位数。所有新生儿均定期随访 3 个月。

1.3 检测指标

1.3.1 评价两组早产儿生长发育情况 测量两组早产儿出生时、出生 42 天、3 个月时的体重。参照我国 9 市儿童体格发育数值表[6]，计算出生 42 天、3 个月时体重标准差(SDS)，SDS 数值参照文献[6]计算。SDS＞0 代表受试对象实际值大于平均值，SDS＜0 代表受试对象实际值小于平均值。

1.3.2 两组早产儿血清脂联素、IGF-Ⅰ、PA 水平比较 分别采集各入组新生儿出生 1 天及 14 天时的静脉血 1.5 mL，经静置离心后，收集血清于 -80℃冰箱储存。用酶联免疫法测定血清脂联素、IGF-Ⅰ水平，采用免疫比浊法测定 PA 水平。脂联素及 PA 检测试剂盒购于上海江莱生物科技有限公司，IGF-Ⅰ检测试剂盒购于广州固康生物科技有限公司，所有操作步骤均严格按照操作说明书。

1.4 统计学分析

使用 SPSS18.0 软件，计数资料采用卡方检验，计量资料采用 t 检验进行统计学分析，P<0.05 为差异有统计学意义。

2 结果

2.1 两组新生儿基线资料比较

依据分组标准 321 例早产儿中有 179 例发生宫外发育缓慢(EUGR)，EUGR 发生率为 55.76%。两组早产新生儿在胎龄、性别方面比较，差异无统计学意义(P＞0.05)。EUGR 组新生儿出生体重显著低于非 EUGR 组(P＜0.05)。

表 1 两组新生儿基线资料比较

Table 1 Comparison of the baseline information between two groups

Groups	Number	Gender(n)		Gestational age (week)	Birth weight (g)
		Male	Female		
EUGR	179	94	85	33.4± 1.27	1550± 149
Non-EUGR	142	75	67	33.6± 1.30	1657± 117a

Note: compared with EUGR, [a]P<0.05.

2.2 两组新生儿生长发育情况比较

EUGR 组新生儿在出生后第 42 d 及三个月时体重与非 EUGR 组比较明显较低，且差异具有统计学意义(P＜0.05)。两组早产新生儿出生后第 42 d 及三个月时体重与我国 9 市儿童体格发育数值表相比，体重标准差(SDS)均为负值，表明两组早产新生儿的体重与同龄新生儿相比，体重较轻。EUGR 组新生儿的体重标准差(SDS)显著低于非 EUGR 组(p＜0.05)。

表 2 两组新生儿生长发育情况比较($\bar{x}\pm s$)

Table 2 Comparison of the growth and development between two groups($\bar{x}\pm s$)

Groups	Number	Body weight(Kg)		SDS	
		42 d	3 month	42 d	3 month
EUGR	179	3.40± 0.97	4.60± 0.70	-2.33± 0.87	-3.04± 1.11[a]
Non-EUGR	142	3.88± 1.03[a]	5.80± 1.16[a]	-1.64± 1.33[a]	-1.59± 1.57[a]

Note: compared with EUGR, [a]P<0.05.

2.3 两组新生儿血清脂联素、IGF-Ⅰ、PA 水平比较

出生后第 7 天，EUGR 组与非 EUGR 组新生儿血清脂联素、IGF-Ⅰ、PA 水平均显著低于对照组，且 EUGR 组的 PA 水平显著低于非 EUGR 组(p＜0.05)。出生第 14 天，EUGR 组血清

脂联素水平与第 7 天相比，差异无统计学意义 (p＞0.05)，非 EUGR 组的血清脂联素水平明显增加，显著高于 EUGR 组，但显著低于对照组(p＜0.05)；出生第 14 天，EUGR 组和非 EUGR 组新生儿血清 IGF-Ⅰ水平均无明显改善(p＞0.05)；EUGR 组血清 PA 水平与第 7 天相比，差异无统计学意义(p＞0.05)；非 EUGR 组的血清 PA 水平明显增加，显著高于 EUGR 组(p＜0.05)，且血清 PA 水平与对照组相比，差异无统计学意义(p＞0.05)。

表 3 两组出生后不同时点血清脂联素、IGF-Ⅰ、PA 水平比较($\bar{x}\pm s$)

Table 3 Comparison of the level of serum adiponectin, IGF-Ⅰ, PA levels at different time points after birth between two groups ($\bar{x}\pm s$)

Groups	Number	Adiponectin(mg/L)		IGF-Ⅰ(μg/L)		PA(mg/L)	
		7 d	14 d	7 d	14 d	7 d	14 d
EUGR	179	9.16± 3.97[a]	13.15± 4.07[a]	24.97± 1.7[a]	26.0± 2.11[a]	80.5± 6.3[a]	82.7± 5.2[a]
Non-EUGR	142	12.84± 4.03[a]	21.72± 3.36[abc]	25.09± 2.3[a]	26.47± 1.16[a]	93.1± 8.7[ab]	104.3± 9.2[ab]
Control	20	23.17± 3.77	26.53± 4.21	28.36± 1.9	28.91± 2.2	105.7± 10.6	106.4± 9.5

Note: compared with control group, [a]P<0.05; compared with the EUGR group, [b]P<0.05; compared with the7 d after birth, [c]P<0.05.

3 讨论

早产儿由于出生时机体系统器官发育尚未完全成熟，营养物质储存有限，抵抗力不佳等因素使得宫外发育缓慢现象十分常见[7]。以体重计，我国早产儿宫外发育缓慢发生率近 50%。本研究纳入的 321 例早产儿中，宫外发育缓慢发生率为 55.76%，与文献报道一致，且出生时低体重新生儿发生宫外发育缓慢的可能性更大，因此及时做好围产期保健对于宫外发育缓慢的预防有重要的意义。

血清脂联素是由脂肪组织表达的蛋白质类激素，可促进脂肪细胞分化、增加胰岛素敏感性，在新生儿生长发育方面有着重要的意义[8]。研究发现大部分早产儿在儿童期均易表现出胰岛素抵抗，早产儿在宫外生长早期是胰岛素敏感性改变的重要时期，如果此时营养不足可引起发育缓慢[9-11]。血清前清蛋白(PA)是一种快速转换蛋白，随着蛋白摄入量增加而快速升高，在临床上被认为反应能量摄入的营养指标。出生体重越低的早产儿 PA 水平低下与胃肠道发育水平不佳，喂养困难，存在吸收障碍等密切相关[12-14]。本研究结果显示出生第一天 EUGR 组新生儿血清脂联素、IGF-Ⅰ、PA 水平显著低于非 EUGR 组及足月新生儿，出生第 14 天非 EUGR 组新生儿血清脂联素、PA 水平显著增加 (p＜0.05)，而 EUGR 组在上述指标上无显著改善(p＞0.05)，这可能是非 EUGR 组新生儿后期生长追赶，未发生宫外发育缓慢的原因，该结果与王爱武[15]，尚利宏[16]等人的报道一致。IGF-Ⅰ是一种与胰岛素结构类似的活性多肽，可促进生长激素发挥生理作用，刺激核酸合成与细胞增殖，在新生儿早期生长发育过程中起积极的调节作用。胎儿 IGF-Ⅰ水平主要来源于母体，且收营养水平、胰岛素的调控。早产儿营养供给不足且存在吸收障碍导致 IGF-Ⅰ水平低下[17-20]。文献报道出生 3 个月后 EUGR 组血清 IGF-Ⅰ明显低于非 EUGR 组，然而本研究中发现两组新生儿血清 IGF-Ⅰ水平显著低于对照组，在出生后 2 周并未有明显变化，这可能与测定时间较短有关。

综上所述，较低的血清脂联素、IGF-Ⅰ、PA 水平与早产儿宫外发育缓慢密切相关，可作为临床上早期判断宫外发育迟缓的参考指标，对实施早期干预降低宫外发育迟缓发生率有积极的意义。

参 考 文 献(References)

[1] Pampanini V, Boiani A, Marchis CD, et al. Preterm infants with severe extrauterine growth retardation (EUGR) are at high risk of growth impairment during childhood [J]. European Journal of Pediatrics, 2015, 174(1): 33-41

[2] Freitas BACD. Extrauterine growth restriction: Universal problem among premature infants[J]. Revista De Nutricao-brazilian Journal of Nutrition, 2016, 29(1): 53-64

[3] Cao W, Zhang Y H, Zhao D Y, et al. Risk factors for extrauterine growth restriction in preterm infants with gestational age less than 34 weeks [J]. Chinese journal of contemporary pediatrics, 2015, 17(5): 453-458

[4] Lunde D, Lunde D. Extrauterine growth restriction: What is the evidence for better nutritional practices in the Neonatal Intensive Care Unit?[J]. Newborn & Infant Nursing Reviews, 2014, 14(3): 92-98

[5] Andersson O. The transition to extra-uterine life by extremely preterm infants - handle with care[J]. ActaPaediatrica, 2016, 105(4): 337-338

[6] 武文艳, 王俊怡, 徐小静. 早产儿、小于胎龄儿体质量追赶生长及其与 IGF-1 的相关性[J]. 山东医药, 2015, 55(1): 69-71
Wu Wen-yan, Wang Jun-yi, Xu Xiao-jing. The catch-up growth of premature infants and infants with less than gestational age and its relationship with IGF-1 [J]. Shandong Medical Journal, 2015, 55(1): 69-71

[7] Desnoulez L, Truffert P, Putet G, et al. 70 Risk Factors of Extrauterine Growth Restriction of Very Preterm Newborns. Results from The Epipage Nord Pas De Calais Cohort [J]. Pediatric Research, 2004, 56 (3): 476-476

[8] Nakano Y, Itabashi K, Sakurai M, et al. Preterm infants have altered adiponectin levels at term-equivalent age even if they do not present with extrauterine growth restriction [J]. Hormone Research in Paediatrics, 2013, 80(3): 147-153

[9] Nagasaki H, Ohta T. Extra-uterine growth and adipocytokines in appropriate-for-gestational-age preterm infants [J]. Pediatrics International Official Journal of the Japan Pediatric Society, 2015, 58 (7): 584-588

[10] Yoshida T, Nagasaki H, Asato Y, et al. Early weight changes after birth and serum high-molecular-weight adiponectin level in preterm infants [J]. Pediatrics International Official Journal of the Japan Pediatric Society, 2011, 53(6): 926-929

（下转第 5180 页）

Henoch-Schönlein purpura nephritis and IgA nephropathy: comparative analysis of data from the Japan Renal Biopsy Registry (J-RBR)[J]. Clinical and Experimental Nephrology, 2016, 20(4): 1-9

[5] Chen JY, Mao JH. Henoch-Sch (o)nlein purpura nephritis in children: incidence, pathogenesis and management [J]. World Journal of Pediatrics, 2015, 11(1): 29-34

[6] Lu S, Liu D, Xiao J, et al. Comparison between adults and children with Henoch-Schonlein purpura nephritis [J]. Pediatric Nephrology, 2015, 30(5): 791-796

[7] O'Neil KM, Varma C, Farooq O, et al. Glucocorticoid-responsive hypertension in Henoch-Schonlein purpura [J]. Clinical Pediatrics, 2010, 49(7): 702-706

[8] Shin E, Hideaki T, Masao O. Nuclear factor erythroid 2-related factor 2 is a critical target for the treatment of glucocorticoid-resistant lupus nephritis[J]. Arthritis Research & Therapy, 2016, 18(1): 1-12

[9] Chen JY, Mao JH. Henoch-Sch (o)nlein purpura nephritis in children: incidence, pathogenesis and management [J]. World Journal of Pediatrics, 2015, 11(1): 29-34

[10] Baek CH, Kim H, Yu H, et al. Low dose of mycophenolate mofetil is enough in desensitized kidney transplantation using rituximab [J]. BMC Nephrology, 2015, 16(1): 1-9

[11] Kizawa T, Nozawa T, Kikuchi M, et al. Mycophenolate mofetil as maintenance therapy for childhood-onset systemic lupus erythematosus patients with severe lupus nephritis [J]. Modern Rheumatology, 2015, 25(2): 210-214

[12] Kirpalani A, Filler G, Grimmer J, et al. Steroid Retrial After Rituximab and Mycophenolate Mofetil in Pediatric Refractory Nephrotic Syndrome[J]. World J Nephrol Urol, 2016, 5(2): 33-36

[13] Allison AC, Eugui EM. Mycophenolate mofetil and its mechanisms of action[J]. Immunopharmacology, 2000, 47(2-3): 85-118

[14] Taylor A, Neave L, Solanki S, et al. Mycophenolate mofetil therapy for severe immune thrombocytopenia [J]. British Journal of Haematology, 2015, 171(4): 625-630

[15] Howard J, Hoffbrand AV, Prentice H G, et al. Mycophenolate mofetil for the treatment of refractory auto-immune haemolytic anaemia and auto-immune thrombocytopenia purpura [J]. British Journal of Haematology, 2002, 117(3): 712-715

[16] Van Dieren JM, Kuipers EJ, Samsom JN, et al. Revisiting the immunomodulators tacrolimus, methotrexate, and mycophenolate mofetil: their mechanisms of action and role in the treatment of IBD [J]. Inflammatory Bowel Diseases, 2006, 12(4): 311-27

[17] Bazsó A, Szappanos Á, Patócs A, et al. The importance of glucocorticoid receptors in systemic lupus erythaematosus [J]. Autoimmunity Reviews, 2015, 14(4): 349-351

[18] Aida K, Miyakawa R, Suzuki K, et al. Suppression of Tregs by anti-glucocorticoid induced TNF receptor antibody enhances the antitumor immunity of interferon-α gene therapy for pancreatic cancer[J]. Cancer Science, 2014, 105(2): 159-167

[19] Cattaneo D, Perico N, Gaspari F, et al. Cattaneo D, Perico N, Gaspari F, Gotti E, Remuzzi G. Glucocorticoids interfere with mycophenolate mofetil bioavailability in kidney transplantation. Kidney Int 62: 1060 [J]. Kidney International, 2002, 62(3): 1060-1067

[20] 陈艳霞, 房向东, 占锦峰,等. 吗替麦考酚酯治疗过敏性紫癜肾炎的 Meta 分析[J].中国临床药学杂志, 2016(1): 20-25
Chen Yan-xia, Fang Xiang-dong, Zhan Jin-feng, et al. Meta analysis of the clinical effect of mycophenolate mofetil on patients with henoch-schonlein nephritis [J]. Chinese Journal of Clinical Medicine, 2016(1): 20-25

(上接第 5130 页)

[11] Savvidou M D, Sotiriadis A, Kaihura C, et al. Circulating levels of adiponectin and leptin at 23-25 weeks of pregnancy in women with impaired placentation and in those with established fetal growth restriction[J]. Clinical Science, 2008, 115(7): 219-22

[12] Rafati M, Nakhshab M, Ghaffari V, et al. Evaluation of Nutritional Status in a Teaching Hospital Neonatal Intensive Care Unit[J]. Iranian Journal of Neonatology, 2015, 5(4): 23-27

[13] Ortiz E M, Gil C M, Muñoz Villanueva M C, et al. Metabolic changes in prepuberty children with extrauterine growth restriction[J]. Anales De Pediatrí a, 2012, 77(4): 247-253

[14] Lee SJ, Park EA, Seo JW. Usefulness of Serum Prealbumin Concentration as a Marker for Nutritional Adequacy in Premature Infants[J]. Korean Journal of Pediatrics, 2001, 24(12): 108-116

[15] 王爱武. 早产儿宫外发育迟缓与血清前清蛋白的关系研究[J].重庆医学, 2011, 40(10): 1000-1001
Wang Ai-wu. The relations between extrauterine growth restriction and the prealbumin in premature infant [J]. CHONGQING MEDICINE, 2011, 40(10): 1000-1001

[16] 尚利宏, 杨真录, 王颖源. 早产儿宫外生长发育迟缓与血清脂联素的关系[J].中国妇幼保健, 2015, 30(34): 6011-6014
Shang Li-hong, Yang Zhen-lu, Wang Ying-yuan. Relationship between premature extrauterine growth retardation and serum adiponectin[J]. Maternal & Child Health Care of China, 2015, 30(34): 6011-6014

[17] Hellström A, Ley D, Hansen-Pupp I, et al. Role of Insulinlike Growth Factor 1 in Fetal Development and in the Early Postnatal Life of Premature Infants [J]. American Journal of Perinatology, 2016, 33 (11): 1067-1071

[18] Teng R J, Wu T J, Hsieh F J. Cord blood level of insulin-like growth factor-1 and IGF binding protein-3 in monochorionic twins [J]. Journal of the Formosan Medical Association, 2015, 114(4): 359-362

[19] Deeney S, Powers K, Dodson B, et al. Reciprocal Serum Levels of Insulin-Like Growth Factor-1 and IGF-Binding Protein-3 in a Murine Surgical Model of Intrauterine Growth Restriction [J]. Journal of the American College of Surgeons, 2015, 221(4): S99-S99

[20] Keswani S G, Balaji S, Katz A B, et al. Intraplacental gene therapy with Ad-IGF-1 corrects naturally occurring rabbit model of intrauterine growth restriction[J]. Human Gene Therapy, 2015, 26(3): 172-182