Cylindrical intensive vs. double surface LED phototherapy for neonatal hyperbilirubinemia

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Abstract

Background
High bilirubin levels may lead to complications such as bilirubin encephalopathy or even death. Therefore, neonatal hyperbilirubinemia patients require appropriate treatment in the form of phototherapy or exchange transfusion. With the advancement of technology, various types of phototherapy, such as the cylindrical intensive phototherapy (bilisphere) and double LED, are now available.

Objective
To compare cylindrical intensive phototherapy to double surface LED phototherapy in neonatal hyperbilirubinemia.

Methods
This cohort study was conducted in neonates with hyperbilirubinemia at Syamsudin SH Hospital, Sukabumi, West Java, who were treated with either cylindrical intensive phototherapy or double surface LED phototherapy. The variables observed were subjects’ characteristics, bilirubin levels pre- and post-therapy, duration of phototherapy, length of stay, and total treatment cost. The data were analyzed using univariate and bivariate analyses.

Results
Of 47 neonates, the mean bilirubin levels were 19.36 mg/dL pre-therapy and 12.26 mg/dL post-therapy. Subjects’ overall mean duration of phototherapy was 24 hours, mean length of stay was 1 day, and mean cost of treatment was IDR 813,175. There was no significant difference in the bilirubin decrease between the cylindrical intensive phototherapy and double LED groups. However, there were significant differences between the cylindrical intensive phototherapy and double LED groups in duration of phototherapy (10.75 vs. 7.17 hours, respectively (P<0.000), mean length of stay (1 vs. 3.13 days, respectively (P<0.000), and total cost of treatment (IDR 598,918 vs. IDR 1,036,747, respectively P<0.000).

Conclusion
While the decrease in bilirubin is not significantly different in neonatal hyperbilirubinemia patients who undergo cylindrical intensive phototherapy compared to double LED therapy, cylindrical intensive phototherapy relates to significant shorter phototherapy duration, length of stay, and total treatment cost. Hence, cylindrical intensive phototherapy is considered to be more time-efficient and cost-efficient than double LED phototherapy.

Keywords: neonatal hyperbilirubinemia; cylindrical intensive phototherapy; double LED phototherapy

Neonatal hyperbilirubinemia is a condition of excessive bilirubin in the blood in neonates. Hyperbilirubinemia clinically appears in newborns if blood bilirubin levels reach 5-7 mg/dL. During the first week of birth, hyperbilirubinemia is present in 60% of full term infants and 80% of premature infants. In Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, reported prevalences of 58% of infants with bilirubin levels ≥5 mg/dL and 29.3% of infants with bilirubin levels ≥12 mg/dL, in 2003. Dr. Sardjito Hospital, Yogyakarta, reported that 85% of healthy infants had bilirubin levels ≥5 mg/dL, and 23.8% had bilirubin levels ≥13 mg/dL. In the uterus, fetal bilirubin is excreted from the blood, through a process carried out by the placenta. After birth, this function is taken over by the liver, which may take several weeks of adjustment. During this period, the liver works hard to remove bilirubin from the blood. However, some bilirubin remains and builds up inside the infant’s body. Because bilirubin is yellow, high bilirubin may turn the infant’s skin, sclera, and other body tissues yellow.

Elevated levels of bilirubin may cause a dangerous complication called kernicterus, also known as bilirubin encephalopathy.

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encephalopathy, in which brain damage occurs due to indirect bilirubin adhesion to the brain, specifically in the corpus striatum, thalamus, nucleus, hippocampus subthalamus, red nucleus, and nucleus at the base of the fourth ventricle. Clinically, kernicterus may cause unusual eye movements, lethargy, seizures, feeding disorders, muscle spasms, and increased muscle tone. If left untreated, it may cause high-frequency hearing loss, speech disorders, and mental retardation. This condition should be treated through phototherapy or exchange transfusion, though phototherapy is the method of choice because it is widely available and has fewer side effects than exchange transfusion.  

Phototherapy is a medical treatment that utilizes a light wavelength of 420-480 nm, which can reduce bilirubin levels in neonates through a process called photo-oxidation. The phototherapy unit used to treat infants with neonatal hyperbilirubinemia converts accumulated unconjugated bilirubin on the skin surface area. Bilirubin exposed to the appropriate light wavelength is converted into non-toxic, water-soluble isomers, making it easier for the liver to break them down and excrete them from the blood. Mean while, there were several consideration to decrease the bilirubin concentration in neonates by using the phototherapy treatment such as an adequate light's exposure to the skin surface area, spectrum of light used (wavelength 460 +10 nm), and irradiance. Current guidelines from the American Academy of Pediatrics (AAP) recommend a light intensity of no more than 30 μW/cm²/nm for phototherapy utilizing blue light, distance of at least 10 cm between the light source and body surface, as well as close monitoring of the infant's body's temperature. 

Phototherapy units utilize different light sources such as fluorescent lights, optical fiber, compact fluorescent lamps (CFL), and light-emitting diodes (LED). Several factors influence the phototherapy unit's efficacy, such as the released radiation energy, distance between the light source and the neonate, body surface area exposed to the light, and spectrum of light emitted. As technology advances, new types of phototherapy units have been developed, from single to double surface LED phototherapy. More recently, a new, 360 degree intensive unit capable of multidirectional (circular-shaped) intensive phototherapy, under brands such as Cradle 360 by Mediprema company and Bilisphere 360 by NOVOS medical system company. The Bilisphere manufacturer claims to be able to significantly reduce the duration of therapy compared to other phototherapy units like single or double LED. A study of 200 neonates with hyperbilirubinemia reported that cylindrical intensive phototherapy might reduce the need for exchange transfusion to only 16% compared to the control group (66%) (P<0.001), reduce the duration of phototherapy by 1.7 days compared to control group (4.1 days) P<0.001), and reduce bilirubin levels up to 5.7 mg/dL. Another study reported that in 157 neonates with hyperbilirubinemia using conventional phototherapy, total serum bilirubin significantly decreased (from 17.23 (SD 5.04) mg/dL to 10.18 (SD 2.02) mg/dL, with an average duration of treatment 4.48 (SD 4.47) days and rate of bilirubin decrease of 0.12 mg/dL per hour. They also showed that conventional phototherapy was less efficient compared to intensive phototherapy, with four times longer duration of therapy. Cylindrical intensive phototherapy is considered to be more cost-efficient, because the shorter duration of phototherapy shortens the hospital length of stay.

At Syamsudin SH District Hospital, Sukabumi, West Java, two types of phototherapy are available: cylindrical intensive 360 degrees phototherapy and double surface LED phototherapy. The LED phototherapy has been available since 2016, while cylindrical intensive phototherapy is relatively new, as it was first implemented in early 2020. Studies that compared the effectivity between these two phototherapy units have been limited, which we became aware of while seeking studies to decide whether to procure a new additional cylindrical intensive phototherapy 360 degrees for RSUD Syamsudin SH. Therefore, we aimed to compare the two units, with regards to mean decrease of bilirubin levels, mean duration of phototherapy, mean length of stay, and mean total cost of treatment in neonatal hyperbilirubinemia patients.

Methods

This was a cohort study with consecutive sampling technique (non-random sampling) which was conducted in 2020 at Syamsudin SH District Hospital, a B type general hospital in Sukabumi City, West Java. Subjects were neonates with hyperbilirubinemia who were
treated with either cylindrical intensive phototherapy or double LED phototherapy. Inclusion criteria were neonates ≥ 37 weeks gestation, birth weight ≥ 2,500 grams, and neonatal hyperbilirubinemia, which was defined as bilirubin levels >12 mg/dL in infants aged 2-13 days, and the absence of other conditions such as underlying disease (vomiting, lethargy, trouble breastfeeding, sudden weight loss, apnea, tachypnea, or unstable temperature), as well as direct bilirubin levels > 2 mg/dL. Exclusion criteria were incomplete medical record data, neonates with congenital abnormalities, and neonates who died or returned home independently during the study. Unpaired numerical sample size formula was used to determine the minimum required sample size for two groups, cylindrical intensive phototherapy vs. double LED phototherapy, resulting in 16 subjects per group, with a total minimum of 32 subjects.

Subjects’ secondary data were collected from medical archives and included age, gender, birth weight, bilirubin level at diagnosis, type of delivery, length of stay, cost of treatment, type and duration phototherapy duration, and the last was payment method. The payment method were classified into two groups cash and by using insurance. In Indonesia there were several Indonesian universal health coverages such as Jaminan Kesehatan Nasional Umum (JKN Umum) as a general national health insurance, Jaminan Kesehatan Penerima Bantuan Iuran (JKN PBI) as a non-contributory health insurance, Jaminan Kesehatan Daerah (Jamkesda) as a local health insurance, dan Jaminan Kesehatan Persalinan (Jamkersal) as a universal delivery care.

Subjects’ bilirubin levels were observed daily. The discharge criterion was bilirubin level reduction to ≤ 12 mg/dL. Neonates with normal final bilirubin levels were declared cured, and their total duration of phototherapy, total length of stay, and total cost of treatment during the phototherapy procedure were recorded. Intravenous blood bilirubin levels were assessed at the RSUD Syamsudin SH laboratory. The total duration of phototherapy was recorded until the bilirubin levels reached normal levels. The length of stay was determined from the time of admission until discharge. The total cost of treatment was the total amount of expenses charged by the hospital to the patient for the overall treatment received (administration, treatment, healthcare service, and laboratorium test). The SPSS 25 software was used to analyze the data. Data analysis comprised univariate and bivariate data analysis.

This study was approved by the Health Research Ethics Commission at RSUD Syamsudin SH, Sukabumi.

Results

Subjects’ characteristics are shown in Table 1, with proportions and mean/median, depending on the data type. The 47 subjects were mostly males (61.7%) and underwent vaginal delivery (70.2%). Almost half (48.9%) of them used Jaminan Kesehatan Nasional Umum (general national health insurance).

Subjects had median birth weight of 3,020 grams (SD 420) and mean age 6.36 days (SD 3.84). Mean initial bilirubin was 19.36 (SD 3.27) mg/dL and mean bilirubin after phototherapy was 12.26 (SD 10.43) mg/dL, which was a mean decrease of 8.93 (SD 3.46) mg/dL. In addition, subjects’ median duration of phototherapy was 24 hours (SD 33.7), median length of stay was 1 day (SD 1.12), and mean cost of treatment was IDR 813,175 (SD 307,743) (Table 1).

Table 2 shows the comparison of the cylindrical

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**Table 1. Subjects’ characteristics**

| Characteristics                        | (N=47) |
|----------------------------------------|--------|
| Gender, n (%)                          |        |
| Male                                   | 29 (61.7) |
| Female                                 | 18 (38.3) |
| Median birth weight (range), grams     | 3,020 (2,550-4,370) |
| Median age (range), days               | (3-20) |
| Mean initial bilirubin level (SD), mg/dL| 19.36 (3.27) |
| Median duration of phototherapy (range), hours | 24 (2-96) |
| Median length of stay (range), days    | 1 (1-4) |
| Mean cost of treatment (SD), IDR       | 813,175 (307,743) |
| Delivery type, n (%)                   |        |
| Vaginal                                | 33 (70.2) |
| Caesarian section                      | 14 (29.8) |
| Payment method, n (%)                  |        |
| Cash                                   | 7 (14.9) |
| JKN Umum                               | 23 (48.9) |
| JKN PBI                                | 13 (27.7) |
| Jamkesda/Jampersal                     | 4 (8.5) |
| Type of phototherapy, n (%)            |        |
| Cylindrical intensive phototherapy     | 24 (51.1) |
| Double LED                             | 23 (48.9) |
intensive phototherapy and double LED phototherapy groups. Mean birth weight was not significantly different between the two groups (P=0.873). However, mean age was significantly higher in the cylindrical intensive phototherapy group (higher by 2.75 days; (P=0.003). Nevertheless, the initial and the final bilirubin levels were not significantly different between the two groups.

Table 2 also shows a significantly shorter mean phototherapy duration in the cylindrical intensive phototherapy group than in the double LED group (10.75 vs. 75.17 hours; P<0.001). The mean length of stay was also significantly shorter in the cylindrical intensive phototherapy group than in the double LED group (1 vs. 3.13 days; P<0.001). Additionally, the mean cost of treatment using cylindrical intensive phototherapy (IDR 598,918) was significantly lower than that of double LED (IDR 1,036,747) (P<0.001). However, the decrease in bilirubin levels before and after phototherapy were not significantly different between groups (P=0.307). Thus, we conclude that while both cylindrical intensive phototherapy and double LED phototherapies were effective in decreasing bilirubin levels in our subjects, cylindrical intensive phototherapy was more efficient than double LED phototherapy with regards to time and cost.

Discussion

To our knowledge, there has been no study that directly compared intensive cylindrical intensive phototherapy with double surface LED phototherapy. In our study, subjects were predominantly male (61.7%), which was in line with a previous study (cylindrical intensive phototherapy vs. conventional phototherapy) that also predominantly male.10 A study reported that 95.5% of male patients responded to intensive phototherapy, while fewer female patients (84.8%) did so. However, kernicterus and death after exchange transfusions were more prevalent in male than in female patients. This observation could have been due to male infants’ significantly higher risk of developing neonatal icterus.13

The management of neonates with unconjugated hyperbilirubinemia is phototherapy with distance of 10-50 cm. Phototherapy is recommended if the total serum bilirubin level is > 12 mg/dL in neonates aged 25-48 hours after birth, and is mandatory if the total serum bilirubin level is 15 mg/dL.1,14 Thus, in this article, there are several aspects that are reviewed as effective parameters:

The first is related to evaluating the decrease in bilirubin levels that needs to be monitored regularly. When viewed descriptively, the difference in the decrease of bilirubin levels after taking measurements pre and post-phototherapy showed a higher decrease in bilirubin levels by using cylindrical intensive phototherapy [7.71 (SD 22) mg/dL], compared to double LED phototherapy [4.96 (SD 26.09) mg/dL]. In addition, the mean of initial bilirubin level before phototherapy was not much different even though the mean initial bilirubin level in the double LED group was higher than cylindrical intensive phototherapy. Unfortunately, statistically the mean difference between the two groups was not significant (P=0.307). A study at Prof. Dr. Margono Soekarjo Hospital, Purwokerto, Central Java, with conventional phototherapy, fluorescent lamps had an average decreased bilirubin level in neonates of 7.05 (SD 5.05) mg/dL.2 This result

| Table 2. Comparison of cylindrical intensive phototherapy and double LED phototherapy groups |
|-----------------------------------------------|---------------------------------|-----------------|-----------------|
| Variables                                | Cylindrical intensive phototherapy | Double LED | P value |
| Mean birth weight (SD), grams            | 3,071 (24.31)                  | 3,037 (23.670) | 0.873 |
| Mean age (SD), days                      | 7.71 (29.75)                   | 4.96 (18)      | 0.003 |
| Mean initial bilirubin (SD), mg/dL       | 18.52 (20.63)                  | 20.24 (27)     | 0.087 |
| Mean final bilirubin (SD), mg/dL         | 10.41 (22.48)                  | 10.46 (25.59)  | 0.437 |
| Mean duration of phototherapy (SD), hours| 10.75 (12.5)                   | 75.17 (36.00)  | 0.000 |
| Mean length of stay (SD), days           | 1.00 (12.5)                    | 3.13 (36.00)   | 0.000 |
| Mean cost of treatment (SD), IDR         | 598,918 (13.92)                | 1,036,747 (34.52) | 0.000 |
| Mean decrease in bilirubin level (SD), mg/dL | 7.71 (22.0)                  | 4.96 (26.09)   | 0.307 |
was not much different from the use of cylindrical intensive phototherapy. Another study at Cairo University Hospital, Kairo, Mesir, was conducted on subject with severe and extreme neonatal unconjugated hyperbilirubinemia who had a mean duration of cylindrical intensive phototherapy of 14 hours. Cairo study showed a decrease of mean total serum bilirubin from 26.8 (SD 6.2) mg/dL to 1.019 mg/dL/day. Based on the comparison of the studies above, it can be seen that the severity of hyperbilirubinemia, the initial condition of the neonate, and the phototherapy used have an impact on decreasing bilirubin levels.

The duration of phototherapy can also affect the decrease in bilirubin levels in neonates. In a study conducted at Prof. Dr. Margono Soekarjo Hospital, the average duration of irradiation was 60.27 (SD 30.74) hours, while the average irradiation time was lower in cylindrical intensive phototherapy, which was 10.75 (SD 12.5) hours, but irradiation on double LED had an average duration of irradiation of 75.17 (SD 36.00). The difference in irradiation duration in the two groups had a statistically significant mean difference. Based on the explanation of the clinical evidence journal from Jardine and Woodgate, the duration of phototherapy has a different time span according to the type of phototherapy used. However, the majority based on RCT studies, there are still many who do not know the appropriate duration of phototherapy, this is because the average quality of RCTs is low-quality evidence.

There is a difference in the duration of the intervention depending on the dose used. In general, the provision of phototherapy needs to pay attention to several things: (1) spectral qualities of the light source used (wavelength range and peak). The most effective light sources for degrading bilirubin emit light in a relatively narrow wavelength range (400 to 520 nanometers, or nm), with a peak of 460 10 nm; (2) Intensity of the light (irradiance). Intensive phototherapy requires a spectral irradiance of 30 W/cm²/nm, delivered over as much of the body surface as possible; (3) Distance between the light and the infant's skin, and (4) body surface area exposed by the irradiated field or "footprint".

The length of treatment also needs to be considered to determine the response to therapy for the neonate. In this study, patients with double LED treatment had a longer duration of stay in the hospital, namely 3.13 days ± 36 hours, while cylindrical intensive phototherapy had a shorter stay, which was only one day. The difference in length of stay between the two groups had a statistically significant mean difference, therefore if based on the average length of stay, the use of cylindrical intensive phototherapy was certainly more effective based on our findings. Other study that evaluate the effectiveness examination of phototherapy using a conventional phototherapy device (a fluorescent lamp) shown the average result was 4.48 (SD 4.47). Based on these findings, it shows that cylindrical intensive phototherapy has the potential to improve the condition of neonates with hyperbilirubinemia seen from a shorter length of hospital stay compared to other phototherapy, but the difference in length of stay has not been proven to be statistically significant, and still needs further research with similar population.

In this study, which evaluated the types of LED and cylindrical phototherapy, there was a significant mean difference between the duration of phototherapy, length of hospital stay and spending on treatment (P=0.000). Judging by the expenditure per treatment, double LED phototherapy has a higher expenditure of IDR 1,036,747 cylindrical intensive phototherapy which was only about half of double LED, which was IDR 598,918. The difference in mean cost of treatment was statistically significant (P=0.000). However, we cannot absolutely say that double LED phototherapy is more expensive than cylindrical intensive phototherapy. We need to look at the duration of the intervention given by each treatment, where the duration of the double LED intervention is longer than cylindrical intensive phototherapy. This condition can be a factor in the significant price difference between the two intervention groups. In some people the phototherapy intervention may be quite expensive in a few hours, but in Indonesia the majority have been covered by government insurance, where in this study the majority used JKN umum (48.9%), although some people still used their personal money (14.9%). Unfortunately, there is not much literature that discusses the cost-treatment of phototherapy, however several studies focus more on cost-effectiveness analysis of a system-based approach for managing neonatal jaundice and preventing kernicterus.

A limitation of our study waere not assessing several variables related to phototherapy, such as hourly bilirubin decrease (due to invasive blood sampling),
urine lumirubin levels, use of exchange transfusion, oxidative stress index, and side effects of phototherapy, we also could not evaluate the bilirubin level changes in certain hour. However, the strength of our study was the novelty of comparing bilisphere to double surface led phototherapy, as past studies made the comparison to conventional (single surface), led, or fluorescent phototherapy.

In conclusion, while the decrease in bilirubin was not significantly different in neonatal hyperbilirubinemia patients who underwent cylindrical intensive phototherapy compared to double LED therapy, cylindrical intensive phototherapy patients had significantly shorter phototherapy duration, length of stay, and total treatment cost. Hence, cylindrical intensive phototherapy is considered to be more time-efficient and cost-efficient than double LED phototherapy.

Conflict of Interest
None declared.

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