Effect of Jaundice on Trace Elements Levels Children

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Abstract

- **Objective:** In the present study, the levels of Zinc (Zn), Copper (Cu) and Iron (Fe) in children with Jaundice aged (1-2 yr) were investigated.

- **Methods:** 25 children diagnosed with Jaundice and (25) healthy children were included in the study. Serum Zinc (Zn), Copper (Cu) and Iron (Fe) levels were measured by Atomic Absorption Spectrophotometry. (GOT), (GPT), and total Bilirubin levels were measured by colormetric methods, while hemoglobin concentration was measured by cynomethmeglobin method.

- **Results:** Cu and Fe levels were found to be significantly high in jaundice group ($p<0.05$) also, Zn levels were found to have tendency to increase ($p<0.05$)than control group. A significant positive correlation between serum Cu, Fe, and total serum bilirubin was established in Jaundice children.

- **Conclusion:** Our findings showed that serum trace elements (Zn, Cu, Fe) levels changed in children with Jaundice. These changes might partially be due to pathological causes during this disease.

الخلاصة

الهدف: تمت دراسة مستويات العناصر: الزنك، النحاس والحديد لدى الأطفال المصابين بمرض اليرقان وفي عمر (1-2) سنة.

طرق العمل : تضمنت الدراسة (25) طفلا مصابين بمرض اليرقان و(25) طفلا آخرين أصحاء لمجموعة سيطرة: مستويات الزنك، النحاس والحديد في مصول الدم يتم قياسها بواسطة تقنية مطيافية الامتصاص الذري. مستويات الإنزيمات الناقلة (GPT, GOL) ومستوى البيليروبين الكلي قد تم قياسها بواسطة الطرق اللونية وباستخدام عدة الاختبار(kit) ، بينما تم قياس تركيز الهيموغلوبين بواسطة طريقة سيتاميثوغلوبين\.

النتائج: أظهرت مستويات النحاس والحديد ارتفاعا معنويا ($p<0.05$) في مجموعة الأطفال المصابين باليرقان. أيضا لوحظ ميل مستويات الزنك إلى الارتفاع ($p<0.05$) لدى الأطفال المصابين باليرقان. أيضا وجد علاقة ارتباط موجبة بين مستويات النحاس، الزنك ومستوى البيليروبين الكلي لدى الأطفال المصابين باليرقان.

الاستنتاجات: أظهرت نتائج دراستنا تغيرات في مستويات العناصر النزرة: الزنك، النحاس والحديد لدى الأطفال المصابين باليرقان. تلك التغيرات تعزى جزئيا إلى التغيرات المرضية التي تحدث أثناء مرض اليرقان.

Introduction

Jaundice is a yellow discoloration of the skin or sclera of eye. This is due to the elevation of bilirubin in the plasma and is not usually detectable until the concentration is greater than about 40µmol/L. Normally, the bilirubin concentration in plasma is less than 22µmol/L.[1]

Bilirubin is the final product of heme degradation. At physiologic pH, bilirubin is insoluble in plasma and requires protein binding with albumin. After conjugation in the liver, it is excreted in bile (2,3,4). New borns produce bilirubin at a rate of approximately (6 to 8) mg per kg per day. This is more than twice the production rate in adults, primarily because of relative polycythemia and increased red blood cell turnover in neonate.[4] Bilirubin production by typically declines to the adult level within (10 to 14) days after birth.[5] Jaundice classification is into three types: prehepatic, hepatic and cholestatic. There is much overlap, particularly between the hepatic and cholestatic varieties.[6]

Trace elements are important in human nutrition, their deficiency has been documented in Malnourished and Straving populations in industrialized countries, where marginal deficiency is now recognized to be fairly common, especially in children and the elderly.[7] Most of the trace elements are metabolized by the liver; damage to hepatic cells usually results trace element deficiency but in some conditions an altered excretion may cause toxicity. Zinc, iron, copper, selenium, manganese and calcium have been studied more extensively whereas the importance of other trace elements and minerals are as yet unknown.[8]

Dietary zinc (Zn) deficiency has been well documented in humans and animals and low Zn status has been linked to many diseases including diabetes[9], abnormal immune function[10], teratogenesis[11] and nerological disorder.[12]

Copper is an essential component of many enzymes involved in cellular respiration, free radical defense and cellular iron metabolism. Cu is known to be toxic in human with prevalent hepatic damage[8]. Cu absorption occurs in the duodenum and jojunm. The efficiency of absorption is relatively high compared with that of other trace elements[8].

Iron (Fe) is required for the synthesis of the oxygen transport proteins, hemoglobin and myoglobin and for the formation of heme enzymes participating

in electron transfer and oxidative-reductive reactions. (Fe) is absorbed in the duodenum through an active, saturable process. The regulation of Fe homeostasis is controlled by variations in absorption. The excess Fe is stored as ferritin or hemosiderin in the liver, spleen, and bone marrow(10). The liver is particularly sensitive to the toxic effects of Fe, reflecting it role in storage and metabolism Hepatic Fe overload induces lipid peroxidation and leads to structural and/or functional alterations in various cell organelles. (Fe) may also enhance the cell-damaging effects of other hepatotoxic factors, such as alcohol, Cu, or viruses[13].

The aim of this study was to evaluate the importance of zinc (Zn), copper (Cu), and iron (Fe) in the pathogenesis of Jaundice in children.

Materials and Methods

Totally, 50 children were enrolled in the study, (25) children with Jaundice (13 males, 12 females), with age ranged between 1- 2 years (1.6 ±SD 0.9) who admitted to the Maternity and Children Teaching Hospital in Diwaniyah City inIraq during(may –July 2005)in which all clinical information was established

The control group consisted of (25) healthy children (15 males and 10 females). With age ranged between 1 – 2 year(1.8 ± SD 0.7 year)

Methods

Blood samples were drown from 25 child of jaundice and control group into sterile, disposable plastic syringes for determination of serum Zn, Cu and Fe levels. All plastic and glass ware used in the experiment were treated with deionized water and then dried. The serum was separated within 2 hr. after blood withdrawal and stored at (-22C°) until analyzed. Serum samples were diluted with deionized water. Zn, Cu and Fe were determined by atomic absorption spectrophotometer (Z-8200 polarized Zeeman).[14]

Serum GOT, GPT level were measured by colormetric method using a kit obtained from biomerieux, France[15], while serum hememoglobin concentration was measured by cynamethoglobin method[16]. Serum total protein was determined by Biuret method.[17]

Total serum bilirubin level was measured using bedside bilirubin meter that uses the direct spectrophotometric method[18].

Statistical Analysis

Results were expressed as the (mean ±, standard deviation [SD]), the difference of parameters between patients

and controls were tested by student's (t-test) for paired value. A ($p<0.05$) was considered to statistically significant. Correlation coefficient was used to test the correlation between two variables.

Results

The clinical characteristics of patients stidied and control groups are summarized in table (I). There were no significant differences in age. The data showed a significant difference ($p<0.05$) in the levels of (GOT, GPT, Hb and total protein) between children with jaundice as compared with control group

Serum Zn, Cu and Fe levels of the groups are shown in table (II). Serum Zn levels in children with Jaundice were significantly increased ($p<0.05$) than that found in the control group. Serum Cu levels in jaundice group were significantly increased ($p<0.05$) as compared with control group. Levels of serum Fe in Jaundice group was also high ($p<0.05$) as compared with control group.

The correlation factor between serum trace elements (Zn,Cu,Fe) levels and total serum bilirubin are shown in table (III). A negative correlation ($R = -0.61$) between serum Zn level and total serum bilirubin concentration was established, while a positive significant noncorrelation between serum Cu and Fe levels with total serum bilirubin concentration ($R=0.25$), ($R=0.14$) respectively.

Table (I): The characteristics in children with Jaundice and control group expressed as (mean + SD)

Parameter	Jaundice group (n=25)	Control group (n=25)	P-value
Sex (M/F)	(13/12)	(5/10	
Age (year)	1.6 $\pm$ 0.9	1.8 $\pm$ 0.7	
Total serum bilirubin (mg/dL)	20.7 $\pm$ 9.3	8.11 $\pm$ 4.1	< 0.05
GOT (µ/L)	129.72 $\pm$ 61.7	32.4 $\pm$ 13.08	< 0.05
GPT (µ/L)	148.8 $\pm$ 49.7	35.72 $\pm$ 14.6	< 0.05
Hb (g/dL)	13.24 $\pm$ 3.1	8.02 $\pm$ 1.22	< 0.05
Total protein (g/dL)	4.87 $\pm$ 0.917	7.02 $\pm$ 0.81	< 0.05

Table (II): Serum Zn, Cu and Fe concentrations (µg/dL) in children with Jaundice and control expressed as (mean ±SD)

Parameter	Jaundice group (n=25)	Control group (n=25)	P-value
Zn (µg/dL)	72.84 ± 25.4	39.7 ± 12.2	< 0.05
Cu (µg/dL)	59.22 ± 31.09	29.0 ± 21.17	< 0.05
Fe (µg/dL)	227.3 ± 113.17	156.22 ± 60.69	< 0.05

Table (III): Correlation factor between total serum bilirubin and the level of Zn, Cu, and Fe in children with Jaundice

Parameter	Correlation factor	P-value
Zn	-0.25	< 0.05
Cu	+0.165	< 0.05
Fe	+0.14	< 0.05

Discussion

A trace element is considered as essential for both man and animals it meets the following criteria: (a) It is present in all healthy tissues. (b) Its concentration from one species to the next is fairly constant. (c) Depending on the species studied, the amount of each element has to be maintained within its required limit if the functional and structural integrity of tissues is to be safe guarded and the growth, health and fertility to remain unimpaired. (d) Its withdrawal induces reproducibly the same physiological and/or structural abnormalities. (e) Its addition to the diet either prevents or reverses the abnormalities.[19]

In our study, the resultsindicated show abnormalities which mild increased in serum aminotransferase levels (GOT, GPT) in children with jaundice than control. Also, the levels of total protein show significant decrease in jundice group than control. These abnormalities are due to acute damage to hepotocytes and reduced in rate of synthesis of total protein.[1]

Zinc (Zn) is necessary trace element in liver cell activity. Zinc deficiencies are common in patients who have advanced cirrhosis.[20]

In our study, we found increased in serum Zn level 2in children with Jaundice, ($p<0.05$). Phillips et al [21] reported an association between sever chronic cholestatic liver disease progressing to end stage biliary cirrhosis and the presence of excess hepatic Zn in six children on the waiting list for liver transplant, who were receiving total parenteral nutrition Zn was deposited in both hepatocytes and canaliculi. Excess hepatic Zn is unexplained. However, reduced liver weight due to weight loss may have resulted in increased liver metal concentrations.[21]

Impaired (Zn) metabolism has been well documented in patients with liver disease, who can develop (Zn) depletion for several reasons: poor diet, impaired intestinal absorption, or excessive urinary loss. (Zn) may exert protective effects on liver cells through inhibiting lipid peroxidation and stabilizing cell membranes.[20]

Copper (Cu) is an essential trace element in animals and man an both deficiency and excess may lead to disease.[22] The liver and specifically the hepatocytes play a pivotal role in the metabolism of copper.[23] Although copper (Cu) is an essential element, an excessive amount is toxic. The symptoms of (Cu) poisoning which is frequently associated with suicidal intent, are clearly documented including: nausea, vomiting, diarrhoea, Jaundice, haematuria, anuria, coma and death.[24]

Since (Cu) balance is greatly influenced by biliary excretion, hepatic (Cu) overload is quite common in cholestatic disease, such as primary biliary cirrhosis and extrahepatic biliary obstruction.[8]

Gross et a [25] was reported during both primary sclerosing cholangitis and primary biliary cirrhosis, hepatic (Cu) concentration are increased. The distrubted (Cu) metabolism may play a role in the pathogenesis of the diseases. Our findings were compatible with those studies. We found an increased in serum (Cu) levels in children with Jaundice ($p<0.05$). Some cases demonstrated a familiar predisposition and an inherited abnormalities in (Cu) metabolism has been proposed, in other cases, the combination of excessive dietary intake, perhaps from household utelkils and an immature biliary excretory mechanism has been implicated.

Several reports describe childhood syndrome distinct from Wilson's disease, and cirrhosis.[26] Some cases of pediatric chronic liver disease have been noted in Europe and North America. Affected patients are generally between four months

and five years of age. Symptoms including jundice, hepatomegaly, and fever develop insidiously and rapidly progress to hepatic failure. The pathogenesis is obscure, but excessive copper deposition appear to prim factor.[27]

The in-utrerotransfer of significant amount of excess (Cu) to the fetus may also account for the dramatic increase in the number of babies being born with Jaundice today. The excess (Cu) is stored primarily in the liver and in the brain. The liver storage can be contributing to the increasing incident rates of jaundice in newborn babies.[28]

The liver serves as a major storage depot for iron, although sizable quantities of iron may accumulate without undue effect, hepatic damage may result when the physiologic capacity is exceeded, with fibrosis and cirrhosis as the ultimate consequences.[29]

Increase in serum (Fe) concentration in children with Jaundice ($p<0.05$) in our study excess amount absorbed from the gut is transported through the portal vein to the liver, where it is predominantly stored in hepatocytes.[2] Iron accumulation is one of the most straight features of hepatic pathology.[30] Increased concentration of (Fe) in hepatocytes play a catalytic role in the initiation of free radical mediated reactions. In humans, chronic (Fe) overload causes progressive fibrosis and ultimately, cirrhosis.[31]

Interaction between minerals can be either positive or negative. A positive action takes place where an element requires the presence of at least one other or its metabolic efficiency. An example of synergy is between copper (Cu) and iron as both are required in the promotion of hematotesis. A negative (antagonistic) interaction occurs whenever a normal metabolic function of an element is impaired by relative excess of another[32]. Our findings were not compatible completely with the previous these studies. We did not find any correlation between the serum levels of zinc (Zn) and serum total bilirubin. The only significant correlation determined was between serum (Cu) and (Fe) levels and serum total bilirubin.

Conclusion

In this study our results showed that serum trace elements levels (Cu , Zn , Fe) changed in children with jaundice These changes might partially be due to pathological causes during this disease.

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