RESEARCH PAPER

Effect of Conventional and LED Phototherapy on the Antioxidant-Oxidant Status in Preterm Neonates with Jaundice

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Objective: To compare oxidative stress due to conventional and LED phototherapy among jaundiced preterm neonates. **Methods:** Cross-sectional study conducted in NICU on 82 neonates (equal numbers received conventional and LED phototherapy). Total antioxidant capacity (TAC), total oxidant status (TOS) and Oxidative stress index (OSI) were assessed. **Results:** Post-phototherapy, mean (SD) OSI increased significantly compared to baseline in both conventional [0.26 (0.24) *vs*. 0.61 (0.41); *P*<0.001] and LED groups [0.24 (0.20) *vs*. 0.32 (0.23); *P*<0.001]. Across groups, mean (SD) TAC was lower [0.28 (0.16) *vs*. 0.53 (0.27); *P*<0.001] mmol Trolox equiv/L; mean (SD) TOS higher [15.6 (10.9) *vs*. 14.6 (10.2); *P*=0.711] µmol H_2O_2/L and mean (SD) OSI higher [0.61 (0.42) *vs*. 0.33 (0.23); *P*<0.001] in conventional as compared to LED phototherapy. **Conclusion**: Both modes increased oxidative stress index; however, conventional phototherapy resulted in higher oxidative stress.

Keywords: *Antioxidant capacity, Hyperbilirubinemia, Oxidative stress*.

Phototherapy is widely used to treat neonatal hyperbilirubinemia. Currently conventional compact fluorescent lamp, light emitting diode lights (LED) are used in phototherapy systems. There are reports that phototherapy generates oxygen free radicals and causes oxidative stress [1-3]. Studies have compared oxidative stress in term neonates after conventional and LED phototherapy [4,5]. However, preterm neonates have an immature antioxidant system and are more susceptible to oxidative stress [6]. The objective of the present study was to compare the effect of conventional and LED phototherapy on oxidative stress parameters exclusively among preterm neonates.

METHODS

This cross-sectional study was conducted in NICU of a government tertiary-care hospital from April 2015 to April 2016 after approval by institutional ethics committee.

Convenience sample of 82 preterm neonates with indirect hyperbilirubinemia requiring phototherapy in the first week of life were included after obtaining consent from parents. Neonates with hemolytic jaundice, with jaundice within 24 hours of life, requiring ventilation, and with birth asphyxia were excluded. Total oxidant status (TOS), total antioxidant capacity (TAC) and Oxidative stress index (OSI) were estimated to assess the effect of phototherapy on oxidant-antioxidant status of neonates.

Sample size was calculated with 80% power and confidence of 95% to demonstrate difference of 16 µmol H_2O_2/L between groups after phototherapy [4].

Neonates were treated by either LED or by conventional phototherapy. Neonates were exposed completely except for eyes and genitalia, kept at 30-40 centimeters from light-source. Continuous phototherapy was calculated in hours, minimally interrupted for feeding and cleaning. In conventional group, the single surface phototherapy equipment had Compact Fluorescent Light tubes with wave length 450 nm and irradiance 8-12 µW/cm^2/nm. (Neocare Equipments, Mumbai, India). For LED phototherapy, equipment with irradiance 30-40µW/cm^2/nm was used (Fanem Medical Devices, India).

Venous sampling was done prior to and at 48 hours after phototherapy to determine total bilirubin, TOS and TAC. TOS and TAC were measured by Erel's method with an autolyser using a kit (Rel Assay Diagnostics, Mega Tip Company, Gaziantep, Turkey) [7,8]. OSI was calculated as TOS/TAC /100 [3,4]. Relevant baseline demographic, clinical and biochemical parameters were recorded in all subjects.

Data were analyzed using SSPS version 16. The OSI before and after phototherapy within the same group were compared using Wilcoxon signed rank test. The change between the pre- and post-phototherapy values were

TABLE I BASELINE CHARACTERISTICS OF THE STUDY GROUPS

	Conventionaln=41	*LEDN=41*
Birth weight (kg)	1.64 (0.34)	1.57 (0.33)
Gestational age (wks)	33.7 (1.6)	32.1 (1.8)
Age at initiation of phototherapy (h)	69 (16.8)	62.7 (15.4)
Duration of phototherapy (h)	82 (30.4)	73.8 (21.6)
Serum total bilirubin before phototherapy (mg/dL)	11.3 (2.6)	10.6 (1.9)
TAS before phototherapy (mmol Trolox equiv/L)	0.53 (0.36)	0.65 (0.37)
TOS before phototherapy (μmol H_20_2/L)	10.9 (8.3)	11.8 (7.9)
OSI before phototherapy	0.26 (0.24)	0.24 (0.20)
Sepsis positivity, *N* (%)	27 (65.8)	20 (48.7)
Surfactant administered, *N* (%)	1 (2.4)	4 (9.7)
Oxygen administered, *N* (%)	10 (24.3)	10 (24.3)

TAC: Total antioxidant capacity; TOS: Total oxidant status; OSI: Oxidative stress index; All values mean (SD) unless indicated.

calculated for TOS, OSI and TAC. ÄTOS and ÄTAC were compared across groups using Mann-Whitney test.

The mean ΔOSI for all neonates was calculated. Neonates were divided into higher oxidative stress group (ΔOSI > mean ΔOSI) and the lower oxidative stress group (ΔOSI < mean ΔOSI). Binary logistic regression analysis was done to identify the risk factors for higher oxidative stress by entering gestational age (very preterm *vs*. moderate to late preterm), type of phototherapy (conventional/LED phototherapy), birth-weight (<1500/ >1500 grams), sepsis (present/absent), surfactant (administered/not administered), oxygen (received/ not received) as co-variants. *P* value of <0.05 was considered significant.

RESULTS

Forty-one preterm neonates each received LED and conventional phototherapy. The mean (SD) gestational age was 32.9 (1.9) weeks and mean (SD) birth weight 1.6 (0.33) kg. ***Table* I** depicts baseline characteristics of the two groups. There were no statistically significant differences except for gestational ages (*P* <0.001).

Post-phototherapy, mean (SD) OSI increased significantly compared to baseline in both conventional [0.26 (0.24) *vs* 0.61 (0.41); *P* <0.001] and LED groups [0.24 (0.20) *vs* 0.32 (0.23); *P* <0.001]. ***Table* II** compares the post phototherapy parameters indicating that conventional phototherapy resulted in higher oxidative stress.

There was statistically significant difference between the conventional and LED groups with respect to ΔTAC and ΔTOS. The reduction in post-phototherapy TAC (ΔTAC) and increase in post-phototherapy TOS (ΔTOS) [mean (SD)] were more pronounced in the conventional group [0.25 (0.34) *vs*. 0.12 (0.23) mmol Troloxequiv/L; *P*=0.026] and [4.6 (4.6) *vs*. 2.8 (4.2) μmol H_20_2/L; *P*=0.029], respectively.

Binary logistic regression analysis showed that conventional phototherapy [odds ratio (95% CI) 30.8 (5.0-188.9)] and sepsis positivity [odds ratio (95% CI) 12.1 (2.5-51.2)] were significant in predicting higher oxidative stress index when controlled for gestational age, birthweight, surfactant administration and oxygen administration.

DISCUSSION

The present study, done exclusively among preterm neonates, compared antioxidant-oxidant parameters following conventional and LED phototherapy. Both conventional and LED phototherapy resulted in increased oxidative stress index. However, derangement of antioxidant-oxidant parameters was more pronounced after conventional as compared to LED phototherapy.

The study had a convenience sample and randomization would have increased the strength of

TABLE II COMPARISON OF OXIDANT AND ANTIOXIDANT PARAMETERS AFTER CONVENTIONAL AND LED PHOTOTHERAPY

	Conventional (n=41)	*LED (n=41)*
*TAC	0.28 (0.16)	0.53 (0.27)
TOS	15.6 (10.9)	14.6 (10.2)
*OSI	0.61 (0.42)	0.33 (0.23)

TAC: Total antioxidant capacity (mmol Trolox equiv/L); TOS: Total oxidant status (μmol H_20_2/L), OSI: Oxidative stress index. All values in mean (SD); P<0.001.*

WHAT THIS STUDY ADDS?

- Conventional phototherapy tilted the oxidant-antioxidant parameters in preterm neonates towards the oxidant side to a greater extent compared to LED phototherapy.

evidence. The two groups compared had statistically significant difference in the gestational ages. However, since baseline TAC, TOS and OSI levels were comparable, the difference in gestational ages alone is unlikely to have affected the results.

The baseline TAC in the present study were lower than values reported by Demirel, *et al*. [4]. The lower TAC could be due to lower gestational age of neonates in the present study. The finding supports the evidence that preterm neonates have immature antioxidant system [9]. Our observation of increase in OSI after both conventional and LED phototherapy is in agreement with the study done by Kale, *et al*. [5]. However, another study reported increased oxidative stress following conventional but found no significant change following LED phototherapy [4]. The differences observed could be due to dissimilarities in characteristics of the study population, phototherapy equipment, used and timing of sample collection.

When conventional and LED phototherapy groups were compared, both TAC and TOS significantly altered towards the oxidant side among neonates of conventional group. An earlier study reported significant increase in TOS without difference in TAC values [4]. Our findings also support evidence in an earlier study that show that sepsis contributes to oxidative stress [10].

We conclude that both conventional and LED phototherapy altered the antioxidant oxidant status towards the oxidant side with the effect of the former being more pronounced than the latter. In light of the findings, we recommend judicious use of phototherapy among preterm neonates who have a lower baseline antioxidant capacity.

Contribution: AA: conceived and designed the study, prepared the protocol, collected data, drafted the manuscript; SRR: designed the study, supervised data collection, analyzed and interpreted the data, revised the manuscript for important intellectual content; BSB: conceived the study, co-ordinated in data collection, provided critical inputs to the manuscript writing; KB: designed the study, critically reviewed the manuscript; NJ: designed the study, guided in analyzing the data. All authors approved the final version of manuscript.
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