

A Clinical Application of Transcutaneous Bilirubinometer in the Newborn Infants¹

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Abstract—A total of 390 transcutaneous bilirubin measurements were performed in 318 Korean fullterm and 72 preterm infants on forehead. 100 test samplings for reproducibility rendered a mean coefficient of variation less than 5% and the calculated coefficients of variation for technique dependence ranged from 1.98 to 4.78%. We obtained a correlation coefficient of 0.78 and $p < 0.01$ between transcutaneous bilirubin measurements and total serum bilirubin concentrations. We consider that infants with a total serum bilirubin concentration exceed 12.9mg/100ml have significant hyperbilirubinemia. We set forehead transcutaneous bilirubin index of 19 as a useful dividing level. The specificity and sensitivity of the test are 98% and 74% respectively. Positive and negative predictive value are 76% and 97% respectively. It can be used as a screening test but further investigation will be necessary.

Key words : *Transcutaneous bilirubinometer, Neonatal hyperbilirubinemia*

INTRODUCTION

Hyperbilirubinemia is the most common problem experienced by infant during the immediate neonatal period. There are many methods to measure serum bilirubin level of the newborn. But its accurate assessment still requires a measurement of the serum bilirubin concentration. It has been observed that dermal icterus has a typical progression from cephalad to caudad direction. Now it has been confirmed that there are direct relationship between serum bilirubin levels and the extent of the dermal progression.

In 1980 Yamanouchi and coworkers developed a new noninvasive bilirubinometer for the transcutaneous measurement of bilirubin levels in newborn by a joint effort with the Minolta Camera Company, Ltd. This device, if accurate, could be a noninvasive monitor of neonatal hyperbilirubinemia and reduce the requirement

for numerous serum bilirubin determination. Initially Yamanouchi *et al.* obtained a highly significant correlation coefficient of 0.95 between transcutaneous bilirubin measurements and serum total bilirubin concentrations measured by the American Optical bilirubinometer. However others found that correlation was not so good.

This study is performed to observe that transcutaneous bilirubin measurement would be a screening test that would reduce the invasive test and necessity for laboratory analysis and be more reliable than visual inspection of the skin color.

MATERIALS AND METHODS

We obtained 390 transcutaneous bilirubin measurements in 318 full term infants and 72 preterm infants admitted to the Well Baby Nursery and Neonatal Intensive Care Unit of Seoul National University Children's Hospital. The babies neither have medical complications nor take drugs which could cause hyperbilirubinemia.

The transcutaneous bilirubin measurements

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were obtained from each infant on forehead as previously described. Measurements were made in triplicate and the mean result was used. None were received phototherapy at the time of study. Total serum bilirubin was measured by American Optical bilirubinometer manufactured by American Optical Corporation using capillary blood obtained by heel pricks at bedside.

First we attempted to identify the reproducibility of the transcutaneous bilirubin measurement. The transcutaneous bilirubinometer was tested on twenty different neonatal patients by the same operator on forehead with three minute interval for five times.

Second the test was performed by five different operators (Doctor 1, Doctor 2, Nurse 1, Nurse 2, Student) to check technique dependence on five different patients.

Third in order to identify the linear relationship between total serum bilirubin concentration and transcutaneous bilirubin measurement, we obtained total 390 transcutaneous bilirubin measurements.

RESULTS

Reproducibility of transcutaneous bilirubin measurement

The test sampling for reproducibility rendered a mean coefficient of variation ranged from 0 to 4.86%, which is similar to that reported by Yamanouchi *et al.* The percentage of variation does not appear to increase with the level of total serum bilirubin concentration.

Technique dependence in transcutaneous bilirubin measurement

The data show that the coefficients of variation range from 1.98 to 4.78%. In any case the percentage of variation did not exceed 5.0% and did not increase with the level of total serum bilirubin concentration.

Correlation between transcutaneous bilirubin and total serum bilirubin measurement

We obtained 390 transcutaneous bilirubin measurements in 72 preterm and 318 full term infants of which 207 male and 183 female, mean gestational period is 38+5 wk range 32+5 wk to 41+3 wk. The mean total serum concentration for all infants was 8.9±3.9 (SD) mg/100 ml, range 3.1 to 23.0mg/100 ml. The population was divided into two groups according to gestational period; GP≥37 Wk and GP<37 Wk.

Next the population is divided into two groups according to body weight; BWt≥2.5 Kg, BWt<2.5 Kg. Correlations between transcutaneous bilirubin measurement and total serum bilirubin concentration with respect to body weight and gestational period are expressed in the table and Fig. 1-4. As illustrated in Fig. 5, we obtained a correlation coefficient between total serum bilirubin and transcutaneous bilirubin measurements which can be expressed as: r=0.78; p<0.01; n=390.

Table 1. Correlation coefficients between total serum bilirubin concentration and transcutaneous bilirubin measurement

Group	case No.	r	R ²	p value
≥2500 gm	341	0.82	0.67	p<0.01
<2500 gm	49	0.78	0.61	p<0.01
≥37 week	318	0.82	0.67	p<0.01
<37 week	72	0.81	0.66	p<0.01
Total	390	0.78	0.61	p<0.01

DISCUSSION

The definitions of physiologic and nonphysiologic jaundice are based on the natural history of neonatal hyperbilirubinemia and normal serum bilirubin levels in the first weeks of life. Several criteria which rule out the diagnosis of physiologic jaundice have been established by several investigators. Of which the most important one is total serum bilirubin level. There are two methods to measure total serum bilirubin concentration which are used world widely, American Optical bilirubinometer and alkali azobilirubin method.

Standard method to measure total serum bilirubin level still requires a measurement of serum bilirubin concentration by laboratory technique using blood obtained by repetitive heel pricks. But invasiveness of this technique of blood sampling serves as a source of discomfort and of serious infection. So to provide a noninvasive method for the screening test of neonatal hyperbilirubinemia a reflectometer system was investigated. In 1960, Gosset developed an inctrometer that determined the depth of the jaundice by comparing skin color with different shades of transparent yellow strips. Hannemann and coworkers demonstrated a noninvasive method

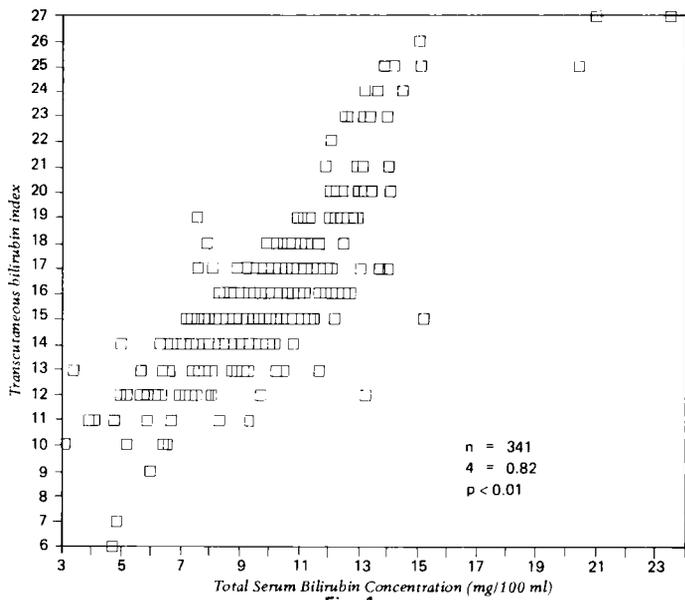


Fig. 1.

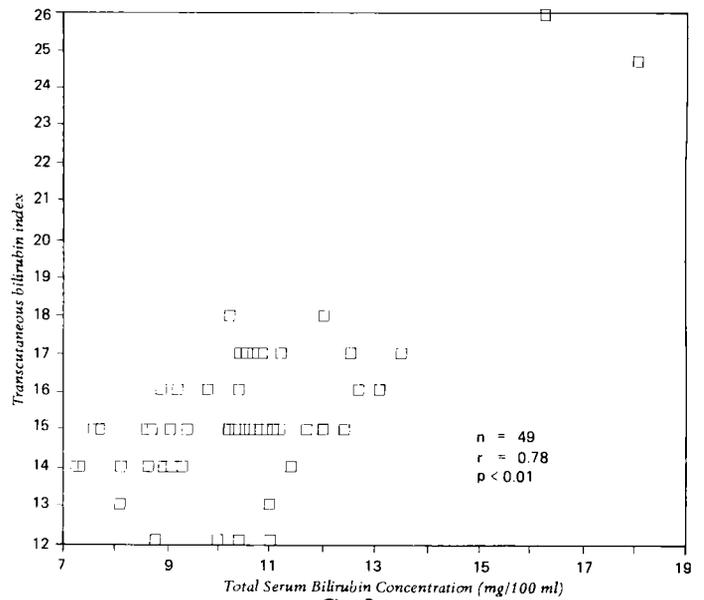


Fig. 2.

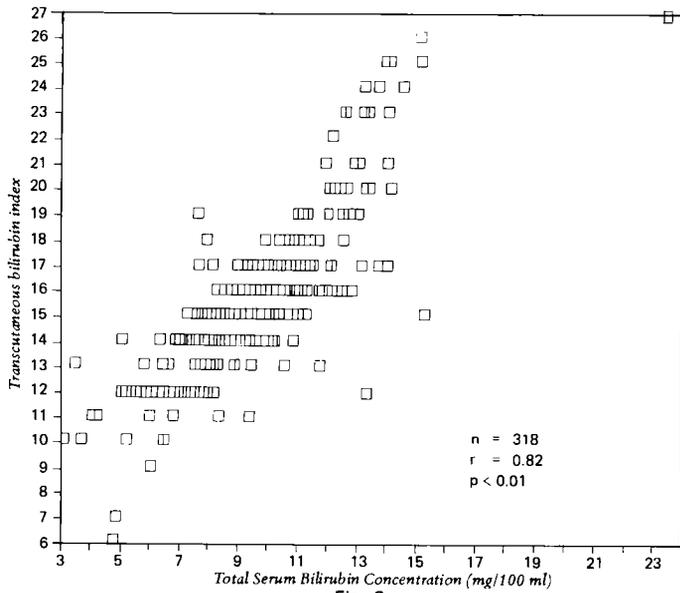


Fig. 3.

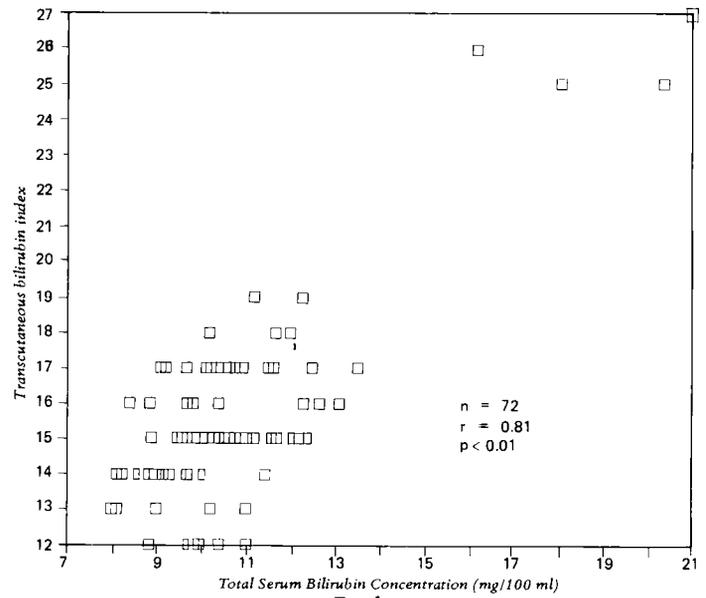


Fig. 4.

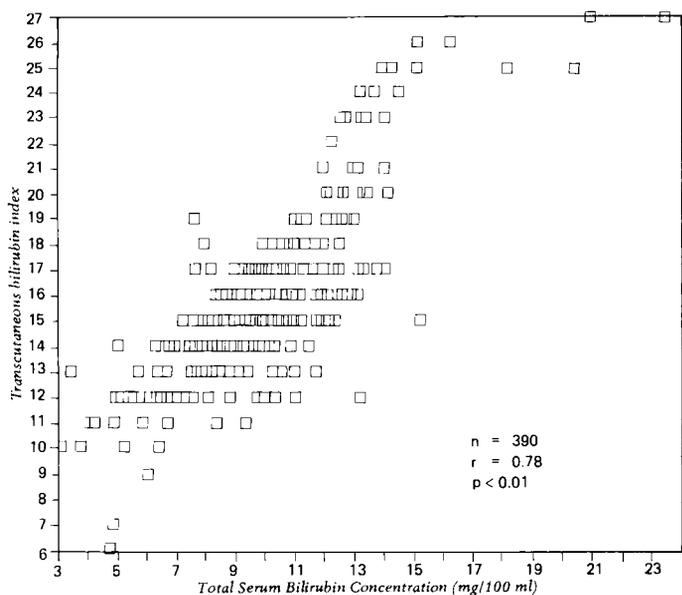


Fig. 5.

Fig. 1. Correlation between transcutaneous bilirubin index and total serum bilirubin concentration Body weight ≥ 2.5 kg.

Fig. 2. Correlation between transcutaneous bilirubin index and total serum bilirubin concentration Body weight < 2.5 kg.

Fig. 3. Correlation between transcutaneous bilirubin index and total serum bilirubin concentration Gestational period ≥ 37 WK.

Fig. 4. Correlation between transcutaneous bilirubin index and total serum bilirubin concentration Gestational period < 37 WK.

Fig. 5. Correlation between transcutaneous bilirubin index and total serum bilirubin concentration Total.

for the serum bilirubin determination by measuring skin spectral reflectance. The reflectometer was operated over the spectral region 400–750 nm with a 30 second scan time on the blanched skin.

In 1980 Yamanouchi and coworkers described the use of transcutaneous bilirubinometer, a small hand hold rechargeable instrument. A strobo light (2w/sec) travel through a fibroptic filament and penetrates the blanched skin and transilluminates the subcutaneous tissue. The scattered light comes back through a second fibroptic filaments and is carried to the spectrophotometric module where the intensity of the hemoglobin-corrected yellow color is obtained as the difference between optical density of blue and green.

Using principles of reflectometry these investigators demonstrated significant correlations between transcutaneous bilirubin measurement using the Minolta bilirubinometer and serum bilirubin measurement using American Optical bilirubinometer. Transcutaneous bilirubin measurements from the forehead and mid sternum have been shown to be convenient and acceptable for its measurement. But as previously described by Yamanouchi, the forehead is recommended as the site of choice for its measurement because: (1) It is usually acceptable; (2) the frontal bone structure offers the necessary resistance to activate the xenon tube mechanism; and (3) the skin surface of the forehead is taut and firm. We also used forehead as a site of measurement.

Report originally described by Yamanouchi and coworkers resulted in highly significant correlation ($r=0.95$, $p<0.001$), good reproducibility (coefficient of variation; 0 to 4.90%) and little technique dependence (coefficient of variation; 2.13 to 4.98%) between transcutaneous and serum bilirubin measurement.

We obtain correlation coefficient of 0.78, which is lower than that reported by Yamanouchi (1980), but is higher than that reported by Pereira (1982; $r=0.76$) and Goldman (1982; $r=0.70$). We also obtain good reproducibility and little technique dependence and the coefficients of variation are 0 to 4.86% and 1.98 to 4.78% respectively, which are similar to those reported by Yamanouchi *et al.* (1981).

As transcutaneous bilirubin measurement detects the skin reflectance, its value is influenced

by many factors as gestational period, phototherapy, exchange transfusion, reading site, level of hemoglobin and color of the skin. Increasing skin reflectance was found with increasing gestational age by Krauss and Post (1976), which suggested that transcutaneous bilirubin measurement was influenced by gestational period. But Yamanouchi reported that transcutaneous bilirubin measurement in premature and low birth weight had statistically significant correlation. Infants receiving phototherapy show a fall in skin reflectance by tanning of the skin. Correlation study by Hegyi *et al.* indicated that transcutaneous bilirubin measurements from infants who received phototherapy are not clinically useful in predicting serum bilirubin. However due to the large scatter of data in the trials, Hanneman *et al.* (1982) question the usefulness of the transcutaneous bilirubin measurements as a clinical tool and suggest incorporation of additional wavelengths to improve accuracy. In spite of the above limitations the transcutaneous bilirubinometer can be best applied initially in healthy neonates as a screening device that inform the clinician when to obtain a blood sample to determine serum bilirubin concentration.

As we attempted to use the transcutaneous bilirubin measurement as a screening test for the identification of neonatal hyperbilirubinemia, we examined the sensitivity and specificity of the measurements. Many investigators suggest that total serum bilirubin concentrations exceed a level of 12 to 12.9 mg/100 ml in full term infant requires diagnostic investigation. We consider that infants with a total serum bilirubin concentration exceed 12.9 mg/100 ml have significant hyperbilirubinemia as previously described by Avery 1987. We calculate the sensitivity and specificity at the levels of transcutaneous bilirubin measurement ranged from 13 to 27. Review of 15 paired data suggests that forehead transcutaneous bilirubin measurement of 19 is a useful dividing level.

The specificity is 98% and sensitivity is 74%. We also calculate positive and negative predictive value; 76% and 97% respectively. Though it seems to be useful device to reduce invasive technique there are a little false negative determinations and low sensitivity. The transcutaneous bilirubin measurement has occasionally a large range of variation as 13 at the same

serum bilirubin concentration. Since an individual transcutaneous index did not predict a serum bilirubin level accurately, we would not agree with Yamanouchi that the instrument could serve as a viable alternative to traditional invasive procedures used to determine serum concentration.

So we determine that this device could be used a useful screening test not an alternative to traditional invasive procedures and have a role to act as clinical screening test in determining which neonates are likely to have total serum bilirubin concentrations greater than 12.9 mg/100 ml, in other words, have significant hyperbilirubinemia. But other contributing factors which could influence a skin reflectance are not considered in the analysis including race, skin color, postnatal age, disease status and hemoglobin level, further investigation will be necessary.

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= 국문초록 =

신생아에서 경피 빌리루빈 측정기의 임상적 이용

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신생아 황달은 신생아에 있어서 가장 흔히 접하는 문제이다. 저자들은 서울대학교 병원의 신생아실과 신생아 중환자실에 입원한 390명의 신생아에 대해서 경피 빌리루빈 측정기를 사용해서 연구한 결과 다음과 같은 결과를 얻었다. 측정자에 따른 차이는 변이계수가 5%이하로 의미가 없으며 동일 측정자에 의한 반복측정에 대한 차이도 변이계수가 5%이하로 의미가 없었다. 경피 빌리루빈 측정치와 혈청 빌리루빈 측정치간에는 의미있는 상관관계를 보였다($r=0.78$ $p<0.01$). 의미있는 고 빌리루빈혈증은 혈중 빌리루빈 치가 12.9 mg/100 ml 이상일때로 기준을 삼았으며 경피 빌리루빈 치는 19이상을 기준으로 삼았다. 이를 기준으로 하면 특이도와 민감도는 각각 98%와 74%이며 양성 적중도와 음성 적중도는 각각 76%와 97%인데 경피 빌리루빈 측정치는 동일한 혈청 빌리루빈에 대하여 최고 13까지 차이를 보이므로 혈청 빌리루빈 측정치를 대신할 수는 없다. 그러나 이를 응용하면 관혈적 방법에 의한 혈청 빌리루빈 측정 빈도를 줄이는데 크게 기여할 것이다.