• Original Article in English •

Blood motilin and gastrin levels in term newborns with hyperbilirubinemia

Li AN, Ping ZHAO, Ji-Ying WU

Department of Pediatrics, Jinan Central Hospital, Clinical Medical College of Shandong University, Jinan 250013, China

Abstract: Objective Most newborn infants with hyperbilirubinemia have gastrointestinal tract symptoms. The aim of this study is to investigate the effect of hyperbilirubinemia on gastrointestinal hormone levels in newborn infants. **Methods** Fasting plasma motilin and serum gastrin levels were measured using a radioimmunoassay in 50 term newborns with hyperbilirubinemia (Hyperbilirubinemia group). Fasting plasm motilin and serum gastrin levels from thirty normal term newborns were used as controls. **Results** The plasma motilin level in the Hyperbilirubinemia group (659±37 ng/L) was significantly higher than that of the controls (486±28 ng/L) ($P<0.01$). The plasma motilin level was positively correlated with the serum bilirubin level. The serum gastrin level in the Hyperbilirubinema group was not different from that of the controls. **Conclusions** The plasma motilin level is correlated with the level of bilirubin in the newborn. The abnormal increase in the level of motilin may be related to the development of gastrointestinal symptoms newborns with hyperbilirubinemia.

[**Chin J Contemp Pediatr, 2004, 6(4): 247−250**]

Key words: Hyperbilirubinemia; Motilin; Gastrin; Radioimmunoassay; Infant, newborn

新生儿高胆红素血症与胃动素 胃泌素水平的相关性研究

安丽，赵平，武际英 山东大学临床医学院济南市中心医院儿科，山东 济南 250013

[**摘 要**] **目的** 新生儿高胆红素血症患儿常出现胃肠道症状。该研究目的是探讨高胆红素血症(高胆)对新生儿胃肠激素水平的影响及其可能的发生机制。**方法** 应用放射免疫分析法(RIA)对 50 例高胆患儿空腹状态下血中胃动素、胃泌素浓度进行测定，并以 30 例正常新生儿作为对照。**结果** 高胆组患儿血浆胃动素浓度(659±37 ng/L)明显高于对照组(486±28 ng/L)，差异有显著性意义($P<0.01$)，且与血清胆红素水平呈正相关；血清胃泌素浓度(128±9 ng/L)与对照组(132±11 ng/L)比较差异无显著性($P>0.05$)。**结论** 高胆红素血症新生儿的某些胃肠道症状可能与胃动素分泌异常有关。

[**中国当代儿科杂志，2004, 6(4): 247−250**]

[**关 键 词**] 高胆红素血症；胃动素；胃泌素；放射免疫测定；婴儿，新生

[**中图分类号**] R722 [**文献标识码**] A [**文章编号**] 1008−8830(2004)04−0247−04

Most newborn infants with hyperbilirubinemia have gastrointestinal tract symptoms such as anorexia, abdominal distension and vomiting. To study the changes of gastrointestinal hormone levels in neonates with hyperbilirubinemia, fasting plasma motilin and serum gastrin concentrations were measured in 50 term newborns with hyperbilirubinemia and the relationship between their concentrations and other clinical factors were investigated.

Subjects and methods

Subjects

Fifty term neonates with hyperbilirubinemia (Hyperbilirubinemia group) and 30 normal term

[Received] December 8, 2003; [Revised] April 12, 2004
[Biography] Li AN(1967−), Female, M.D., Associate Professor, Specializing in neonatology and pediatric neurology.
[Correspondence Author] Li AN, Department of Pediatrics, Jinan Central Hospital, Clinical Medical College of Shandong University, Jinan 250013, China (Email:doctordiane@163.com).

neonates (Control group) were enrolled in this study. In the Hyperbilirubinemia group, there were 28 males and 22 females, with gestational ages ranging from 37 weeks to 41 weeks (mean 39.5 weeks), with day ages ranging from 1 day to 18 days (mean 11 days), with episode ages ranging from 0.5 day to 6 days (mean 3.5 days), and weighing ranging from 2 600 to 3 750 g (mean 3 250 g). Their total bilirubin levels ranged from 208.2 μmol/L to 265.8 μmol/L (mean 239.7 μmol/L). Twenty-three were delivered by cesarean section, and the others by vaginal delivery. None had congenital malformations and all of then accorded with the diagnostic standards of pathological jaundice[1]. The Control group was matched to the Hyperbilirubinemia group in gender, gestational age, day age and body weight.

Methods

Sample collection and process

Four ml fasting femoral vein blood was obtained from the two groups in the early morning. Two ml blood was added to cold test tubes containing 30 μl 10% edathamil disodium and 30 μl aprotinin, and then thoroughly mixed. After the processed blood and the other un-processed blood samples had been centrifuged at 4 ℃ for 20 minutes, plasma and serum were taken out and were preserved at −20℃.

Detection of motilin and gastrin levels

The motilin level was detected using motilin radio-immunity analysis box labeled by ^{125}I which was provided by the East Asia Immune Technology Research Institute of Liberation Army Hospital. The gastrin level was detected using gastrin radio-immunity analysis box labeled by ^{125}I which was provided by the Beijing Furui Biology Engineering Company. The error was 4.5% and 3.2% respectively. The measuring instrument was a FJ-2003 automatic γ-immune counter which was made in Xi'an 262 Factory.

Statistics analysis

All data were expressed as $\bar{x} \pm s$. SAS software packet was employed to conduct statistical calculations. The t-test and step by step regression analysis were used for analysis of differences and correlations. $P < 0.05$ was considered statistically significant.

Results

Plasma motilin concentration

The fasting plasma motilin concentration was 659±37 ng/L in the Hyperbilirubinemia group. It was significantly higher than that in the Control group (Table 1).

Table 1 Plasm motilin concentrations in the Hyperbilirubinemia and Control groups ($\bar{x} \pm s$, ng/L)

Group	n	Motilin
Control	30	486±28
Hyperbilirubinemia	50	659±37
t		3.312
P		<0.01

Serum gastrin concentration

The fasting serum gastrin concentration was 132±11 and 128±9 ng/L in the Control and Hyperbilirubinemia groups respectively. There was no statistically significant difference between the two groups (Table 2).

Table 2 Serum gastrin concentration in the Hyperbilirubinemia and Control groups ($\bar{x} \pm s$, ng/L)

Group	n	Gastrin
Control	30	132±11
Hyperbilirubinemia	50	128±9
t		0.875
P		>0.05

The correlation between plasm motilin concentration and the other clinical factors in the Hyperbilirubinemia group

The plasm motilin concentration in the Hyperbilirubinemia group was regarded as a variable and was compared with the other factors using step by step regression analysis. The self-variables, including gestational age (x_1), episode age (x_2), day age (x_3), body weight (x_4), bilirubin concentration (x_5) and motilin concentration (x_6), were in-

troduced into the equation. Those factors which had a significant level of less than 0.15 were selected for the next analytical stage. As a result, variables such as x_1, x_2, x_4 and x_6 were rejected. In the other variables, x_5 played the most important role in influencing the plasm motilin level followed by x_3. See Table 3.

Table 3 Results of regression analysis

Variable	Dedication to R_2	R_2	C(p)	F	P
Bilirubin concentration	0.3026	0.3026	5.290	15.617	<0.01
Day age	0.0842	0.3867	2.554	4.803	<0.05
Gastrin concentration	0.0217	0.4312	2.003	1.980	>0.05
Gestational age	0.0129	0.4535	1.375	1.842	>0.05
Episode age	0.0113	0.4861	1.219	1.821	>0.05
Body weight	0.0067	0.5328	1.032	1.625	>0.05

Discussion

Neonatal jaundice is the most common problem in the perinatal period. It is regarded as pathological jaundice when any one of the following conditions occurres: ① Jaundice occurs within the first 24 hours of life, with serum bilirubin level being more than 102 μmol/L; ② Serum bilirubin level in full-term neonates exceeds 220.6 μmol/L, or exceeds 255 μmol/L in preterm infants; ③ Serum direct bilirubin level exceeds 26 μmol/L; ④ Serum bilirubin level increases by over 85 μmol/L daily; ⑤ Jaundice lasts for 2 to 4 weeks, or becomes more and more serious. Hyperbilirubinemia is confirmed when the serum bilirubin concentration is higher than that of physiological jaundice, which can induce injuries of nervous system. Hyperbilirubinemia is the most common in neonatal admission cases in many hospitals[2,3]. The cause of this disorder could not be confirmed in about 20% hospitalized patients[4]. Recent investigations have indicated that many patients with digestive tract diseases have abnormal secretion of gastrointestinal hormones. The patients with hyperbilirubinemia often have gastrointestinal tract symptoms, such as gastric retention, abdominal distension, vomiting and slowing of weight growing. Hyperbilirubinemia also contributes to the changes of the liver and cholecyst functions and is related to the abnormal secretion of gastrointestinal hormones. This study showed that the plasma motilin level in newborns with hyperbilirubinemia was significantly higher than that of Control group and that the serum gastrin level was not statistically different from that of the Control group.

Motilin is a brain-gut peptide[5]. It exists as a hormone in mucosae recessus's endocrine cells of stomach, dodecadactylon jejunum and near tip of jejunum, and also exists as a neurotransmitter in peripheral nerves of digestive system and brain tissues. To some extent its contents can reflect the growth and development level of endocrine cells and neurons. Motilin has a stronger stimulation to the mechanical movement and electrical action of the upper digestive tract, which is of great significance on the movement of the upper digestive tract after eating. The increased level of motilin can result in coordination disturbance and movement disorder of the intestine and stomach and can make gastric emptying slower, yielding digestive tract symptoms such as gastric retention, abdominal distension and vomiting. The following factors may be related to abnormal increased plasma motilin level in newborns with hyperbilirubinemia: ① Liver is one of the major organs to clear and inactivate motilin. Hyperbilirubinemia of the newborn and the decreased ability to clear motilin due to immaturity of liver development can increase the plasma motilin level. ② Unconjugated bilirubin is toxic to brain cells, especially to neurons. It can lead to the disturbance of neuron functions and then stimulate

abnormal secretion of motilin. The higher the serum bilirubin concentration, the more serious the nervous system injuries. The step by step regression analysis in this study showed that the serum bilirubin level increased and was positively correlated with the plasma motilin level in newborn infants with hyperbilirubinemia, which corresponded with clinical manifestations. ③ Infection is one of the principal causes of hyperbilirubinemia of the newborn. Some inflammation mediums can affect the function of endocrine cells which secrets motilin. ④ The dysfunction of the intestine and stomach of patients with hyperbilirubinemia can induce motilin secretion by feedback mechanism.

Gastrin released by G-cell in gastrointestinal tract can stimulate the secretion of gastric acid and pepsin and promote peristalsis of the intestine and stomach and the growth of gastrointestinal mucous membrane. Blood capillary bed and kidneys play a major role in gastrin's metabolism, while the liver is not involved in the inactivation and clearing of gastrin. This study showed that the serum gastrin level in the newborns with hyperbilirubinemia was not statistically different from that of the normal newborns. It suggests that the serum gastrin level has no significant correlation with hyperbilirubinemia of the newborn.

The step regression analysis also showed that the plasma motilin level was positively correlated with day age of patients. This correlation reflected the developmental level and physiological condition of the secretory cells, and it confirmed that motilin played a positive auxo-action in development of neonatal digestive tract. Foreign research[7] has indicated that motilin may take part in the integration between behavior (ingestion) and emotion (anxiety) when regarded as neurotransmitter or medium. It is necessary to make thorough investigations about mechanism and comprehensive effects of gastrointestinal hormones' abnormal secretion in hyperbilirubinemia.

[**References**]

[1] Jin H-Z, Huang D-M, Guan X-J. Practical Pediatrics [M]. 2nd ed. Beijing: People's Health Publishing House (in Chinese), 1997, 217—225.

[2] Akaba K, Kimura T, Sasaki A, Tanabe S, Wakabayashi T, Hiroi M, et al. Neonatal hyperbilirubinemia and a common mutation of the bilirubin uridine diphosphate-glucuronosyl transferase gene in Japanese [J]. J Hum Genet, 1999, 44(1): 22—25.

[3] Di Maio M, Langevin L. Management of hyperbilirubinemia of the term newborn in matermity wards [J]. Arch Pediatr, 1998, 5(10): 1156—1161.

[4] Huang D-M. How to decrease the morbidity, mortality and mutilation rate of hyperbilirubinemia of the newborn [J]. Chin J Pediatr (in Chinese), 1996, 34(4): 219—220.

[5] Peeters TL, Depoortere I. Motilin receptor: a model for development of prokinetics [J]. Dig Dis Sci, 1994, 39 (12 Suppl): 76s—78s.

[6] Wei Z-T. Gastroenterology [M]. 2nd ed. Beijing: People's Health Publishing House (in Chinese), 1993, 1201—1207.

[7] Momose K, Inui A, Asakawa A, Ueno N, Nakajima M, Kasuga M. Anxiolytic effect of motilin and reversal with GM-109, a motilin antagonist, in mice [J]. Peptides, 1998, 19(10): 1739—1742.

(Edited by Le ZHONG)