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PATTERN OF PHYSIOLOGIC JAUNDICE AND INCIDENCE OF "EXAGGERATED PHYSIOLOGIC" HYPERBILIRUBINEMIA IN IRANIAN FULL-TERM INFANTS USING TRANSCUTANEOUS BILIRUBINOMETRY

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ABSTRACT

Normal full-term infants were followed by serial transcutaneous bilirubinometry over the first week of life. The pattern of physiologic jaundice in our population was similar to that shown for white infants. Mean maximum bilirubin peak was seen on day four of life and was also similar to that shown for American white infants. The incidence of nonphysiologic hyperbilirubinemia defined as 2 SD above the mean maximum peak was about three times that reported for white infants, but similar to that reported for oriental populations. Oxytocin and the type of delivery did not seem to affect this high incidence. The role of breast feeding and G6PD deficiency needs to be further defined.

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INTRODUCTION

During the first week of life about ninety percent of white full- term newborn infants will develop physiologic jaundice: that is, a transient hyperbilirubinemia with serum unconjugated bilirubin concentration rising from 1.7 mg/dl at birth to a peak of 6 mg/dl by day three, falling to 3 mg/dl by day five, remaining so for about three days with a gradual decline to normal thereafter.

In about five percent of white infants serum bilirubin values grater than two standard deviations from the mean (that is 12.9 mg/dl) are seen. This may be due to pathologic reasons, but as is the case in most such infants no etiologic factor can be found for these «exaggerated physiologic» or «nonphysiologic» bilirubin levels.

Oriental infants, on the other hand, have mean maximum bilirubin concentrations about double those of non- oriental infants, and the incidence of «nonphysiologic» jaundice is also higher.

The purpose of this study was to define pattern of jaundice as well as the incidence of «nonphysiologic» hyperbilirubinemia in the Iranian population. To our knowledge such a study has not been previously reported in Iran.

METHOD

Preliminary to using the Minolta/Air- Shields Jaundice Meter 101, in order to define the linear relationship of transcutaneous bilirubin index (TcB index) to serum bilirubin concentration in our populatio simultaneous serum bilirubin and TcB index were obtained from 36 full- term newborns, a single data set for each patient. Serum bilirubin was performed manually by a single technician at the hospital's clinical laboratory using the manual diazo method. Regression line for our population of infants was then calculated as suggested by the operator's manual.[1]

First or second- born infants of mothers delivering

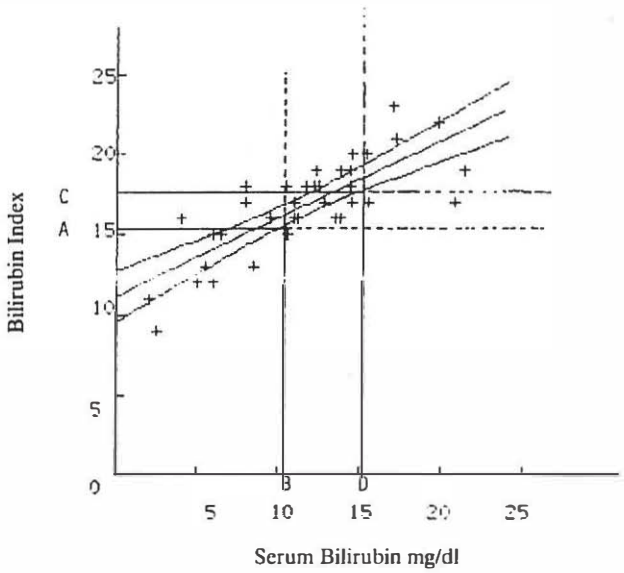

Fig. 1. Serum versus transcutaneous bilirubin. Population: Iranian term newborns.

vaginally or infants born by caesarian were eligible for the study, provided they had no other problems.

The reason for selecting these infants was the duration of their stay in the hospital. (Most multipara mothers are discharged within hours of a normal delivery). TcB index was obtained daily while they were in hospital and after discharge for the first eight days of life, using the Minolta- Air Shields Jaundice Meter 101 over the forehead. In three babies, sternum was used due to the presence of nevi or hematoma over the forehead. Any infant requiring phototherapy was excluded from the study. Blood group of all mother-infant pairs were obtained, and those who had an ABO set up were excluded. Rhesus positive infants whose mothers were Rh negative were excluded only if they had a positive Coombs.

RESULTS

The correlation of TcB index and serum bilirubin was linear: the regression line obtained is shown in Fig. 1. Mean serum bilirubin for the group was 11.5 ± 4.99 mg/dl; individual values ranged from 2 to 21.4 mg/dl; prevalence of values >12.9 mg/dl was 38.8% and for bilirubin >15 mg/dl was 19.4%. The correlation coefficient (r) was 0.63, slope 0.49, intercept 11.18 and the standard error of estimate (sy. n) was 1.49.

Of the 360 eligible infants 330 entered the study, 146 of them being females and 184 males*. All except six weighed 2500 gms or more; four of them weighing 4000

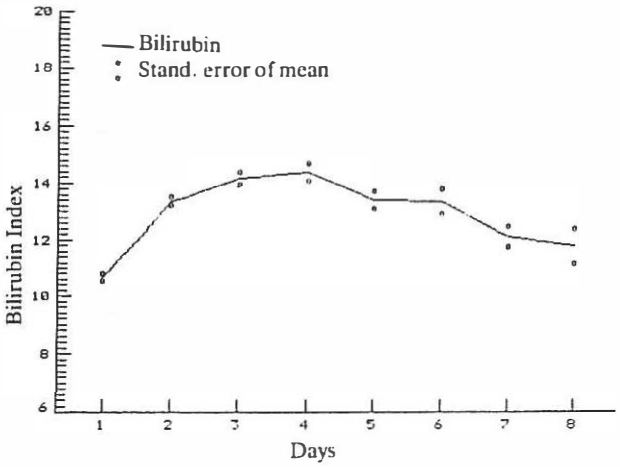

Fig. 2. Mean daily transcutaneous bilirubin in Iranian term newborns.

gms or more. All of them were 38 weeks or more in gestation. 54 infants were born by caesarian, 22 being elective repeat and the remaining 32 due to CPD, breech presentation and other indications for a primary caesarian. Of the 276 babies born vaginally, 32 were born by vacuum. All infants were fair- skinned except 47 who were a shade darker. 187 mothers (59%) received oxytocin during labour. Amniotic fluid was reported meconial in 26, blood- tinged in two and clear in the remaining cases.

Mean daily TcB index for this group of infants is shown in Fig.2. Mean TcB index was 10.7±2.02 SD on Day 1, 13.27±2.18 SD on Day2, 14.19±3 SD on Day3, 14.42±3.5 SD on Day 4, 13.45±3.95 SD on Day 5, 13.4±3.9 on Day 6, 12.16±3.2 SD on Day 7, and 11.78±3.25 SD on Day 8. Thus peak mean TcB index was 14.4 on Day 4 of life.

The total number of values of TcB index daily from Days 1 to 8 were 205, 201, 172, 114, 137, 70, 88 and 32 successively. (The numbers are less than the total of 330 because of early discharges from the hospital and weekend days). 184 babies of the total group (56%) returned for follow-up for five days or more and had at least 4 TcB index values successively. 19% of these infants had a TcB index of 18 sometime during the first week of life, that is more than 2 SD of the mean maximum peak of 14.4. 26.6% of the total group were followed up for more than seven days, and the incidence of TcB index 18 in this group was 14.4%. 12 infants required phototherapy for a serum bilirubin exceeding 15 mg/dl.

The incidence of TcB index 18 in born by caesarian versus those born vaginally was 11% and 19% respectively, (difference not statistically significant); 26% of infants whose mothers received oxytocin versus 22% of infants whose mothers did not receive oxytocin had TcB index 18 (difference not statistically significant).

* (30 babies were excluded due to ABO or Rh set up).

DISCUSSION

Jaundice meter is a simple instrument which quantifies the yellow colour of the skin by measuring colour as a function of wavelength when light is reflected from the skin and subcutaneous tissue. The intensity of yellow colour thus measured is displayed as arbitrary units: The transcutaneous bilirubin index. This instrument was introduced for the first time in 1980 by Yamanouchi[2] and coworkers. Using the meter in Japanese infants, Yamanouchi showed a correlation of 0.95 between the TcB index and serum bilirubin. Maisles[3] also obtained an r value of 0.93 for white infants. Compared to these studies the r value of 0.63 in our population is quite poor. The reason though, may not be the insensitivity of the instrument in our population, but rather the inaccuracy that may be present in the manual diazo method for serum bilirubin in our hospital laboratory where control bilirubin solutions are not easily available for standardization. Using a hospital clinical lab with a standard error of ± 1.8 for a bilirubin of 19, Goldman[4] obtained an r value of 0.7 for white infants and 0.5 for black infants.

Other factors that affect the r value are race, colour of skin and homogeneity of the population. Our population of infants were nonhomogenous and of variable skin colour. This too might account to some degree for the low r value. When a more standardized automated bilirubin assay is available, however, the correlation study should be repeated in Iranian infants.

Thus we feel that the jaundice meter cannot be used to replace serum- bilirubin levels, and it has been marketed not to replace serum bilirubin estimation but as a screening tool to predict which babies need the blood test.

Measurements with the transcutaneous bilirubin meter (or jaundice meter) are highly reproducible, there is virtual absence of interobservervariability, and it is better than the eye in screening jaundiced infants. It also could be a useful tool for following jaundiced infants. Its utility in our population needs to be further tested, especially where laboratory facilities are not available.

Whether the relation of TcB index with serum bilirubin be 100% or not, TcB index measures indirectly a compartment of bilirubin, that amount deposited in the subcutaneous tissue and skin, which is probably in equilibrium with the total body bilirubin. As such, it can be a useful non- invasive method to evaluate various aspects of jaundice in the newborn such as the progress of jaundice in a baby, effect of types of feeding or preventive therapy on jaundice or as in our case defining the curve of physiologic jaundice in our infants, provided that phototherapy or exchange transfusion has not been used to change the normal dynamics between total body bilirubin and skin bilirubin.

The infants in this study were representative of a healthy full- term population, and there was apparently no pathologic cause for their jaundice. Mean TcB index, in this group, rose from 10.7 (±2 SD) on Day 1 to 14.4 (±3.9 SD) on Day4 and then fell to 11.8 (±3.4 SD) by Day 8. This curve is rather similar to that obtained by Gartner.[5] The peak TcB index of 14.4 corresponds to a serum bilirubin of about 6.6 mg/dl using the regression equation for our infants. Gartner[5] showed a biphasic pattern of physiologic jaundice: in phase 1 serum bilirubin rose to 6 mg/dl by day 3 then fell to 3 mg/dl by day 5. In phase 2, serum bilirubin remained between 2 and 3 mg/dl for about 3 days then declined slowly to normal by 11 to 12 days of life.

We cannot identify two distinct phases in our neonates because we are using TcB index and not serum bilirubin per se. The mean maximum in our study is however quite similar to that reported for American white infants by several investigators. 2 SD above the mean maximum at three days of life in the combined data from seven studies was 12.7 mg/dl. In several studies the incidence of hyperbilirubinemia above 12.7 or 12.9 mg/dl has been about 6% even when sick infants and those with hemolytic disease were included.

184 (or 56%) of our babies were followed up for more than five days. In this group the incidence of hyperbilirubinemia defined as 2 SD above the peak TcB index, that is 14.4 + 3.9 or about 18, was 19%. This is about three times the incidence reported for white infants but similar to that observed in oriental populations. The incidence of hyperbilirubinemia >15 mg/dl was shown to be 6.9, 2.2 and 19% for white, black and oriental infants respectively in a study of more than 12,000 infants.[4]

Besides oriental infants, a higher incidence of jaundice has also been reported in American Indian and Greek neonates while that in Black infants is lower than that reported for White infants. It is not quite clear whether genetic or environmental factors are responsible for these differences. For example Japanese infants living in the United States have a higher incidence of hyperbilirubinemia while infants of Greek migrants to Australia do not.[8]

The high incidence of nonphysiologic hyperbilirubinemia is not explained by the use of oxytocin or the type of delivery as these were not found to be significant. It could be that infants who returned for follow-up were more likely to have been clinically jaundiced, hence falsely elevating the incidence of nonphysiologic hyperbilirubinemia. However we feel that this factor is probably not important because mothers in our society tend to consider jaundice as something normal and not to be worried about. Again the incidence of significant hyperbilirubinemia, that is requiring phototherapy,

was about 6% of those who returned for at least five days.

G6PD deficiency was not investigated in any of our infants. This too is unlikely to account for the increased incidence of hyperbilirubinemia based on our clinical experience in this population. In Greek infants the incidence of hyperbilirubinemia and kernicterus has been shown to be equally high in infants with or without G6PD deficiency.

We feel that the most likely reason for this nonphysiologic jaundice in our population is breast feeding. Most of our mothers were breast feeding their infants, although accurate feeding history was not recorded. Infants of mothers who had caesarian delivery were more likely to have been formulated because of the hospital policy of not letting these mothers nurse their infants for 48 to 72 hours. In these infants the incidence of hyperbilirubinemia was lower but did not reach significance. Maisels[9] studied 1260 breast-fed and 1026 bottle-fed babies and showed that the mean maximum bilirubin for bottle-fed babies was 5.7 versus 7.3 mg/dl for breast fed babies; 2% of formulated versus 9% of breast fed infants had bilirubin levels >12.9 mg/dl.

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