CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Phototherapy Devices for Neonatal Jaundice: Clinical-Effectiveness, Cost-Effectiveness, and Guidelines
SUMMARY OF ABSTRACTS

Phototherapy Devices for Neonatal Jaundice

Authors: Casey Gray, Lorna Adcock


Acknowledgments:

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Research Questions

1. What is the comparative clinical effectiveness of different phototherapy devices used to treat jaundice in newborns?
2. What is the comparative clinical effectiveness of phototherapy devices used with or without incubators to treat jaundice in newborns?
3. What is the clinical effectiveness of double phototherapy treatment for the treatment of newborn jaundice?
4. What is the comparative cost-effectiveness of different phototherapy devices used to treat jaundice in newborns?
5. What are the evidence-based guidelines regarding phototherapy devices with or without incubators for the treatment of newborn jaundice?

Key Findings

One systematic review, nine randomized controlled trials, seven non-randomized studies, and two evidence-based guidelines were identified regarding phototherapy used to treat jaundice in newborns.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases and a focused Internet search. No methodological filters were applied to limit retrieval by publication type. The search was limited to English language documents published between January 1, 2013 and April 24, 2018. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Newborns (birth – 2 months) with neonatal jaundice (hyperbilirubinemia)</th>
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</thead>
</table>
| Interventions | Q1.4-5: Phototherapy devices  
Q2: Phototherapy devices used in conjunction with an incubator  
Q3: Double phototherapy treatment |
| Comparators | Q1.4: Other phototherapy devices  
Q2: Phototherapy devices used without an incubator  
Q3: Single phototherapy treatment  
Q5: No comparator |
| Outcomes | Q1-3: Clinical effectiveness  
Q4: Cost-effectiveness outcomes  
Q5: Evidence-based guidelines |
| Study Designs | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines |
Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

One systematic review, nine randomized controlled trials, seven non-randomized studies, and two evidence-based guidelines were identified regarding phototherapy used to treat jaundice in newborns. No relevant health technology assessments or economic analyses were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One systematic review, nine randomized controlled trials, seven non-randomized studies, and two evidence-based guidelines were identified regarding phototherapy used to treat jaundice in newborns. No studies were identified regarding cost-effectiveness or use of incubators in conjunction with phototherapy. Detailed study characteristics are provided in Table 2.

One systematic review was identified regarding different wavelengths, intensities, total doses, and threshold for commencement of hospital phototherapy. Results were not reported in the study abstract.

Three randomized controlled trials examined double- versus single phototherapy. No differences in reduction of total bilirubin concentration during the first four or 10 hours of treatment were observed. However, after 12 and 24 hours greater reductions in bilirubin were recorded for double versus single phototherapy. In other research, infants treated with high intensity LED bed phototherapy experienced greater reductions in bilirubin and lower rates of hyperthermia, dehydration, and skin rash compared with triple phototherapy. There was no difference in rebound jaundice between groups.

Four randomized controlled trials examined blue (LED) phototherapy (Studies 3 and 4 likely reported on the same participant sample). Among the two studies that examined blue versus turquoise LED, serum concentrations of specific bilirubin isomers differed in blue versus turquoise LED after 24 hours in one study, whereas total serum bilirubin concentrations did not differ between groups over the same timeframe. In the third study, total serum concentrations of bilirubin did not differ between blue LED and a 7-bulb daylight device, however hypothermia was more frequent with blue LED. Finally, blue LED phototherapy was less effective than broad-spectrum light phototherapy, with longer duration of treatment and greater probability of remaining in phototherapy for infants treated with blue LED in the fourth study.

One randomized controlled study compared in-house LED phototherapy with conventional phototherapy, and showed a shorter duration of treatment, faster reduction in average serum bilirubin, and fewer cases of hypothermia in LED versus conventional phototherapy.
Five non-randomized studies examined LED (colour not specified) versus conventional phototherapy on various outcomes. Body temperature was elevated in infants exposed to LED phototherapy of higher irradiance, but not for LED with lower irradiance or for conventional phototherapy in one study. Two studies examined oxidative stress; total antioxidant capacity was higher and total oxidant stress and mean oxidative stress index were lower in LED versus conventional phototherapy in one study, while serum total antioxidant capacity decreased and total oxidant status and oxidative stress increased with both conventional and intensive LED phototherapy (differences between groups not reported). Authors of one study reported that LED-, enhanced LED-, and conventional phototherapy caused increases in the frequency of sister chromatid exchange (statistical differences between groups were not examined). There was no difference between LED and conventional phototherapy in the incidence and extent of skin eruptions.

Three non-randomized studies examined other phototherapy devices. Bilisphere 360 was associated with greater reductions in the duration of phototherapy and the need for exchange transfusion compared with conventional phototherapy. Fiberoptic phototherapy was not associated with total oxidative status, whereas there were increases with conventional phototherapy with blue fluorescent lamps and intensive LED phototherapy. Serum total antioxidant capacity and oxidative stress index changed in the same direction across all groups (statistical differences were not reported). Lastly, intensive compact fluorescent tube phototherapy did not differ from intensive LED phototherapy for rate of bilirubin reduction between groups. A slightly elevated mean body temperature was seen with compact fluorescent tube but not LED.

Two evidence-based guidelines were identified. The Canadian Pediatric Society recommends use of intensive phototherapy for “severe hyperbilirubinemia or those at greatly elevated risk of developing severe hyperbilirubinemia”, and consideration of conventional phototherapy for infants with a moderately elevated risk. The National Institute for Health and Care Excellence (NICE) recommends phototherapy, and provides guidance about when to consider intensified phototherapy to treat significant hyperbilirubinemia in infants. NICE advises use of incubators according to clinical need, and advises against white curtains routinely used with phototherapy.

Table 2: Summary of Included Studies Phototherapy Devices for Neonatal Jaundice

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Results</th>
<th>Authors’ Conclusions</th>
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</thead>
<tbody>
<tr>
<td><strong>Systematic Reviews and Meta-Analyses</strong></td>
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<tr>
<td>Woodgate, 2015¹</td>
<td>Hospital phototherapy</td>
<td>Different wavelengths, intensities, total doses, and threshold for commencement of hospital phototherapy</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td><strong>Randomized Controlled Trials</strong></td>
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<tr>
<td>Donneborg, 2018²</td>
<td>Double phototherapy N = 41</td>
<td>Single phototherapy N = 42</td>
<td>After 12 hours, percentage decreases of total serum bilirubin were greater for double</td>
<td>Even with intensive phototherapy increasing spectral power by increasing the irradiated</td>
</tr>
<tr>
<td>Author, year</td>
<td>Intervention</td>
<td>Comparison</td>
<td>Results</td>
<td>Authors’ Conclusions</td>
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<td>Ebbesen, 2016³ (Participants likely to be a subset of Ebbesen 2016⁴)</td>
<td>LED light centered at 497 nm (turquoise) N = 40</td>
<td>LED light centered at 459 nm (blue) N = 43</td>
<td>After 24 hours, percentage decreases of total serum bilirubin were greater for double vs. single phototherapy.</td>
<td>Body surface area, the efficacy of phototherapy is improved.²</td>
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<td>After 24 hours, serum concentration of total bilirubin isomers and Z,Z-bilirubin did not differ between groups.</td>
<td>Infants treated with phototherapy of equal irradiance with LED light centered at 497 nm (turquoise) vs. 459 nm (blue) had different distribution of serum bilirubin isomers</td>
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<td></td>
<td>Serum concentrations of Z,E-bilirubin and total bilirubin isomers formed during therapy were highest for infants receiving light centered at 459 nm (blue).</td>
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<tr>
<td></td>
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<td></td>
<td>Serum concentrations of E,Z-bilirubin formed during therapy was highest for infants receiving light centered at 497 nm (turquoise).</td>
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<td>No between groups difference for serum concentrations of E,Z-lumirubin.</td>
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<tr>
<td>Ebbesen, 2016⁴</td>
<td>LED light centered at 497 nm (turquoise) N = 46</td>
<td>LED light centered at 459 nm (blue) N = 45</td>
<td>After 24 hours there was no difference in total serum bilirubin concentrations between groups.</td>
<td>Reduction of total serum bilirubin did not differ between neonates treated with phototherapy with LED light centered at 497 nm (turquoise) vs. 459 nm (blue) of equal irradiance</td>
</tr>
<tr>
<td>Sherbiny, 2016⁵</td>
<td>High-intensity LED bed N = 100</td>
<td>Conventional intensive phototherapy with triple fluorescent tube units N = 100</td>
<td>Greater reduction in bilirubin for high-intensity LED bed vs. conventional phototherapy.</td>
<td>High-intensity LED bed phototherapy is safe for treatment of severe neonatal hyperbilirubinemia</td>
</tr>
<tr>
<td>Author, year</td>
<td>Intervention</td>
<td>Comparison</td>
<td>Results</td>
<td>Authors’ Conclusions</td>
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<tr>
<td>Brandao, 2015</td>
<td>17-bulb blue LED N = 74</td>
<td>7-bulb daylight device N = 76</td>
<td>After 24 hours there was no difference in reduction of total serum bilirubin concentrations between groups. Hypothermia was more frequent in 17-bulb blue LED than with 7-bulb daylight device.</td>
<td>Blue was as effective as daylight phototherapy. There is a greater need for rigorous control of room temperature with blue light phototherapy.</td>
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<tr>
<td>Mreihil, 2015</td>
<td>Intervention 1: Double fluorescent light phototherapy; N = NR</td>
<td>Single fluorescent light phototherapy N = NR</td>
<td>Reductions in total bilirubin concentrations did not differ between groups during the first 4 hours of intensive phototherapy. Total N = 42</td>
<td>Formation of bilirubin photoisomers is rapid, and occurs early during intensive phototherapy for neonatal jaundice. The rate and level of photoisomerization was not influenced by irradiance and light source.</td>
</tr>
<tr>
<td>Pratesi, 2015</td>
<td>Broad-spectrum light phototherapy N = 20</td>
<td>Blue LED phototherapy N = 20</td>
<td>Shorter duration of treatment, and higher probability of remaining in phototherapy for broad-spectrum light phototherapy vs. blue LED phototherapy</td>
<td>Broad-spectrum light phototherapy is more effective than blue LED phototherapy for the treatment of hyperbilirubinemia. Our data suggest that these results are not due to the different irradiance of the two phototherapy systems, but probably depend on their different peak light emissions.</td>
</tr>
<tr>
<td>Abd Hamid, 2013</td>
<td>Single phototherapy with reflecting curtains N = 80 (2 were excluded post-hoc)</td>
<td>Double phototherapy N = 80 (2 were excluded post-hoc)</td>
<td>The mean decrease of total serum bilirubin did not differ between groups after 4 hours or after 10 hours. Total dose of phototherapy did not differ between groups. No significant adverse events were noted</td>
<td>Single phototherapy with reflecting curtain is as effective as double phototherapy for the treatment of neonatal hyperbilirubinemia.</td>
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<tr>
<td>Author, year</td>
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<tr>
<td>Ek-isariyaphom, 2013&lt;sup&gt;10&lt;/sup&gt;</td>
<td>In-house LED phototherapy N = 25</td>
<td>Conventional phototherapy N = 25</td>
<td>Shorter duration of treatment with LED vs. conventional phototherapy</td>
<td>In-house LED phototherapy equipment is more effective than conventional phototherapy in the reduction of serum bilirubin level and occurrence of hyperthermia during treatment is less.&lt;sup&gt;10&lt;/sup&gt;</td>
</tr>
<tr>
<td>Allam, 2017&lt;sup&gt;11&lt;/sup&gt;</td>
<td>LED phototherapy N = 41</td>
<td>Conventional phototherapy N = 41</td>
<td>Total antioxidant capacity was higher, total oxidant stress was lower, and mean oxidative stress index was lower in LED vs conventional phototherapy</td>
<td>LED and conventional phototherapy both increased oxidative stress index. Oxidative stress was higher with conventional phototherapy</td>
</tr>
<tr>
<td>Kanmaz, 2017&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Enhanced LED phototherapy N = 25</td>
<td>Comparison 1: LED phototherapy N = 25</td>
<td>Increase in sister chromatid exchange frequency after phototherapy was observed in all three intervention groups</td>
<td>Phototherapy causes an increase in the frequency of sister chromatid exchange regardless of the irradiance. Phototherapy could have some genotoxic adverse effects on chromosomes; however, further investigations are warranted to enlighten as to whether these effects are permanent or clinically important.&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>Aydemir, 2014&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Group 1: LED phototherapy of 26-60 μW/cm(2)/nm irradiance N = 30</td>
<td>Conventional phototherapy with fluorescent lamps (10-15 μW/cm(2)/nm irradiance) N = 30</td>
<td>Group 1: Increased body temperature ≥ 38 °C in 1/30 infants Group 2: 30/30 reached body temperature ≥ 37.5°C and 77% reached ≥ 38°C</td>
<td>LED phototherapy of ≥ 60 μW/cm(2)/nm intensity increases body temperature in newborns with hyperbilirubinemia.</td>
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<td></td>
<td>Group 2: LED phototherapy of 60-120 μW/cm(2)/nm</td>
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<tr>
<td>Author, year</td>
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<td>Comparison</td>
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<tr>
<td>Edris, 2014&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Bilisphere 360 N = 183</td>
<td>Conventional phototherapy N = 177</td>
<td>Reduced need for exchange transfusion and shorter duration of phototherapy with Bilisphere 360 vs. conventional phototherapy</td>
<td>Bilisphere 360 is effective in reducing needs for exchange transfusion and duration of phototherapy.</td>
</tr>
<tr>
<td>Kale, 2013&lt;sup&gt;15&lt;/sup&gt;</td>
<td>fiberoptic phototherapy N = NR</td>
<td>Conventional phototherapy with blue fluorescent lamps N = NR Intensive LED phototherapy N = NR</td>
<td>Serum total antioxidant capacity decreased in all infants Total oxidant status increased with conventional phototherapy and intensive LED phototherapy, whereas there was no change for fiberoptic phototherapy. Oxidative stress index increased in all infants</td>
<td>As indicated by increased OSI, oxidant/antioxidant balance is disturbed in favor of oxidants after blue fluorescent light, LED and fiberoptic phototherapy. &lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Surmeli-Onay, 2013&lt;sup&gt;16&lt;/sup&gt;</td>
<td>LED phototherapy N = 33</td>
<td>Conventional phototherapy N = 25</td>
<td>Similar percentages of skin eruptions were reported between groups.</td>
<td>For preterm infants undergoing conventional vs. LED phototherapy, there was no difference between groups in the incidence and extent of skin eruptions.</td>
</tr>
<tr>
<td>Takci, 2013&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Intensive compact fluorescent tube N = 20</td>
<td>Intensive LED phototherapy N = 23</td>
<td>Rate of bilirubin reduction did not differ between the LED and compact fluorescent tube phototherapy Mean body temperature was slightly elevated in compact fluorescent tube and not LED.</td>
<td>Intensive phototherapy with compact fluorescent tube or LED were equally effective and can provide rapid decrease in bilirubin levels in the first few hours.</td>
</tr>
</tbody>
</table>

LED = light-emitting diode; NR = not reported
References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses
   PubMed: PM25998618

Randomized Controlled Trials
   PubMed: PM29095431

   PubMed: PM27331354

   PubMed: PM26484622

   PubMed: PM25844870

   PubMed: PM25234100

   PubMed: PM25794186

   PubMed: PM25545446

9. Abd Hamid UJ, MI MI, Ibrahim NR, Abd Majid N, Ramli N, Van Rostenbergh H. Randomised controlled trial of single phototherapy with reflecting curtains versus
PubMed: PM23573836

PubMed: PM24511717

Non-Randomized Studies

PubMed: PM28891476

PubMed: PM29483799

PubMed: PM24037476

PubMed: PM24605703

PubMed: PM24090867

PubMed: PM24016282

PubMed: PM23692829
Economic Evaluations
No literature identified.

Guidelines and Recommendations

Appendix — Further Information

Previous CADTH Reports


Additional References


Guidelines – Uncertain Methodology

