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Original Article

Covered Skin Bilirubin Measurement during Phototherapy, in Comparison with Total Serum Bilirubin in Full Term Neonates

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ABSTRACT

Background: Jaundice is a prevalent problem among neonates. Patients undergoing phototherapy need a close follow-up of their serum bilirubin levels to determine the treatment response. To make a comparison between transcutaneous bilirubin measurements (TcB) from covered skin areas during phototherapy and total serum bilirubin (TSB) levels.

Methods: This prospective observational study was conducted on 30 full-term neonates with indirect hyperbilirubinemia requiring phototherapy. Some parts of the skin (forehead and sternum) were covered in each neonate using the BiliEclipsephoto opaque patch and this covered site was used to measure TcB during phototherapy and compare it with TSB. Both TSB and TcB estimation were performed on icteric newborns before, as well as 24 and 48 h of exposure to phototherapy.

Results: As demonstrated by the obtained results, TSB was not significantly different from TcB measured at forehead and sternum before phototherapy. Moreover, no significant difference was detected between TSB and TcB from the covered forehead and sternum in 24 and 48 h of phototherapy initiation. There was a highly significant positive correlation between TSB and covered forehead/sternum TcB during phototherapy. There was no significant difference in both covered forehead and sternum TcB according to different used TcB devices.

Conclusion: Measurement of TcB from the covered area of the skin during phototherapy using transcutaneous bilirubin meters is a reliable method to assess TSB in full-term neonates and could lead to a reduction in blood sampling and its complications.

Keywords: Hyperbilirubinemia, Phototherapy, Transcutaneous bilirubin meter

Introduction

Jaundice is a frequent and usually physiological problem among neonates; nonetheless, it can result in neurological sequelae. Up to 10% and 25% of term and preterm newborns develop significant hyperbilirubinemia requiring phototherapy (1). Transcutaneous bilirubin measurement has been recommended by the American Academy of Pediatrics (AAP) as a reasonable alternative to total serum bilirubin for screening neonates with jaundice (2).

Jaundiced neonates under phototherapy require close monitoring of total serum bilirubin (TSB), which means frequent blood sampling. Bilirubin in the skin exposed to phototherapy is decreased and significantly alters transcutaneous bilirubin (TcB). Phototherapy converts the bilirubin to more water-soluble lumirubin excreted by the body. This process results in skin blanching and alters TcB levels. Nonetheless, the reliability of TcB measurement during phototherapy is still unclear. Some studies reported that more accurate approximations of TSB could be made with TcB measurement by covering the skin during phototherapy, (3). In light of the

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aforementioned issues, the present study aimed to compare TcB measurements from covered skin areas during phototherapy to total serum bilirubin (TSB) levels.

Methods

Subjects

This prospective observational study was conducted at the neonatal intensive care unit (NICU) of Benha University Hospital from January 2019 to January 2020. Before the commencement of the study, written informed consent was obtained from neonates' parents and the study was approved by the Ethical Committee of Faculty of Medicine, Benha University Hospital. This study was performed on 30 full-term neonates with indirect hyperbilirubinemia who required phototherapy according to AAP (4). The newborns with direct hyperbilirubinemia, major congenital anomalies, or neonatal sepsis were excluded.

Materials and Methods

Each neonate included in this study was subjected to full history taking, including gestational age, mode of delivery, gender, etiology of jaundice, and postnatal age in hours at presentation and thorough clinical examination. Before phototherapy, TSB and TcB were measured in all jaundiced full-term neonates who required phototherapy. Before the initiation of phototherapy, we covered the forehead and sternum using the BiliEclipse phototherapy patch. A photo-opaque patch 2.5 cm in diameter (BiliEclipsephototherapy patch, Respironics, Murrysville, PA, USA) was used to shield this area from light exposure. We avoided areas with ecchymosis, hair, hyperpigmentation, and hemangioma.

Phototherapy was initiated, and different intensities were used according to the level of TSB. During the phototherapy procedure, the patients were taken away from phototherapy only for feeding for 15-20 minutes every 3 h, as well as for a brief examination and blood sampling. Serial serum bilirubin measurements were repeated on a daily basis. The TSB was measured at presentation before phototherapy, as well as after 24 and 48 h after phototherapy initiation by Colorimetric Diazo method using semi-automated analysis(5010), diazotized sulphanilicacid reaction using Diamond reagent (Bilirubin. Photo-analyzer) (5).

Different regular jaundice meter devices were used to measure TcB upon admission before phototherapy. Moreover, 24 and 48 h after phototherapy, the measurements were taken from the covered parts within 5 minutes of blood sampling for TSB estimations. Phototherapy was disconnected during TcB measurements and blood sampling for TSB.

Statistical Analysis

The collected data were analyzed in SPSS software (version 16). Categorical data were presented as numbers and percentages. Quantitative data were tested for normality using the Shapiro-Wilks test assuming normality at P>0.05. Normally distributed variables were expressed as mean±standard deviation, while non-parametric data were presented as median and inter-quartile range (IQR), and analyzed by Kruskal Wallis (KW) tests for more than 2 independent groups. Paired non-parametric variables were analyzed by Friedman tests for more than two paired variables. The correlation among variables was assessed by Person's and Spearman's correlation coefficients for parametric and non-parametric variables, respectively. Bland Altman plot was constructed to detect the mean difference and agreement between the used methods of bilirubin measurement. A p-value less than 0.05 was considered statistically significant (6).

Results

The current study was conducted on 30 full-term newborns (16(, the majority of whom (53%) were male)14(.The mean gestational age was reported as 37.0±0.45 weeks, and the mean±SD of postnatal age at presentation was 72.0±32.4 h (Table 1). There is no significant difference between TSB and TcB measured at forehead and sternum before phototherapy, as well as between TSB and covered forehead and sternum TcB after 24 and 48 h of phototherapy (P=0.06), (P=0.13), and (P=0.27), respectively (Table 2).

Table 1. Description of the studied groups

Variable		No. (N=30)	% (100%)
Gestational age (w)	Mean±SD	37.0±0.45	
	Range	37-38	
	37 w	22	73.3
	38 w	8	26.7
Gender	Female	14	46.7
	Male	16	53.3
Mode of delivery	NVD	5	16.7
	CS	25	83.3
Age at presentation (hours)	Mean±SD	72.0±32.4	
	Range	24-144	

NVD= normal vaginal delivery CS=caesarian section

Table 2. TSB (mg/dl) vs forehead and sternum TcB before phototherapy, and vs covered forehead and sternum TcB after 24 and 48 h of phototherapy

(n=30) before phototherapy	TSB	forehead TcB	sternum TcB	Friedman' test (P)
Median, IQR	14.0 (12.8-16.2)	14.2 (13.0-15.7)	14.4 (13.0-16.5)	5.64 0.06 (NS)
After 24 hours of phototherapy	TSB during phototherapy	Covered forehead TcB	Covered sternum TcB	Friedman' test (P)
Median, IQR	12.1(10.3-13.6)	12.2(11-14.3)	12.0(10.8-14.1)	3.05 0.13 (NS)
After 48 hours of phototherapy				
Median, IQR	9.15(6.8-11.7)	9.0(7.07-11.9)	8.95(7.15-11.9)	2.6 0.27(NS)

Test result before phototherapy = 5.64 P = 0.06 NS=non-significant as P>0.05
Test result after 24 hours = 3.05 P = 0.13 NS= non-significant as P>0.05
Test result after 48 hours = 2.6 P = 0.27 NS= non-significant as P>0.05
TSB = total serum bilirubin TcB = transcutaneous bilirubin

There was a highly significant positive correlation between TSB and covered forehead TCB (r= 0.942) and covered sternum TCB (r=0.903) during phototherapy after 48 h (P<0.001) (figures 1, 3). Bland Altman plot was constructed to detect the mean difference and agreement between the used methods of bilirubin measurements and revealed good agreement (figure 2, 4). Table (4) shows no

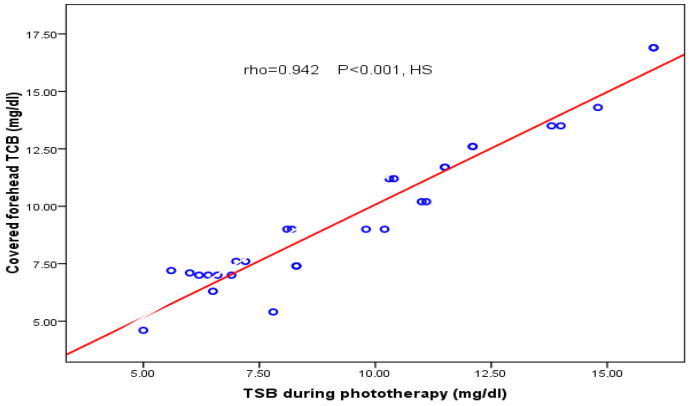

Figure 1. Correlation between total serum bilirubin and covered Forehead transcutaneous bilirubin during phototherapy after 48 h

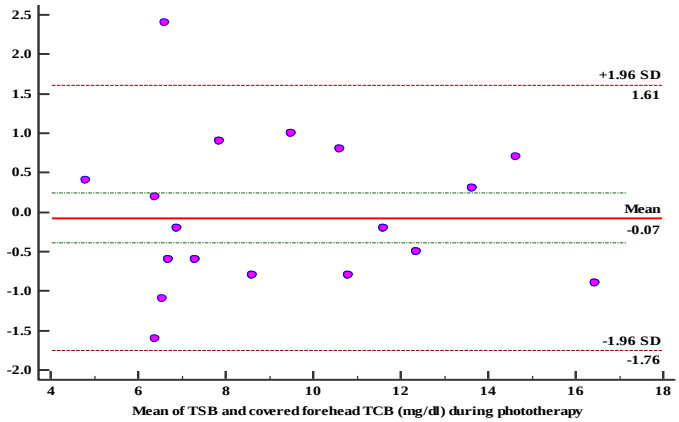

Figure 2. Bland-Altman plot for TSB and covered forehead TcB during therapy, mean difference between TSB and covered forehead TcB= -0.07 (the closer the value to "zero", the more similar and not systematically different are the 2 methods), 95% CI of the agreement= -1.76 to 1.61

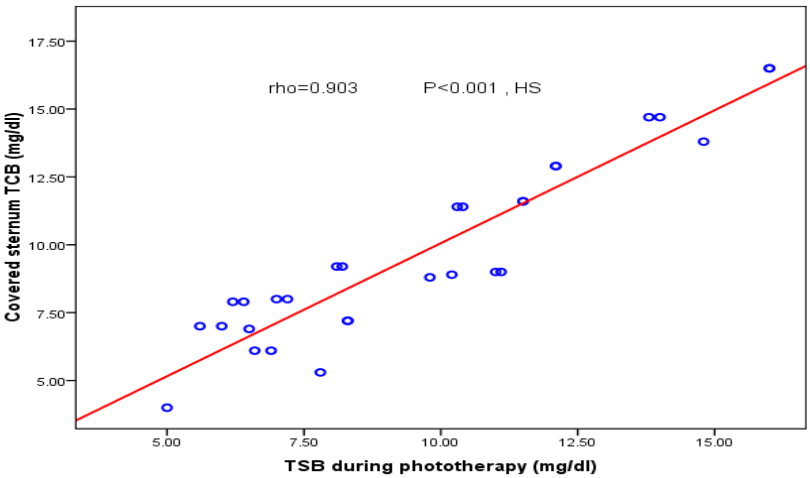

Figure 3. Correlation between total serum bilirubin and covered sternum transcutaneous bilirubin during phototherapy after 48 h

Table 3. Covered forehead and covered sternum TcB during phototherapy after 48 h according to the used device

Device	n.	Covered forehead TcB during phototherapy		Covered sternum TcB during phototherapy	
		Median	IQR	Median	IQR
BILICHECK	6	10.8	7.9-13	10.9	7.6-13.1
Dragger JM	8	11.4	8.1-15.6	11.5	7.4-15.3
MB J20	16	7.5	7.0-9.9	8.0	7.1-9.2
Kruskal Wallis test (P)		4.08 (0.13, NS)		2.87 (0.24, NS)	

Covered forehead test result by different devices = 4.08 P = 0.13 NS= non-significant as P>0.05
Covered sternum test result by different devices = 2.87 P = 0.24 NS= non-significant as P>0.05
TSB=total serum bilirubin TcB=transcutaneous bilirubin

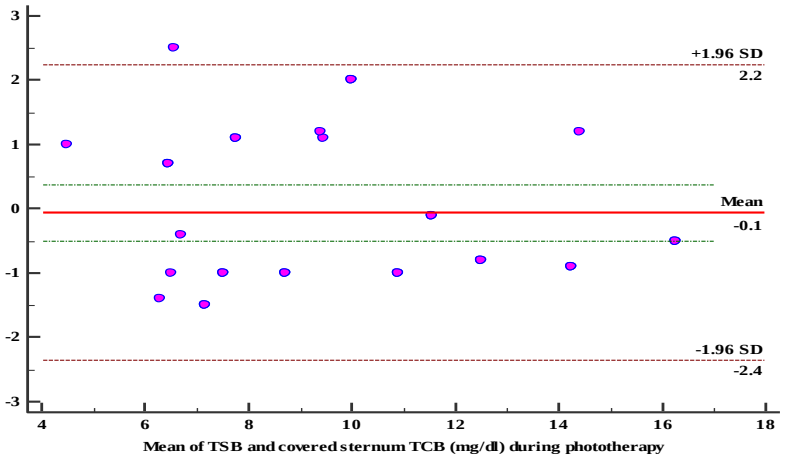

Figure 4. Bland-Altman plot for total serum bilirubin (TSB) and covered sternum transcutaneous bilirubin(TcB) during therapy, mean difference of TSB, and covered sternum TcB, Mean difference= -0.1. 95%CI of agreement= -2.4 to 2.2

significant difference in both covered forehead and sternum TcB according to different devices used as MB J20 used in 16 cases, Dragger JM 103 used in 8 cases, and Bilicheck used in 6 cases.

Discussion

Although the measurement of TSB is still the main method for the assessment of neonatal jaundice, it needs frequent blood sampling which is an invasive and painful procedure in neonates. In this regard, TcB is an easy, non-invasive, painless alternative for TSB estimation. A meta-analysis conducted in 2016 assessed the dubious utility of TcB in skin exposed to phototherapy (7). Therefore, the present study aimed to make a comparison between TcB from covered skin areas

during phototherapy and TSB levels. To the best of our knowledge, it is the first study to compare TSB with TcB during phototherapy using the BiliEclipse photo-patch for skin coverage in Egypt.

Similar to previous studies, the results of the present study revealed that TSB was non-significantly different from TcB measured at forehead and sternum before phototherapy, demonstrating the usefulness of TcB as a screening tool, (8-13). A highly significant positive correlation was found between TcB measured at covered forehead and sternum during phototherapy and TSB. The Bland-Atman analysis denoted good agreement between TSB and covered forehead and sternum TCB during phototherapy. There was no significant difference in the covered forehead and sternum TcB during phototherapy using different devices.

In their study, Zecca et al. (9) assessed the accuracy of TcB estimation on 364 neonates during phototherapy and concluded that BiliCheck can be safely used for the measurement of bilirubin levels in neonates under phototherapy. The accuracy of this bilirubinometer on covered skin of the forehead is high enough to reduce blood withdrawal and determine the safe time to stop phototherapy. Along the same lines, in a study on 39 full-term neonates in the USA, Fonesca et al. (10) aimed to evaluate the accuracy of TcB from patched skin during and after phototherapy in the treatment of neonatal jaundice. They concluded that it is a reliable method in the management of neonatal hyperbilirubinemia.

In the same context, in their study, Radfar et al. (8) included 134 term and 36 preterm neonates in Iran. They concluded that TcB can be used for the measurement of bilirubin levels in preterm and term neonates under phototherapy, and Bilicheck is slightly less accurate in preterm neonates. Katayama et al. (14) performed a study on 125 term Japanese neonates to assess the reliability of TcB measurement from an area unexposed to phototherapy for the estimation of TSB in neonates during phototherapy. The results of the stated study indicated that direct measurement of TcB during phototherapy using a bed type device is a reliable method to measure TSB in term neonates and would decrease frequent blood sampling.

In a similar vein, a study was conducted by Alsaedi (15) in Saudi Arabia on 151 term neonates to assess the correlation between TcB estimation during phototherapy and TSB. The findings of the mentioned study revealed that it correlates with TSB and can be used to assess bilirubin levels during phototherapy. However, if the neonate is found to have significant jaundice, a confirmatory TSB should be performed. Posada et al. (16) in Spain performed a study on 217 full-term and preterm neonates to investigate the suitability of TcB as a tool to assess the efficacy of phototherapy on covered skin. They concluded that covered skin TcB estimation is useful for evaluating the response to phototherapy in term and preterm infants.

The accuracy of TcB estimations from the forehead skin area covered with a patch in neonates receiving phototherapy was demonstrated in numerous studies (9, 10, 12). All these studies used only one TcB device; nonetheless, the present research employed three devices: (BILICHECK, Dragger JM 103, and MB J120). No significant difference was found in the covered forehead and sternum TcB measurements during phototherapy according to different devices. This is in agreement with the results of the study performed by Romagnoli et al. (17)who compared Respironics BiliCheck and JM-103 in a normal newborn population and concluded that both BiliCheck and JM 103 showed similar diagnostic accuracy. Nevertheless, Rylance et al. (18) reported a moderate correlation between TcB measured by JM-103 (Minolta) and TSB in African neonates during phototherapy.

Numerous studies approved a good correlation between TSB and TcB measurement from covered skin areas before and during phototherapy. Nonetheless, Murli et al. (19) assessed the reliability of TcB on shielded skin in neonates receiving phototherapy. The results of the mentioned study demonstrated that TcB is not reliable for estimating serum bilirubin in late preterm and term neonates during phototherapy. The variations in the results of these different studies can be ascribed to different study populations, the inclusion of preterm neonates, and the different irradiance of phototherapy. Reyes et al. (20) found that TcB estimated by BiliCheck device during phototherapy has a negative mean bias which worsens as TSB level > 238μmol/L, as compared to TSB. Engle et al. (21) reported that BiliCheck TcB underestimated bilirubin in term Hispanic newborns with relatively high TSB >15mg/dl.

Conclusion

As evidenced by the obtained results, there is a significant correlation between TSB and TcB measured from a patched area of the skin during

phototherapy. Therefore, TcB can be used to monitor bilirubin levels during phototherapy.

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Conflicts of interest

The authors declare that they have no conflict of interest regarding the publication of the current study.

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