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Changes of serum bile acid concentrations in children associated with gender and age

Zmiany stężenia kwasów żółciowych w surowicy krwi u dzieci w zależności od płci i wieku

INTRODUCTION

In normal conditions bile acids (BA), that are produced in the liver from cholesterol, are enzymatically conjugated with glycine and taurine and thus they form bile acid salts. In this form BA are secreted to bile, temporarily stored in the gall bladder, and then they participate in the process of digestion and absorption of lipids in the duodenum and jejunum. Subsequently nearly all (99%) BA are actively absorbed in the ileum entering entero-hepatic circulation cycle. Non-absorbed BA are metabolised by bacterial flora of the large bowel into secondary BA that are partially reabsorbed into the (portal) blood stream, thus entering entero-hepatic circulation cycle of BA, and the remaining quantity of BA is excreted with faeces [4, 5].

In normal conditions, the vast majority of BA that were absorbed in the bowel, is uptaken by the liver and only the minor quantities of BA enter the systemic circulation. Therefore, serum BA concentrations are very low (in adults normal level is 5 μmol/l) and they reflect a balance between their intestinal absorption and hepatic clearance [5, 6].

Invasive diagnostic methods, like endoscopic retrograde or percutaneous transhepatic cholangiography, or non-invasive imaging techniques (ultrasound, computed tomography) tremendously improved early diagnosis of hepatic diseases, especially focal hepatic lesions. Diagnosis of diffuse hepatic disorders remains difficult. Significant progress in this matter was made when determination of serum concentrations of BA was introduced, especially in regard of sub-clinical hepatic disorders and

cholestasis. Serum BA concentrations determination is non-invasive, simple (commercially available test kit) and very sensitive diagnostic test in evaluation of liver disorders [2, 6]. However its usefulness is limited by lack of data on normal value range of serum BA concentrations in children, especially newborns and infants. Therefore, the aim of the study was to:

1. evaluate serum total bile acids concentrations according to the age and gender of children, and
2. compare thus obtained results with the normal values of adults (5 μmol/l).

MATERIAL

Two hundred sixty one children (135 females and 126 males) in age ranging from 1st day of life to 16 years old were included in the study. These were healthy children without any abnormalities on physical examination. The children were divided into groups according to their gender and age.

METHOD

Determination of serum BA concentrations was made using enzymatic-colorimetric method by means of 3α-hydroxysteroid dehydrogenase (*Enzabile* kit, Nycomed Pharma, Norway). Blood serum samples were taken up 3 hours after last meal in newborns and infants, and on fasting in children over 1 year old. Serum BA concentrations (μmol/l) were presented in mean ± standard deviation (SD).

RESULTS

Results of serum BA determinations in different age groups according to the gender of the investigated children are listed in Table 1.

Table 1. Serum BA concentrations in different age groups of children according to the gender.

Gender	Age	Number of cases (n)	Serum BA concentrations µmol/ (mean ±SD)
Male	1–6 days	11	22.4 ±4.3
	1–6 months	50	19.8 ±4.9
	7–12 months	26	17.1 ±4.9
	2–6 years	25	9.9 ±2.1
	7–16 years	14	4.6 ±1.3
Female	1–6 days	12	21.3 ±4.7
	1–6 months	73	19.3 ±5.3
	7–12 months	13	16.9 ±4.7
	2–6 years	27	9.7 ±1.9
	7–16 years	10	4.4 ±1.4

DISCUSSION

Lack of the literature data on normal values of serum BA concentrations in newborns, infants, and children has limited a clinical application of the diagnostic test that is very sensitive for diagnosis of cholestasis or hepatocellular damage. Results of the present study indicate that there are considerable differences between serum BA concentrations in children and in adults (as normal values for adults given by the test producer). The differences are remarkable also between different age groups of children. The highest serum BA concentrations in newborns and in infants are probably related with the physiologic immature entero-hepatic circulation of the BA. This leads to ineffective digestion of lipids, increased hepatic clearance, and cholestasis [2, 4, 6]. Because of prolonged hepatic clearance, serum BA concentrations in fasting newborns is several times higher than in adults [1]. High serum BA concentrations in newborns observed in the present study, decrease gradually in infant and post-infant age, and this phenomenon is probably associated the maturation of the liver and alimentary tract function. This observation is in agreement with other reports [4, 11]. In the present study no gender-related differences were observed in serum BA concentrations of the children.

Knowledge of range of physiologic serum BA concentration values is extremely important especially in the youngest children because this is very sensitive marker of cholestasis than can be easily found before its clinical manifestation. Early diagnosis of metabolic BA disturbances or congenital biliary atresia, that enables immediate treatment, improves prognosis [6, 7, 8, 9]. When interpreting values of serum BA concentration in children it is mandatory to refer to age of the patient [7].

CONCLUSIONS

1. Serum BA concentrations in newborns are significantly higher than in normal values of adults.
2. Serum concentration of total BA increased gradually after delivery, with peak values occurring at the age of 1 month, which then gradually declined to nearly the adult levels by the age of 6 years.
3. No gender-related differences were observed in serum BA concentrations in children.

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STRESZCZENIE

Celem pracy była ocena zmian stężenia całkowitych kwasów żółciowych (KŻ) w surowicy krwi w zależności od wieku i płci dzieci, a także ich porównanie z normą dla dorosłych (5 μmol/l).

Oznaczeń stężenia KŻ dokonywano przy użyciu testu enzymatyczno-kolorymetrycznego *Enzabile* (Nycomed Pharma, N) w surowicy krwi pobranej 3 godz. po ostatnim posiłku u noworodków i niemowląt oraz na czczo u dzieci > 1 r.ż. Uzyskane wyniki przedstawia tabela:

Płeć	Wiek	Liczba przypadków (n)	Stęż. KŻ w surowicy krwi w μmol/l (średnia ±SD)
Chłopcy	1–6 dni	11	22.4 ±4.3
	1–6 mies.	50	19.8 ±4.9
	7–12 mies.	26	17.1 ±4.9
	2–6 r.ż.	25	9.9 ±2.1
	7–16 r.ż.	14	4.6 ±1.3
Dziewczynki	1–6 dni	12	21.3 ±4.7
	1–6 mies.	73	19.3 ±5.3
	7–12 mies.	13	16.9 ±4.7
	2–6 r.ż.	27	9.7 ±1.9
	7–16 r.ż.	10	4.4 ±1.4

Wnioski: Stężenia KŻ w surowicy krwi noworodków są istotnie wyższe od normy dla dorosłych. Od urodzenia narastają one stopniowo, osiągając wartości szczytowe w wieku 1 mies., po czym obserwuje się ciągłe zmniejszanie się stężenia KŻ, które osiąga wartości zbliżone do stężeń właściwych dorosłym po 6 r.ż. Nie zaobserwowano istotnych różnic stężenia KŻ w zależności od płci.