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## NEONATAL HYPERBILIRUBINEMIA

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**ABSTRACT-** Jaundice is extremely common among infant during the primary days of life. Several factors like maternal and neonatal history need to be considers before implementation drugs therapy. Significant advance are made within the past few years concerning the treatment of jaundice new-born infant. This review specialise in three kinds of treatment of neonatal hyperbilirubinemia; phototherapy, blood transfusion and also the use of medicine to cut back serum bilirubin concentration To review the recent medical literature on the drugs therapy of neonatal jaundice, specializing in practical aspect that relevant to paediatricians and neonatologist .An extensive review of the related literature was performed , also including the authors clinical experience during this field of investigation. Now days ,the in depth knowledge about the mechanism of action of phototherapy ,the development of intensified phototherapy unit and also the use to drugs to scale back bilirubin formation ,have contributed to significantly decrease the necessity for blood transfusion .

**KEY WORDS** – Assess, knowledge, neonatal hyperbilirubinemia, Icterus neonatorum.

**Introduction-** ictus neonatorum, neonatal jaundice has been recognized the term kernicterus was introduced the first 1900 to discuss with the yellow staining of the basal ganglia observed in infant who died with severe jaundice. From the 1950 through the 1970 thanks to a high incidence of Rh haemolytic disease and kernicterus, paediatrician were aggressive in treating jaundice. However several factors have changed the management of jaundice studied in 1980 and 1990 suggested that kernicterus from jaundice was rare which too many infant were being treated unsuccessfully. Also new born infants were being discharged from sooner after birth, limiting the power of physician to detect jaundice during the amount when the serum bilirubin concentration is probably going to rise. Finally low concentration of bilirubin may have some anti oxidant benefits, suggesting that it mustn't be completely eliminated. thanks to these factors physician recede likely to treat jaundice in neonates which successively cause increase in reports of the just about forgotten and a

few time deadly kernites fortunately the change have also stimulated the event of recent approaches to the prevention, detection and treatment of hyperbilirubemia. during this review, we appraise the advance .

## **PATHOPHYSIOLOGY-**

Neonatal hyperbilirubinemia result from a pre-disposition to the assembly of bilirubin in new-born infants and their limited ability to excrete it. Infant specially pre-term infant ,have higher rates of bilirubin production than adults , become they need red cells with the next turnover and a shorter life .in new-born infants , unconjugated bilirubin isn't readily excreted , and also the ability to conjugate bilirubin is proscribed .together these limitation cause physiological jaundice .that is ,high serum bilirubin concentration within the first day of life fully term infants , followed by a decline during the following several week to the worth commonly found in adults .the average term new-born infant features a peak serum bilirubin concentration of 5to6 mg per decilitre .exaggerated physiological jaundice occurs at value above the 7to 17mg per deciliter.serum bilirubin concentration higher then 17 mg per decilitre fully term infants aren't any longer considered physiological , and a reason behind pathological jaundice can usually be identified in such infants .

## **CAUSES**

The predominant sources of bilirubin within the breakdown of haemoglobin in senescent or haemolyzed red cells. heme is degraded by the heme oxygenase, leading to the discharge of iron and also the formation of corban monoxide and biliverdin. Biliverdin is further reduced to bilirubin by biliverdin reductase. bilirubin then enters the liver and is modified to an excretable conjugated from that enters the intestinal lumen but are often deconjugated by bacteria in order that the bilirubin is reabsorbed in to the circulation. Increased production of bilirubin, deficiency of hepatic, impaired conjugation of bilirubin, and increase enterohepatic circulation of bilirubin account for many cases of pathologic jaundice in new-born infants. increase production of bilirubin occurs in infant of assorted racial group, moreover as I infant with blood type incompatibilities, erythrocyte -enzyme deficiency or structural defects of the erythrocytes. the propensity toward hyperbilirubinemia in certain racial groups isn't well under stood.

## **CELLULAR,TOXIC,EFFECTS,OF,BILIRUBIN**

The primary concern with regard to exaggerated hyperbilirubinemia is that the potential for neurotoxic effects, but general cellular injury also occurs. bilirubin inhibits mitochondrial enzymes and might interfere with DNA synthesis, induce DNA -strand breakage and inhibits protein synthesis and phosphorylation. Bilirubin has an affinity for membrane phospholipids and inhibits the uptake of tyrosine, a marker of synaptic transmission. bilirubin also inhibits the function of N-methyl D- aspartate -receptor ion channels. this means that bilirubin can interfere with neuroexcitatory signals and impair nerve conduction. bilirubin can inhibit activity and water transport in renal cells , which can explain neuronal swelling that happens within the bilirubin encephalopathy related to kern ictus . in immature rate, increased level of lactate ,decreased level of cellular glucose , and impaired cerebral glucose metabolism are related to hyperbilirubinemia.

## FACTORS THAT INFLUENCE THE NEUROTOXIC EFFECTS OF BILIRUBIN –

The concentration of bilirubin within the brain and also the duration of exposure to bilirubin are important determinants of the neurotoxic effects of bilirubin, where because the correlation between the serum bilirubin concentration and bilirubin encephalopathy is poor in infants without haemolysis . once reason for this weak corelation is that the duration of hyperbilirubinemia is additionally a vital determinant of the brain expose to bilirubin. serum bilirubin concentration don't provide a reliable estimate of bilirubin production , tissue bilirubin concentration , or serum concentration of albumin – bound bilirubin. Furthermore, phototherapy , which alters the configuration of bilirubin and yields a photograph isomer which will be excreted ,makes it difficult to equate serum bilirubin concentration in treated infants with those in untreated infants in contrast , peak serum bilirubin concentration more than 20mg per decilitre usually predict a poor outcome in infants with Rh haemolytic disease, but some infants with concentration of 25 mg per decilitre or higher are normal .kernicterus was detected in 8 percentage of infants with Rh- associated haemolysis who had serum bilirubin concentration of 19 to 24 mg per decilitre ,33 %of infants with concentration of 25 to29 mg per decilitre and 73 you look after infants with concentration of 30 to 40 mg per decilitre .

## CLINICAL,FEATURES,OF,KERNICTERUS –

The clinical searches of kern ictus vary, and up to fifteen of infants haven't any obvious neurologic symptoms. the disease will be divided into an acute and chronic form. the acute form usually has three phase, and chronic form is characterized by hypotonia within the first year and by extrapyramidal abnormalities and sensorineural deafness thereafter. in a very registry of term and nearly full-term infant born between 1984 and 1999, the fatality rate among infant with kernites was 4%. Specific changes on magnetic reasons imaging namely, increase signal intensity within the global pallidum on T2 weight images are closely correlated with the deposition of bilirubin within the basal ganglia. In approximately 27,000 within the collaborative perinatal project, neurodevelopment during the primary year life was correlated with the maximal serum bilirubin concentration soon after birth .in a multicentre Dutch survey , a dose response relation between the maximal serum bilirubin concentration and therefore the risk of impaired development was found at two year old only among children who had weight but 1500 g at birth . and there was no corelation at five year old .in a very study of fifty term infant with moderate hyperbilirubinemia, the latency of brain -steam auditory evoked response was longer in these infant than in those with lower serum bilirubin concentration, and therefore the abnormality was more pronounced in infant with higher bilirubin concentration .

## PREDICTION OF THE RISK OF SEVERE HYPERBILIRUBINEMIA

An increasing number of new-born infant are discharge from the hospital within 48 hrs after birth and it's therefore not surprising that hyperbilirubinemia is decreed before discharge less often than it had

been within the past .the need for phototherapy is one in all the foremost commonly reported reason for readmission of new-born infant .suggested the requirement for early detection of hyperbilirubinemia and follow up after discharge .Clues to an infant propensity for sever hyperbilirubinemia will be obtain from characteristic of the mother and perinatal and neonatal factored . the evaluation of the serum bilirubin concentration new-born infants by mean of a percentile based nomogram allows physician to predict the danger of hyperbilirubinemia. in one study infant who had serum bilirubin concentration within the high risk category 18 to 72hrs after birth had a 40% probality of subsequent , moderately severe hyperbilirubinemia . where's infant with concentration within the low risk category had a probality of zero . some caution is required in interpreting these data , since meaningful follow up data after hospital discharge were available for less than 2976 of 13003 eligible infant . nonetheless , nomogram can identify infant who are in danger for severe hyperbilirubinemia and might guide follow up

### **TRANSCUTANEOUS MEASUREMENT OF BILIRUBIN**

Estimate of serum bilirubin concentration that are based solely on clinical examination aren't reliable . non-invasive technique for transcutaneous measurement are developed for these purpose, but older device are tormented by variation within the pigmentation of the skin . newer devices that use multiwavelength spectral reflectance can eliminate this variability .in 897 new-born infant from various racial and grouping , the serum bilirubin concentration ranged from 2to28 mg per decilitre and also the results of transcutaneous measuring of bilirubin corelation well with the serum concentration .these devices could help reduce the requirement to draw blood and improve follow up infant reception .

### **MEASUREMENT OF CARBON MONOXIDE TO EVALUATE BILIRUBIN PRODUCTION**

Homolysis and bruising increase the production of bilirubin. although the degree of jaundice and the rate of production of bilirubin are not always correlated because the rate of elimination of bilirubin various among infant , early identification of infant in whom large amount infant of bilirubin are produce is important . because carbon monoxide and bilirubin are produced in equimolar amount when heme is degraded , measurement of carbon monoxide in exhaled air can be used as an index of bilirubin production.exhaled carbon monoxide can be measure reproducibly in new-born infant as well as in adults .since infant with haemolytic disease have high value for exhaled carbon monoxide , measuring end tidal carbon monoxide may allow physician to identify such infant .

### **PREVENTION**

Reduction of bilirubin in the enterohepatic circulation –

New-born infant who do not feed adequately probably have increased enter phatic circulation of bilirubin ,because fasting cause increased accumulation of bilirubin in animals . since increasing the number of oral feeding allow for more rapid excretion of bilirubin ,early , frequent nursing of supplemental feeding with

formula may be effective in reducing serum bilirubin concentration in breast fed infant who are under going phototherapy . in contrast supplementation production of milk resulting in higher serum bilirubin concentration.

No drugs or no other agents that decrease the enteropatic circulation of bilirubin are available .in rates activated charcoal binds bilirubin and promotes its excretion, but the efficacy of charcoal in infant has not been tested . in one study , the administration of agar as an adjust of phototherapy in new-born infant with hyperbilirubinemia significantly reduced the duration of phototherapy from 48 hrs without the use of agar to 38 hrs with its used .cholestyramine ,used the treat obstructive jaundice , in crease bilirubin excretion by binding to bile acid in the intestine and forming a nonabsorbable complex . however in a study involving full-term infant who were receiving phototherapy , treatment with cholestyramine given at a dose of 1.5 g per kilogram of body weight , did not result in serum bilirubin concentration that were lower than those achieved with phototherapy along .

## TREATMENT

### Phototherapy

phototherapy has remained the quality of look after the treatment of hyperbilirubinemia in infant for four decades . efficient phototherapy rapidly reduced the serum bilirubin concentration. The formation of bilirubin , a water soluble compound is that the rate limiting steps within the elimination of bilirubin by phototherapy . two factored determine the speed of lumirubin formation the spectrum and also the total dose of sunshine delivered . because bilirubin could be a yellow pigment , it's likely to absorb blue light . thus blue lamp are only in deducing hyperbilirubinemia but eye strain in health can provider and a discount in there ability to assess cyanosis deter hospital from using them /longer wavelengths penetrate the skin more deeply and should interact more effectively with albumin – bound bilirubin , but fluorescent white light is that the commonest phototherapy

Phototherapy is treatment with a special form of light (not sunlight). It's sometimes accustomed treat new-born jaundice by making it easier for your baby's liver to interrupt down and take away the bilirubin from your baby's blood. Phototherapy aims to reveal your baby's skin to the maximum amount light as possible. Your baby are going to be placed under a light-weight either in an exceedingly cot or incubator with their eyes covered. It will usually be stopped for half-hour so you'll feed your baby, change their nappy and provides them a cuddle. If your baby's jaundice doesn't improve, intensified phototherapy is also offered. This involves increasing the quantity of sunshine used or using another source of sunshine, like a lightweight blanket, at the identical time.Treatment can't be stopped for breaks during intensified phototherapy, so you'll not be able to breastfeed or hold your baby. But you'll be able to give your baby expressed milk. During phototherapy, you baby's temperature are monitored to form sure they are not getting too hot, and they'll be checked for signs of dehydration. Intravenous fluids is also needed if your baby is becoming dehydrated and that they aren't ready to drink enough. The bilirubin levels are tested every 4 to

six hours after phototherapy has started, to test if the treatment is functioning. Once your baby's bilirubin levels have stabilised or began to fall, they're going to be checked every 6 to 12 hours. Phototherapy are stopped when the bilirubin levels fall to a secure level, which usually takes daily or two. Phototherapy is mostly very effective for new-born jaundice and has few side effects. Exchange transfusion

If your baby includes a very high level of bilirubin in their blood or phototherapy has not been effective, they'll need a whole insertion, referred to as an blood transfusion. During an blood transfusion, your baby's blood are going to be removed through a skinny plastic tube placed in blood vessels in their channel, arms or legs. The blood is replaced with blood from an acceptable matching donor (someone with the identical blood group).As the new blood won't contain bilirubin, the general level of bilirubin in your baby's blood will fall quickly. Your baby are going to be closely monitored throughout the transfusion process, which may take several hours to finish. Any problems which will arise, like bleeding, are going to be treated. Your baby's blood are tested within 2 hours of treatment to test if it has been successful. If the extent of bilirubin in your baby's blood remains high, the procedure might have to be repeated.

## PHARMACOLOGIC THERAPIES

Phenobarbital has been used since the mid 1960 to extend the conjugation and excretion of bilirubin but it's not effective immediately . during a study involving 1310 women whose infant were in danger for jaundice , the administration of phenobarbital atdose of quite 1g daily for the last week of pregnancy reduced the incidence of severe jaundice and reduce the necessity for blood transfusion by a factore of six. However , in rate, phenobarbital diminishes the oxidatve metabolism of bilirubin in neural tissue suggesting an increased risk of neurotoxic effects .Unconjugated bilirubin is metabolized by bilirubin oxidase . when human and rat blood is seasoned a filter containing bilirubin oxidase ,more than 90% of the bilirubin is degraded during sunglass .This procedure may prove useful within the treatment of hyperbilirubinemia of the new-born , but it's not yet been tested in clinical trail. Moreover it should pose a risk of sensitivity because the enzyme comes from a fungus .

## PREVENTION OF BILIRUBIN ENCEPHALOPATHY

Once bilirubin has accumulated , raising the brain ph. may help prevent encephalopathy ,because bilirubin is more soluble in Alka line states in primates with hyper bilirubin , correction of respirate acidosis cause the whole reversal of abnormalities and auditory evoked potentials the new-born baby with severe hyperbilirubinemia , moderate alkalinization could even be attempted either by infusing bicarbonate or by using ventilatory strategies to lower the lower the partial pressure of gas and thus raise the ph .

## APPROACH THE JAUNDICE

Many variables affected the severity of hyperbilirubinemia in infant , making in difficult to develop a simple algorithm for intervention. this recommendation for initiating treatment are supported clinical practice , and importance unknown ,preclude the event of a selected serum bilirubin concentration at which therapy is warranted is controversial be cause estimate of safe concentration based totally on historical data from infant with a disease that's rarely seen now . additionally serum bilirubin concentration of more then 25 mg per delimeter are rarely uncounted today. therefore, clinical trails of therapy would be difficult to conduct because of the huge population of patients that may be required . to complicate matters further , there's sustained variability among hospital within the methods of testing for hyperbilirubinemia and also the laboratory values they report. Furthermore the concentration and duration of expose at which bilirubin is neurotoxic don't seem to be known, very premature or sick infants and folks with haemolytic disease are at greater risk for neurotoxic effects.

Therefore , for preventing the event of pathologic jaundice , we are ready to recommend only a carefully history taking to elicit information on risk factor early measurement of serum bilirubin , test to rule out haemolysis , and prudent feeding practice . the serum bilirubin concentration is simply a marker of possible neurotoxic effects and should be evaluated within the context of the infant overall condition . for example the physician should take into consideration the presence ,and sepsis . if severe hyperbilirubinemia is detected , phototherapy should be initiated immediately . we also strongly recommend early follow -up to detect severe jaundice .

## CONCLUSION

With our altered perception of the toxicity of the toxicity of bilirubin and a stress , driven by managed care , on shortened hospital stays ,the incidence of kernicterus has again increased . thus health care providers must re-examine their procedure for follow of new-born .evaluating the serum bilirubin concentration early for all infant with the use of a percentile based nomogram and possibly screening for genetic condition should facilitate the anticipation and diagnosis of pathological jaundice before discharge .improved phototherapy and thus the employment of metalloporphyrin's may decrease the necessity for transfusion and even alter the successfully treatment of hyperbilirubinemia reception. All new-born infants who are discharge 48 hrs or less after delivery should meet the standards of the American academy of paediatrics for early discharge and will be examined for jaundice within two to some days after discharge .

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