A New Approach: The Application and Impact of NeoLight Skylife™ Phototherapy for Hyperbilirubinemia in Newborns

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ABSTRACT

The purpose of the on-going clinical study is to test the equivalence of a new FDA cleared neonatal phototherapy device, Skylife™, against the standard of care, GE BiliSoft, under hospital settings conducted at HonorHealth Scottsdale Shea Medical Center. The results point towards the fact that the investigational device (Skylife™) can considerably reduce the neonatal phototherapy discharge time by 40%, which would be of clinical, operational & economical significance to hospitals, insurance providers and patients.

PROBLEM STATEMENT

Phototherapy devices are indispensable to any hospital administering care to neonates, as neonatal hyperbilirubinemia presents itself in 60% of the term neonates and 80% of the preterm neonates. It is imperative for these devices to be compact and seamlessly integrate with the hospital environment while offering the required treatment dosage on a case-by-case basis. Current phototherapy devices often lack the required treatment dosage and lack ergonomic considerations for maintenance and operation. This forces hospitals to use multiple phototherapy devices – even up to 3 devices – at the same time. Such practices have a negative monetary impact on both hospital and patients; patients receiving insufficient dosage may have longer hospital length of stay, in worse cases this could lead to chronic side-effects; hospitals need to maintain more devices in the inventory to meet the demand; hospital floor is crowded by the use of multiple phototherapy devices affecting patient access; equipment crowding is not an optimal working condition as it could lead to increased caregiver stress, reduced patient comfort, and in effect lower patient safety and hospital quality metrics.

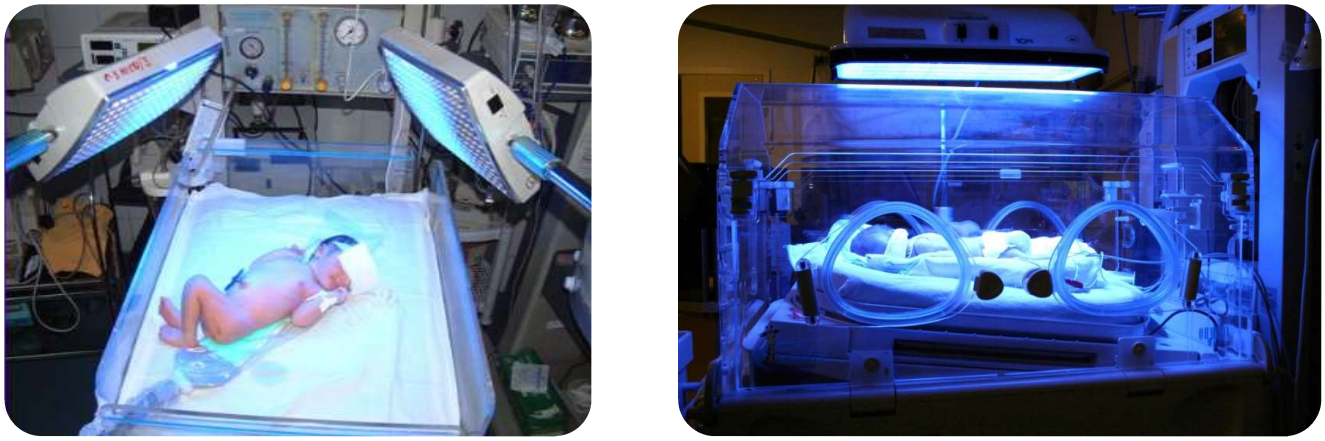

Fig 1: Baby undergoing triple-phototherapy (left) and top-phototherapy in an incubator (right) where access to the patient access is cut off in an already crowded environment.

BACKGROUND

Nearly 60% of normal newborns become clinically jaundiced in the first week of life. Unconjugated (indirect) hyperbilirubinemia is the result of excessive bilirubin formation due to the neonatal liver's inability to clear bilirubin quickly enough from the blood.[1,2] Although most newborns with jaundice are otherwise healthy, they need to be monitored as bilirubin can be toxic to the central nervous system, and elevated levels left unchecked can cause serious problems. Sufficiently elevated levels of bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopmental handicaps and even death.[3]

The goal of phototherapy is to lower the concentration of circulating bilirubin or keep it from increasing. Phototherapy achieves this by using light energy to change the shape and structure of bilirubin, converting it to molecules that can be excreted even when normal conjugation is deficient.[4] Absorption of light by dermal and subcutaneous bilirubin induces a fraction of the pigment to undergo several photochemical reactions that occur at very different rates. These reactions generate yellow stereoisomers of bilirubin and colorless derivatives of lower molecular weight. The products are less lipophilic than bilirubin, and unlike bilirubin, they can be excreted in bile or urine without the need for conjugation.

Bilirubin elimination depends on the rates of formation as well as the rates of clearance of the photoproducts. Photoisomerization occurs rapidly during phototherapy, and isomers appear in the blood long before the level of plasma bilirubin begins to decline. Bilirubin absorbs light most strongly in the blue region of the spectrum near 460 nm, a region in which penetration of tissue by light increases markedly with increasing wavelength. The rate of formation of bilirubin photoproducts is highly dependent on the intensity and wavelengths of the light used. Only wavelengths that penetrate tissue and are absorbed by bilirubin have a phototherapeutic effect. Lamps with output predominantly in the 460-to-490-nm blue region of the spectrum are likely the most effective for treating hyperbilirubinemia.

METHODS

This paper provides initial findings of a prospective, two-arm, randomized, controlled investigation comparing the efficacy and safety of the NeoLight Skylife™ phototherapy with the standard phototherapy treatment (GE Bili Soft Blanket) on 16 healthy newborns (≥ 35 weeks gestational age) in the treatment of hyperbilirubinemia.

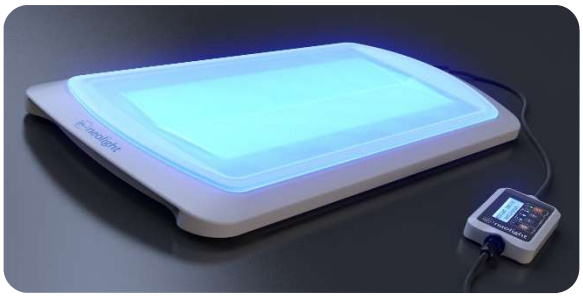

Fig 2a. Skylife™ Phototherapy Device

Fig 2b Standard of care GE BiliSoft Blanket

This investigation was carried out at HonorHealth system in Scottsdale, AZ. The investigation was approved by the HonorHealth Institutional Review Board. All patients included in the analysis were consented and enrolled in the investigation. Participants were randomly assigned to either the Neolight Skylife™ phototherapy condition (n = 7) or to the Natus-Neo Blue Blanket and GE Bili Soft Blanket (standard of care) group (n = 9). Comparisons were made between groups and time-points (baseline, 12 hours, and 24 hours) on total bilirubin levels, frequencies of temperature deviations outside of the normal range, and prevalence of pressure ulcers.

Note: All data were entered and analyzed using IBM SPSS v.24 (IBM Corp, 2016). Data were screened and met the criteria for parametric statistical test assumptions. Missing data, nonadherence and data lost to follow-up were excluded from statistical analysis. The a priori alpha level for all statistical tests was set at .05. A Repeated measures analysis of variance (RM-ANOVA) tests were conducted to examine within-between group differences on unconjugated bilirubin levels. Time until discharge was evaluated with an independent measures t-test.

SOLUTION (FINDINGS)

No initial group differences were observed on baseline bilirubin levels, gestational age, and birth weight. To date, no deviations of the temperature outside the normal range and no presence of pressure ulcers were reported for participants in both treatment groups. Therefore, no formal statistical analysis was conducted to evaluate safety.

Means and standard deviations for bilirubin at each time interval are reported in Table 1. The result of the repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean total bilirubin did not differ significantly

between time points ($F(1.418, 19.846) = 0.698$, $p = .882$. Therefore, we can conclude that the modality of phototherapy treatment showed statistical equivalence in bilirubin rates over a 24-hour treatment period.

	GROUP	*MEAN*	*SD*	*N*
BILIRUBIN AT BASELINE	Skylife™	11.38	1.38	7
	Control	12.44	1.39	9
	Total	11.98	1.45	16
BILIRUBIN AT 12 HOURS	Skylife™	10.96	2.56	7
	Control	11.94	2.61	9
	Total	11.51	2.55	16
BILIRUBIN AT 24 HOURS	Skylife™	10.74	2.32	7
	Control	12.06	2.78	9
	Total	11.48	2.60	16

Table 1: Descriptive Statistics for Total Bilirubin across Time and Condition

Discharge rate comparisons across treatment arms are presented in Fig 3. The results of the independent measures t-test to assess differences in discharge times across conditions showed equivalence ($p = .177$).

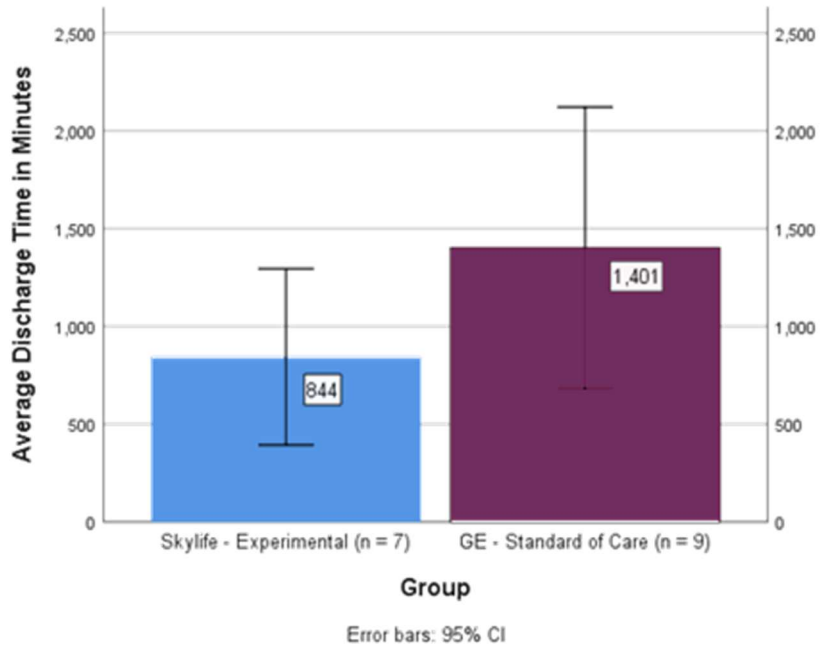

Fig 3. Discharge rates across phototherapy treatment types

With the current sample (n = 16), discharge times for the Skylife™ group (M = 844, SD = 487.17) were, on average, 557 minutes (9 hours, 17 minutes) faster than the GE BiliSoft control condition (M = 1401, SD = 937.13).

DISCUSSION

Phototherapy is a biomolecular process which involves photoisomerization of unconjugated bilirubin[5] found in extravascular skin tissue and capillary flow, and the rate of photoisomerization follows a strong dose-response relationship with the intensity of lights.[6,7] A potential reason for faster discharge times could be due to the ability of Skylife™ offering higher treatment dosage, also known as the spectral power that is the product of body surface area covered by the treatment lights and light intensity. Skylife™ has three treatment levels, and the delivered intensities are one of the highest amongst the currently FDA cleared devices. Its unique 3D treatment light profile, as shown in Fig 4, potentially accounts for the higher body surface area coverage.

Fig 4. Skylife™ 3D Treatment Light Profile

CONCLUSION

The preliminary results of the current investigation provide promising findings that support the use of Skylife™ as a viable, cost-effective phototherapy treatment. The Skylife™ device was found to be efficacious in reducing bilirubin levels for babies with similar rates of bilirubin reduction being observed in each treatment arm across the 24 hour treatment period. No adverse events or safety concerns were observed with the babies undergoing treatment with Skylife™. Observations also indicated that, so far, Skylife can discharge patients 9 hours 17 hours faster than the standard of care (40% quicker).

USER EXPERIENCE:

Designed as a bottom phototherapy device, Skylife™ has a significant advantage over the standard of care devices with its ability to fit inside most of the commonly used neonatal enclosures. Unlike standard of care devices, no additional room in a hospital is required during treatment. The lightweight and compact design of Skylife™ have made it easy to handle and maintain. Most importantly, the form factor of Skylife™ makes efficient use of storage space. Skylife™ also hosts a specially designed mattress pad for neonates that has been well received by the nurses who even expressed their interest for using the pad when the patient is not undergoing phototherapy.

The results should be interpreted with caution and generalizability of these findings is limited due to the small number of participants that were evaluated on study endpoints. Future directions include continuation of the current investigation to assess a larger sample of babies and comparisons across multiple sites and populations. However, the preliminary results show promise in this new and innovative phototherapy treatment approach.

REFERENCES

[1] Kaplan M, Muraca M, Hammerman C, et al. Imbalance between production and conjugation of bilirubin: a fundamental concept in the mechanism of neonatal jaundice. Pediatrics 2002;110(4):e47. (Accessed October 2, 2017, at http://www. pediatrics.org/cgi/content/full/110/4/e47.)

[2] Maisels MJ, Kring E. The contribution of hemolysis to early jaundice in normal newborns. Pediatrics 2006;118:276-9. AAP Subcommittee on Neonatal Hyperbilirubinemia. Neonatal jaundice and kernicterus. Pediatrics 2001;108:763-5.

[3] Newman TB, Escobar GJ, Gonzales VM, Armstrong MA, Gardner MN, Folck BF. The frequency of neonatal bilirubin testing and hyperbilirubinemia in a large health maintenance organization. Pediatrics 1999;104:1198-203. [Erratum, Pediatrics 2001;1(2):126.]

[4] Hansen TWR. Therapeutic approaches to neonatal jaundice: an international survey. Clin Pediatr (Phila) 1996;35:309-16.

[5] McDonagh AF, Lightner DA. “Like a shriveled blood orange” – bilirubin, jaundice, and phototherapy. Pediatrics 1985;75:443–55.

[6] Tan KL. The nature of the dose-response relationship of phototherapy for neonatal hyperbilirubinemia. J Pediatr 1977; 90: 448-52.

[7] Tan KL, Lim GC, Boey KW. Efficiency of ‘‘high-intensity’’ blue light and ‘‘standard’’ daylight phototherapy for non-hemolytic hyperbilirubinemia. Acta Paediatr 1992;81:870–4.

[8] Ferreira, Duarte, Abílio Oliveira, and Alberto Freitas. "Applying data mining techniques to improve diagnosis in neonatal jaundice." BMC medical informatics and decision making 12.1 (2012): 143.