INFLUENCE OF PHOTOTHERAPY ON SERUM LIPIDS OF JAUNDICED NEWBORN INFANTS

THESIS

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BY

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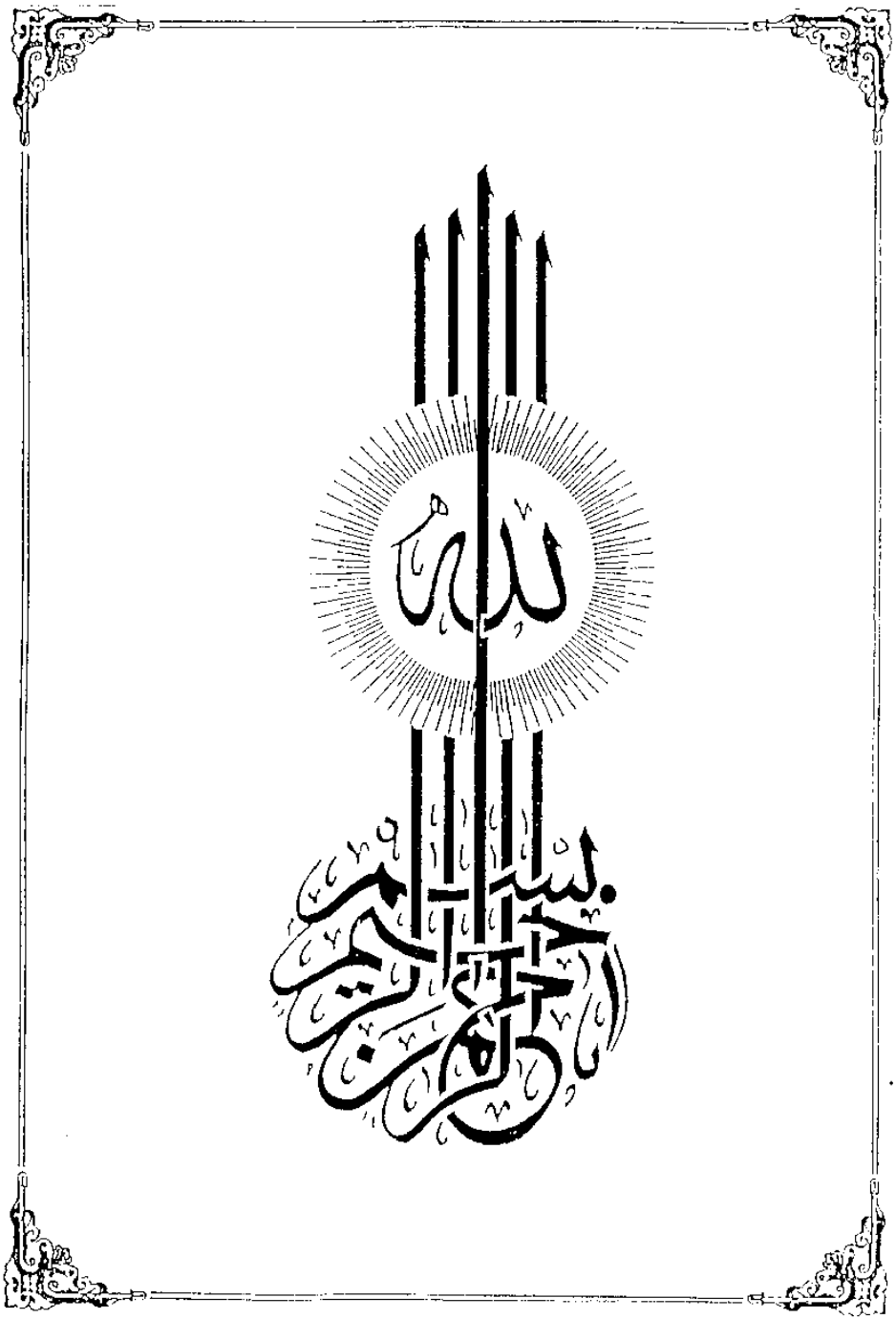

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INTRODUCTION

Hyperbilirubinemia is a common occurance in the newborn period. Some elevation of the serum bilirubin concentration is found in a significant percentage of infants in the first few days of life. Hyperbilirubinemia may be attributable to either pathologic or physiologic causes. The majority of healthy term infants have pathologic etiology discovered for their hyperbilirubinemia, and the therapy of these infants is directed simply toward keeping the serum bilirubin concentration in the range considered safe (Lawrence and Frederick,1984). Phototherapy is an established and effective treatment for neonatal jaundice (Moseley and Fielder, 1988). Phototherapy for neonatal hyperbilirubinemia is based upon a photochemical process with an action spectrum between the 400 and 500 nm range with a peak in the blue region at 450 nm. Light sources with different emission spectra in the 400 to 800 nm range have been used for treatment of neonatal hyperbilirubinemia (Warshow etal.,1980).

Phototherapy is an accepted treatment for neonatal hyperbilirubinemia and reduces the need for exchange transfusions among infants with hyperbilirubinemia due to non hemolytic causes. Phototherapy did not control the increase in bilirubin level in infants with hemolysis, and the rate of exchange transfusion is the same for these infants with or without phototherapy (Brow etal., 1985).

There are three main effects of phototherapy. Configurational photoisomerisation, photoconversion and photo-oxidation (Mc Donagh and Lightner , 1985).

AIM OF THE WORK

The aim of the work is to investigate the influence of phototherapy on serum lipids of jaundiced preterm and fullterm neonates with physiologic jaundice.

REVIEW OF LITERATURE

JAUNDICE

JAUNDICE

Jaundice is yellowish discoloration of the plasma, skin and mucous membrane. Jaundice becomes clinically apparent in childern and adults when the concentration of bilirubin reaches 2-3 mg /dL. In neonates, higher levels may be found without evident icterus. (William,1987).

Bilirubin occurs in plasma in four forms:-

[1] Unconjugated bilirubin tightly bound to albumin
[2] Free or unbound bilirubin
[3] Conjugated bilirubin (The only to appear in urine)
[4] Delta fraction (bilirubin covalently bound to albumin which appears in serum when hepatic excretion is impaired in patients with hepatobiliary disease.

The delta fraction permits conjugated bilirubin to persist in the circulation and delay resolution of jaundice (Frederick,1987).

BILIRUBIN METABOLISM

Bilirubin Production:-

Bilirubin is derived from the catabolism of heme proteins-heme-containing proteins include hemoglobin, myoglobin and heme-containing enzymes such as the cytochromes, catalase and tryptophan pyrrolase. Virtually all cells of the body are a potential source of bilirubin, although, under usual circumstances, this pigment is primarily due to the destruction of hemoglobin contained within erythrocytes.

The catabolism of I gm hemoglobin results in the production of 34 mg of bilirubin (Berlin and Berk,1981).

The red cells are destroyed by reticulo-endothelial system. Hemoglobin is released and eventually, both iron and globin are split off and bilirubin is formed. The released iron is most carefully stored in the body probably by becoming bound with a specific tissue protein called apoferritin to form the iron-containing protein, ferritin. This "reserve iron" is presumably released into the circulation for hemoglobin formation in the red marrow as and when required (Wright, 1984).

Bilirubin is formed by enzymatic breakdown of protein that contain heme. Quantitatively, most of it is derived from hemoglobin. While packaged in the red cell, hemoglobin is protected from catabolic degradation. But once released by hemolysis or phagocytosis of old or damaged red cells, it is converted rapidly to bilirubin and other products.

In babies, red cells turnover more rapidly than in older folk, with a mean life time of about 70 days, compared with 120 days in the adult. The breakdown process is remarkable because it generates two toxic products, carbon monoxide and bilirubin.One of these, (co) is excretable, the other (bilirubin) is not (Mc Donagh and Lightner ,1985) .

This shortened survival time together with the large mass of hemoglobin present in the newborn compared to the older infant or child result in a significantly higher output of bilirubin. This output is corresponding greater whenever any factor increases the rate of hemolysis and in the presence of extravasated blood in the body (ForFar, 1984).

Starvation increases hepatic heme oxygenase enzyme level which increases bilirubin production from pre-existing heme pool, this may contribute to the bilirubin load in the newborn (Beitzer and Boyer, 1982).

Transport And Hepatic Uptake Of Bilirubin

Bilirubin produced in the peripheral regions of the body and the reticulo endothelial system is transported, tightly bound to albumin, to the liver. Binding to albumin is essential for transport because the solubility of unbound at pH 7.4 is extremely low, averaging 0.4 ug per 100 ml (Avery, 1984). When the bilirubin-albumin complex reaches the plasma membrane of the hepatocyte the bilirubin protein, but not the albumin, is transferred across the cell membrane into the hepatocyte where it is bound to soluble proteins. The transfer of bilirubin from plasma into the liver cell is probably carrier-mediated.

Bilirubin within the hepatocyte is bound primarily to ligandin Y and to Z protein. This binding within the cell prevents back flow of bilirubin into the circulation. Phenobarbital increases the concentration of ligandin (Y), thus providing more intracellular binding sites for bilirubin (Wolkoff etal., 1979).

The Y protein does not reach mature levels until the second week of life and is almost absent at birth. Maturation of Z protein occurs in fetal life. Lack of maturity of the acceptor proteins and competition for the binding sites on these proteins results in reduced hepatic uptake of bilirubin (ForFar, 1984)

Conjugation And Excretion

The bound intracellular bilirubin is next transported to the smooth endoplasmic reticulum for conjugation. The unconjugated or (indirect-reacting bilirubin) which is poorly soluble in aqueous solution at a PH of 7.4, is converted to its water soluble conjugate (direct reacting bilirubin) prior to excretion.

In adult, the major product of conjugation is bilirubin diglucoronide. In newborns during the first 48 hours of life, only monoglucoronides are formed. After 48 hours of life, bilirubin diglucoronide is the major excretory product. It appears that two separate enzymes participate in the conjugation process. The first is bilirubin uridine diphosphate glucoronyl transferase (UDPG-T), an enzyme associated with the smooth endoplasmic reticulum inducible by phenobarbital, UDPG-T, catalyzes the formation of bilirubin monoglucoronide. This monoglucoronide may be excreted, stored or converted to the diglucoronide. The formation of the bilirubin diglucoronide appears to be catalyzed by a transferase enzyme located in the plasma membrane of the hepatocyte (Schmid,1978).

The conjugation of bilirubin is of importance to the newborn not only because it converts the pigment into a water soluble form capable of easy excretion but also because conjugated bilirubin does not have the toxic effects of unconjugated bilirubin. Conjugation therefore,is a detoxifying process (ForFar,1984).

Transport Of Bilirubin Into Bile And Intestinal Transport

After conjugation, bilirubin is excreted into the bile. This is an active, energy-dependent process because the conjugated bilirubin is excreted against a large concentration gradient. Conjugated bilirubin is not reabsorbed once it enters the intestinal tract. In the normal adult, most of the conjugated bilirubin is reduced to stercobilin by bacteria and only a very small fraction is hydrolyzed to unconjugated bilirubin and reabsorbed via the enterohepatic circulation. In the sterile intestine of the newborn infant, the reduction of bilirubin to stercobilin does not occur. In addition, the newborn gut is rich in B. glucoronidase, an enzyme that hydrolyzes the ester linkage of bilirubin glucoronide yielding unconjugated bilirubin. This unconjugated bilirubin is now capable of being reabsorbed and returned to the circulation, where it must again be transported to the liver for conjugation and excretion (Odell, 1980).

This enterohepatic phase of bilirubin metabolism appears to play a major role in the hyperbilirubinemia of some newborn infants (Avery, 1984)

There may be as much as 200 mg meconium in the intestine at birth, this will contain up to 175 mg of bilirubin which equals 5-10 times the daily rate of bilirubin production in the normal term infant. A delay in passage of meconium more than 12 hours after birth will cause an increased enterohepatic reabsorption with an increased bilirubin load for conjugation in the liver as in intestinal atresia, meconium plug syndrome and cystic fibrosis (Ballstreri et al., 1983).