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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	3
BACKGROUND	4
OBJECTIVES	4
METHODS	4
Figure 1.	6
Figure 2.	7
RESULTS	7
Figure 3.	9
Figure 4.	10
DISCUSSION	11
AUTHORS' CONCLUSIONS	12
ACKNOWLEDGEMENTS	12
REFERENCES	13
CHARACTERISTICS OF STUDIES	14
DATA AND ANALYSES	19
Analysis 1.1. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 1 Duration of phototherapy.	20
Analysis 1.2. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 2 Rate of decline of serum total bilirubin.	21
Analysis 1.3. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 3 Treatment failure (need of additional phototherapy or exchange transfusion).	21
Analysis 1.4. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 4 Hypothermia.	21
Analysis 1.5. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 5 Hyperthermia.	22
Analysis 1.6. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 6 Skin rash.	22
Analysis 2.1. Comparison 2 Phototherapy with LED versus halogen light source, Outcome 1 Duration of phototherapy.	23
Analysis 2.2. Comparison 2 Phototherapy with LED versus halogen light source, Outcome 2 Rate of decline of serum total bilirubin.	23
Analysis 3.1. Comparison 3 Phototherapy with LED versus compact fluorescent light source, Outcome 1 Duration of phototherapy.	23
Analysis 3.2. Comparison 3 Phototherapy with LED versus compact fluorescent light source, Outcome 2 Rate of decline of serum total bilirubin.	24
Analysis 4.1. Comparison 4 Phototherapy with LED versus non-LED light source and irradiance matched, Outcome 1 Duration of phototherapy.	24
Analysis 4.2. Comparison 4 Phototherapy with LED versus non-LED light source and irradiance matched, Outcome 2 Rate of decline of serum total bilirubin.	25
Analysis 5.1. Comparison 5 Phototherapy with LED versus non-LED light source and distance matched, Outcome 1 Duration of phototherapy.	25
Analysis 5.2. Comparison 5 Phototherapy with LED versus non-LED light source and distance matched, Outcome 2 Rate of decline of serum total bilirubin.	26
Analysis 6.1. Comparison 6 Phototherapy with LED versus non-LED light source in term neonates, Outcome 1 Duration of phototherapy.	26
Analysis 6.2. Comparison 6 Phototherapy with LED versus non-LED light source in term neonates, Outcome 2 Rate of decline of serum bilirubin.	26
Analysis 7.1. Comparison 7 Phototherapy with LED versus non-LED light source in preterm neonates, Outcome 1 Duration of phototherapy.	27
Analysis 7.2. Comparison 7 Phototherapy with LED versus non-LED light source in preterm neonates, Outcome 2 Rate of decline of serum bilirubin.	27
CONTRIBUTIONS OF AUTHORS	28
DECLARATIONS OF INTEREST	28
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	28
INDEX TERMS	28

[Intervention Review]

Light-emitting diode phototherapy for unconjugated hyperbilirubinaemia in neonates

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ABSTRACT

Background

Phototherapy is the mainstay of treatment of neonatal hyperbilirubinaemia. The commonly used light sources for providing phototherapy are special blue fluorescent tubes, compact fluorescent tubes and halogen spotlights. However, light emitting diodes (LEDs) as light sources with high luminous intensity, narrow wavelength band and higher delivered irradiance could make phototherapy more efficacious than the conventional phototherapy units.

Objectives

To evaluate the effect of LED phototherapy as compared to conventional phototherapy in decreasing serum total bilirubin levels and duration of treatment in neonates with unconjugated hyperbilirubinaemia.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library* 2010, Issue 1), MEDLINE (1966 to April 30, 2010) and EMBASE (1988 to July 8, 2009). Handsearches of the proceedings of annual meetings of The European Society for Paediatric Research and The Society for Pediatric Research were conducted through 2010.

Selection criteria

Randomised or quasi-randomised controlled trials were eligible for inclusion if they enrolled neonates (term and preterm) with unconjugated hyperbilirubinaemia and compared LED phototherapy with other light sources (fluorescent tubes, compact fluorescent tubes, halogen spotlight; method of administration: conventional or fibreoptic).

Data collection and analysis

We used the standard methods of The Cochrane Collaboration and its Neonatal Review Group for data collection and analysis.

Main results

Six randomised controlled trials met the inclusion criteria for this review. Four studies compared LED and halogen light sources. Two studies compared LED and compact fluorescent light sources. The duration of phototherapy (six studies, 630 neonates) was comparable in LED and non-LED phototherapy groups (mean difference (hours) -0.43, 95% CI -1.91 to 1.05). The rate of decline of serum total bilirubin (STB) (four studies, 511 neonates) was also similar in the two groups (mean difference (mg/dL/hour) 0.01, 95% CI -0.02 to 0.04). Treatment failure, defined as the need of additional phototherapy or exchange blood transfusion (1 study, 272 neonates), was comparable (RR 1.83,

95% CI 0.47 to 7.17). Side effects of phototherapy such as hypothermia (RR 6.41, 95% CI 0.33 to 122.97), hyperthermia (RR 0.61, 95% CI 0.18 to 2.11) and skin rash (RR 1.83, 95% CI 0.17 to 19.96) were rare and occurred with similar frequency in the two groups.

Authors' conclusions

LED light source phototherapy is efficacious in bringing down levels of serum total bilirubin at rates that are similar to phototherapy with conventional (compact fluorescent lamp (CFL) or halogen) light sources. Further studies are warranted for evaluating efficacy of LED phototherapy in neonates with haemolytic jaundice or in the presence of severe hyperbilirubinaemia (STB $\geq$ 20 mg/dL).

PLAIN LANGUAGE SUMMARY

Comparison of a light-emitting diode with conventional light sources for providing phototherapy to jaundiced newborn infants

Jaundice, or yellowish discolouration of the skin, can occur due to increased amounts of bilirubin pigment in the blood. It is a commonly observed, usually harmless condition in newborn infants during the first week after birth. However, in some babies the amount of bilirubin pigment can increase to dangerous levels and require treatment. Treatment of jaundice in newborn infants is done by placing them under phototherapy, a process of exposing their skin to light of a specific wavelength band. Fluorescent tubes or halogen lamps have been used as light sources for phototherapy for many years. A light-emitting diode (LED) is a newer type of light source which is power efficient, has a longer life and is portable with low heat production. In this systematic review, the efficacy of LED phototherapy was compared with conventional (non-LED) phototherapy. LED phototherapy was observed to be efficacious in bringing down the levels of serum total bilirubin, at rates similar to phototherapy with conventional light sources.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Phototherapy with LED versus non-LED light source for unconjugated hyperbilirubinaemia in neonates

Phototherapy with LED versus non-LED light source for unconjugated hyperbilirubinaemia in neonates

Patient or population: neonates with unconjugated hyperbilirubinaemia

Settings:

Intervention: Phototherapy with LED versus non-LED light source

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Phototherapy with LED versus non-LED light source				
Duration of phototherapy hours		The mean duration of phototherapy in the intervention group was 0.43 hours lower (1.91 hours lower to 1.05 hours higher)	Mean Difference (IV, Fixed, 95% CI [Hours]): -0.43 [-1.91 to 1.05]	630 (6 studies)	⊕⊕⊕⊕ high	
Rate of decline of serum total bilirubin mg/dL/hour		The mean Rate of decline of serum total bilirubin in the intervention group was 0.01 mg/dL/hour higher (0.02 mg/dL/hour lower to 0.04 mg/dL/hour higher)	Mean Difference (IV, Fixed, 95% CI [mg/dL/hour]): 0.01 [-0.02 to 0.04]	511 (4 studies)	⊕⊕⊕⊕ high	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

BACKGROUND

Description of the condition

Neonatal jaundice occurs in 25% to 50% of term newborns, and in a larger proportion of preterm newborns, in the first two weeks of life (Maisels 2005). It is a benign transient physiological event in the majority of newborns but can cause irreversible brain damage and kernicterus in some infants if the serum bilirubin levels are very high. Various mechanisms involved in producing this 'physiological' increase in serum total bilirubin include increased production of bilirubin due to lysis of red blood cells, decreased ability of liver cells to clear bilirubin and increased enterohepatic circulation. Any condition that further increases bilirubin production or alters the transport or metabolism of bilirubin increases the severity of the physiological jaundice. Unconjugated hyperbilirubinaemia in which the direct-reacting bilirubin level is less than 15% of serum total bilirubin is the most common form of jaundice seen in newborn infants. Common risk factors for pathological unconjugated hyperbilirubinaemia include blood group incompatibility, glucose-6-phosphate dehydrogenase enzyme deficiency, prematurity, instrumental delivery and non-optimal breastfeeding. A direct relationship between severe unconjugated hyperbilirubinaemia and neurological damage has been demonstrated (Ip 2004). Interventions such as exchange blood transfusion and phototherapy aim at reducing the serum bilirubin levels in order to prevent bilirubin brain toxicity.

Description of the intervention

Phototherapy is the most frequently used treatment when serum bilirubin levels exceed physiological limits. In normal circumstances, the liver conjugates the bilirubin so that it can be excreted in bile. In the neonate with hyperbilirubinaemia, this conjugating function of the liver is immature. Phototherapy converts bilirubin into water soluble photo-products that can bypass the hepatic conjugating system and be excreted without further metabolism (Ennever 1990). The efficacy of phototherapy is dependent upon wavelength, irradiance, exposed body surface area, distance of the phototherapy, and duration of exposure (American Academy of Pediatrics (2004)). Intensive phototherapy is provided by use of high levels of irradiance in the 430 to 490 nm band (usually 30 $\mu\text{W}/\text{cm}^2$ per nm or higher) delivered to as much of the infant's body surface area as possible.

The commonly used light sources for providing phototherapy are special blue fluorescent tubes, compact fluorescent tubes and halogen spotlights. However, the efficacy and ability of these light sources to provide intensive phototherapy may be limited because of the inability to keep them close to the infant. Fiberoptic blankets attached to a light source can eliminate the heat transmission but are not as effective as conventional units due to exposure of a limited surface area (Mills 2001). These light sources also share the disadvantage of emitting unstable, broad wavelength light output and thereby cause adverse effects like glare, giddiness and headache to healthcare personnel (Tan 1989). In recent years, a new type of light source, light-emitting diodes (LEDs), has been incorporated into phototherapy units. LEDs are power efficient, portable devices with low heat production so that they can be placed very close to the skin of the infants without any apparent untoward effects. They are also durable light sources with an average life span of 20,000 hours (Seidman 2003). Blue LEDs have a narrow spectral band of high intensity monochromatic light that overlaps the absorption spec-

trum of bilirubin (Fasol 1997; Vreman 1998). These unique characteristics of LEDs make them an attractive light source for an optimal phototherapy unit.

How the intervention might work

High luminous intensity, narrow wavelength band and higher delivered irradiance of LED phototherapy can make LED more efficacious than currently available conventional or fiberoptic phototherapy units resulting in more rapid decline in serum bilirubin, shorter duration of phototherapy and lesser number of exchange transfusions. LED phototherapy may also be more cost-effective because of the longer life span of the light source and lower energy consumption.

Why it is important to do this review

Many phototherapy devices incorporating LEDs have come into the market in recent years. LEDs as a light source have many purported advantages. However, there are few published reports comparing the benefits and risks of LED phototherapy with the conventional devices. The aim of this review is to systematically assess and compile the available evidence from randomised and quasi-randomised trials comparing LED phototherapy with conventional phototherapy devices.

OBJECTIVES

To evaluate the effect of LED phototherapy as compared to conventional phototherapy (with fluorescent lamps, compact fluorescent lamps (CFL) or halogen spotlights) in decreasing serum total bilirubin level and duration of treatment in neonates with unconjugated hyperbilirubinaemia during the first 28 days of life. The secondary objectives of the review include evaluation of the efficacy of LED phototherapy in haemolytic versus non-haemolytic jaundice and in term versus preterm neonates.

Predefined outcomes were compared separately for the following subgroups:

- term versus preterm neonates;
- haemolytic versus non-haemolytic jaundice;
- types of non-LED units.

A subgroup analysis was also done for studies using two different approaches, keeping the phototherapy to baby distance similar (which may provide different irradiance) or keeping the irradiance similar between the two groups (by altering the distance).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised or quasi-randomised controlled trials were eligible for inclusion in this review. Trials reported in abstract form were also eligible for inclusion.

Types of participants

Neonates (term and preterm) with unconjugated hyperbilirubinaemia (irrespective of etiology and defined as hyperbilirubinaemia with direct-reacting component less than 2 mg/dL or less than 15% of serum total bilirubin). Hyperbilirubinaemia was de-

defined as any serum bilirubin level needing treatment with phototherapy during the first 28 days of life.

Types of interventions

Comparison of LED phototherapy with other light sources (fluorescent tubes, compact fluorescent tubes, halogen spotlight; method of administration: conventional or fibreoptic).

Types of outcome measures

Primary outcomes

- Duration of phototherapy (hours)
- Rate of fall of serum total bilirubin (mg/dL per hour)

Secondary outcomes

- Need for blood exchange transfusion or additional phototherapy (proportion)
- Duration of hospital stay (days)
- Side effects like hypothermia (body temperature < 36.5 °C), hyperthermia (body temperature > 37.5 °C), skin rash (assigned by investigators to be due to phototherapy), burns (assigned by investigators to be due to phototherapy), diarrhoea (defined as per individual study) and dehydration (cumulative weight loss > 10% in term and > 15% in preterm neonates)
- Nursing staff comfort or satisfaction (measured on Likert type scales), parental comfort or satisfaction (measured on Likert type scales)

Search methods for identification of studies

We used the standard search strategy of the Cochrane Neonatal Review Group, as outlined in *The Cochrane Library*.

Electronic searches

- Cochrane Central Register of Controlled Trials (CENTRAL), *The Cochrane Library* 2010, Issue 1), MEDLINE (1966 to April 30, 2010) and EMBASE (1988 to July 8, 2009) using the Cochrane highly sensitive search strategy for identifying randomised trials: sensitivity- and precision-maximizing version (2008 revision); with the limits: Human, age < 1 month combined with jaundice, neonatal, phototherapy, light-emitting diode, LED as text words using Boolean operators AND and OR (e.g. #1: Cochrane Highly Sensitive Search Strategy for identifying randomised trials with Limits: Human, age < 1 month; #2: #1 AND phototherapy; #3: #1 AND light-emitting diode; #4: #2 OR #3). The clinical trial registers ClinicalTrials.gov (search date: April 30, 2009) and Current Controlled Trials (search date: April 30, 2009) were also searched.

Searching other resources

- Reference lists from the above, and from review articles
- Personal communication with primary authors from the above to retrieve unpublished data related to published articles
- Proceedings of annual meetings of The European Society for Paediatric Research and The Society for Pediatric Research: handsearches of abstracts (up to and including 2010)

Data collection and analysis

We used the standard methods of The Cochrane Collaboration and its Neonatal Review Group ([Cochrane Neonatal Group 2011](#)).

Selection of studies

All three review authors independently identified the studies to be included.

Data extraction and management

Two review authors (PK and DC) independently extracted data using a pretested data extraction form. We resolved differences after discussion among all the three review authors.

Assessment of risk of bias in included studies

All three review authors independently assessed the quality of studies using the following criteria: blinding of randomisation, blinding of intervention, completeness of follow-up and blinding of outcome measurement. We resolved differences after discussion among all the three review authors. Blinding of randomisation was evaluated by assessing the methods of sequence generation and allocation concealment. Blinding of intervention was evaluated by assessing the attempts made to blind the clinical care team regarding type of phototherapy in use. Completeness of follow-up was evaluated by assessing whether information regarding the primary and secondary outcomes was available for all the neonates enrolled in an individual study. Blinding of outcome measurement was evaluated by assessing the attempts made to blind the health-care workers and laboratory personnel measuring serum bilirubin.

Measures of treatment effect

For categorical data the relative risk (RR), risk difference (RD) and number needed to treat (NNT) with 95% confidence intervals (CI) were calculated. Continuous data were analysed using weighted mean difference (WMD).

Unit of analysis issues

We compared LED with any non-LED device in an overall analysis and we also separately compared LED with each specific non-LED device.

Dealing with missing data

We contacted the original investigators for any missing data and requested this data, if feasible.

Assessment of heterogeneity

We estimated the degree of statistical heterogeneity using the I^2 statistic.

Assessment of reporting biases

We used funnel plots to investigate publication bias ([Figure 1](#); [Figure 2](#)).

Figure 1. Funnel plot of comparison: 1 Phototherapy with LED versus non-LED light source, outcome: 1.1 Duration of phototherapy.

Figure 2. Funnel plot of comparison: 1 Phototherapy with LED versus non-LED light source, outcome: 1.2 Rate of decline of serum total bilirubin.

Data synthesis

Results were pooled using a fixed-effect model.

Subgroup analysis and investigation of heterogeneity

Predefined outcomes were compared separately for the following subgroups:

- term versus preterm neonates;
- haemolytic versus non-haemolytic jaundice;
- types of non-LED units.

A subgroup analysis was also done for studies using two different approaches, keeping the phototherapy to baby distance similar (which may provide different irradiance) or keeping the irradiance similar between the two groups (by altering the distance).

Sensitivity analysis

We planned to perform a sensitivity analysis by the methodological quality of trials. However, the quality of trials as assessed by the assessment scheme recommended by the Cochrane Neonatal Review Group was comparable for all the included studies. Therefore, no sensitivity analysis was performed.

RESULTS

Description of studies

Results of the search

A total of 1215 records were retrieved from the literature. There were nine studies reporting efficacy of LED phototherapy. Of them, six randomised controlled trials (Seidman 2000; Seidman 2003; Maisels 2007; Martins 2007; Bertini 2008; Kumar 2010) met the inclusion criteria for this review. Four studies compared LED and halogen light sources (Seidman 2000; Seidman 2003; Martins 2007; Bertini 2008). Two studies compared LED and compact fluorescent light sources (Maisels 2007; Kumar 2010). Two studies by Seidman et al enrolled only term neonates (Seidman 2000; Seidman 2003). Studies by Bertini et al (Bertini 2008) and Martins et al (Martins 2007) enrolled only preterm neonates. Studies by Maisels et al (Maisels 2007) and Kumar et al (Kumar 2010) enrolled neonates born at 35 or more weeks of gestation. The study by Kumar et al (Kumar 2010) was conducted at multiple centres, while the other five were single centre studies. Four studies took measures to keep the irradiance similar in the study groups (Seidman 2000; Seidman 2003; Maisels 2007; Martins 2007) while two studies kept the distance between the light source and the infant similar (Bertini 2008; Kumar 2010). Duration of phototherapy was reported in all six studies. The rate of decline of serum total bilirubin was reported by four studies (Seidman 2000; Seidman 2003; Maisels 2007; Kumar 2010).

One study reported failure of phototherapy (Kumar 2010). LED phototherapy was used in a multi-centre randomised controlled trial comparing aggressive versus conservative phototherapy for extremely low birthweight neonates (Morris 2008). However, information about efficacy of LED phototherapy in this trial has not yet been published (see Characteristics of studies awaiting classification).

Included studies

The randomised controlled trial by Bertini et al (Bertini 2008) enrolled 31 preterm neonates admitted to the neonatal intensive care unit. Neonates were enrolled if born at less than 34 weeks of gestational age, not requiring respiratory support and clinically stable. Neonates with malformations, perinatal asphyxia, respiratory distress, patent ductus arteriosus, intracranial haemorrhage, hypo- or hypertension, infection, anaemia (venous haemoglobin (Hb) < 10 g/dL), polycythaemia (venous Hb > 22 g/dL), or neonates receiving cardiovascular drugs (that is, dopamine, dobutamine) were excluded. The experimental group received phototherapy with a commercial LED device with special blue light emitting diodes. The control group received phototherapy with a device incorporating a metal vapour discharge blue lamp with two filters. Main outcomes reported were trans-epidermal water loss and change in cerebral haemodynamics. Duration of phototherapy was also reported. In both study groups the distance between the infants and the light sources was kept similar at 30 cm.

The study by Kumar et al (Kumar 2010) was a multi-centre randomised controlled trial conducted at four centres in India; 272 newborn infants born at 35 or more completed weeks of gestation with hyperbilirubinaemia needing phototherapy within the first seven days of life were enrolled. Infants with perinatal asphyxia (Apgar score < 4 at one minute or < 7 at five minutes), onset of jaundice within 24 hours of age, evidence of haemolysis (positive direct Coombs test), rhesus haemolytic disease, culture-positive or clinical sepsis, need for exchange transfusion at the time of enrolment, and major congenital malformations were excluded. The experimental group received phototherapy with a prototype device having multiple LED bulbs arranged in an area of about 20 × 15 cm. The control group received phototherapy with a commercial device having six special blue compact fluorescent tubes. Outcomes reported were duration of phototherapy, failure of phototherapy (serum total bilirubin rising or reaching more than 20 mg/dL during phototherapy, which required either use of double surface phototherapy or exchange transfusion), rate of decrease in serum total bilirubin and incidence of hypothermia. A distance of 25 to 30 cm was maintained between the baby and the bulb or lamp surface for both type of units.

Maisels et al (Maisels 2007) reported a randomised controlled trial in well, newborn infants born at 35 or more completed weeks of gestation and needing phototherapy. Among 66 infants enrolled, 30 received phototherapy during birth hospitalisation and 36 during readmission. For infants receiving phototherapy during birth hospitalisation, the LED group received phototherapy using a prototype device. The control group received phototherapy using eight two foot long special blue fluorescent tubes. In both groups a fiberoptic blanket was kept underneath the infant. For infants receiving phototherapy during readmission, the LED group received phototherapy using a commercially available device. The control group received phototherapy using two phototherapy units above the infant with each unit containing four special blue fluorescent tubes. In both groups additional phototherapy was provided from

underneath the infant using four special blue fluorescent tubes. The primary outcome reported was rate of decline of serum total bilirubin. The distance between the lights and the infants was adjusted to provide an irradiance of approximately 40 µW/cm²/nm.

Martins et al (Martins 2007) reported a randomised controlled trial in 88 preterm neonates weighing more than 1000 gm and admitted to the neonatal intensive care unit. Neonates with a direct bilirubin greater than 2 mg/dL, haemolytic jaundice (positive Coombs test), ecchymosis, malformations or congenital infection were excluded. The experimental group received blue LED phototherapy from a system positioned 30 cm from the patient and illuminating an elliptical area of 38 cm x 27 cm diameter. The control group was given treatment with a halogen phototherapy system equipped with a single quartz-halogen lamp with a dichroic reflector, positioned 50 cm from the patient and illuminating a circle of 18 cm diameter. To match the surface area exposed in the two groups, two halogen light phototherapy systems were used for each patient in the control group. Main outcomes reported were rate of decrease of serum total bilirubin concentration in the first 24 hours of treatment and duration of treatment (hours).

In two separate publications, Seidman et al (Seidman 2000; Seidman 2003) reported randomised controlled trials in 69 and 114 healthy, term neonates with hyperbilirubinaemia. The experimental group received LED phototherapy with a prototype device consisting of six focused arrays, each with 100 3 mm blue LEDs. The control group received phototherapy with three halogen-quartz bulbs. The main outcomes reported were rate of decrease in serum total bilirubin and duration of phototherapy. The LED phototherapy device was placed at a distance that provided a light intensity within the measured limits of the conventional phototherapy device.

Excluded studies

Three studies (Vreman 1998; Chang 2005; Karadag 2009) were excluded from this review. Chang et al (Chang 2005) compared the efficacy of a prototype blue gallium nitride LED phototherapy unit with a commercially used halogen quartz phototherapy device by measuring both in vitro and in vivo (in Gunn rats) bilirubin photodegradation. Karadag et al (Karadag 2009) compared chromosomal effects caused by conventional phototherapy and intensive (LED) phototherapy in jaundiced newborns. This was an observational study which also reported the rate of decline of serum total bilirubin. Vreman et al (Vreman 1998) compared the efficacy of a prototype LED device with that of conventional phototherapy devices by measuring the in vitro photo-degradation of bilirubin in human serum albumin.

Risk of bias in included studies

Allocation

Due to an inadequate description of the method used for random number generation in the studies by Bertini et al and Martins et al, the potential for selection bias in these two studies is unclear (Figure 3; Figure 4). The random sequence generation method was described in the other four studies (Seidman 2000; Seidman 2003; Maisels 2007; Kumar 2010) and the risk of potential bias was low. The allocation concealment method was not reported in the studies by Seidman et al (Seidman 2000; Seidman 2003) and Martins et al (Martins 2007). The other three studies reported using a sealed envelope technique and the risk of potential bias was low.

Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bertini 2008	?	+	-	+	+	+
Kumar 2010	+	+	-	+	+	+
Maisels 2007	+	+	-	+	+	?
Martins 2007	?	?	-	+	+	+
Seidman 2000	+	?	-	+	+	+
Seidman 2003	+	?	-	+	+	+

Figure 4. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

Blinding

Due to the nature of the intervention, clinicians making decisions for starting and stopping phototherapy were unblinded to the type of phototherapy (Figure 3; Figure 4). Predefined serum total bilirubin cut-off values based on various clinical practice guidelines were used to start and stop phototherapy in all but one trial (Maisels 2007), and the risk of potential bias was low. Serum total bilirubin was measured in a laboratory or at the bedside and blinding of personnel measuring the bilirubin was not reported by any of the included studies.

Incomplete outcome data

All included studies reported complete outcome data.

Selective reporting

All included studies were assessed to be free of selective reporting.

Other potential sources of bias

In the study by Kumar et al (Kumar 2010) the prototype LED phototherapy units were made available free of cost by the manufacturer. The study by Maisels et al (Maisels 2007) was supported by grant from a manufacturer of phototherapy devices. In both of these studies the role of the manufacturers in the study conduct or analysis was not reported. However, as per additional information provided by the authors of one study (Kumar 2010) the "manufacturer had no role in planning, designing, conduct, analysis or publication of the study and apart from the phototherapy units, no other funds were received". The funnel plots in Figure 1 and Figure 2 indicate no major publication bias. The study by Martins et al (Martins 2007) showed a significantly greater reduction in the duration of phototherapy than the pooled estimate (Figure 1), probably because of using a different LED source that is indium gallium nitrate as compared to the other studies and enrolling only preterm infants.

Effects of interventions

See: [Summary of findings for the main comparison Phototherapy with LED versus non-LED light source for unconjugated hyperbilirubinaemia in neonates](#)

Comparison 1: phototherapy with LED versus non-LED light source

Duration of phototherapy (Outcome 1.1)

The duration of phototherapy was reported in all six included studies (630 neonates) (Seidman 2000; Seidman 2003; Maisels 2007; Martins 2007; Bertini 2008; Kumar 2010). A significant decrease in duration of phototherapy in the LED group was reported in only one study (Martins 2007). This may be because of use of a specific type of LED phototherapy, with a different physical and chemical composition (indium gallium nitrate). According to the authors adding indium to the semiconductor element confers greater power to LEDs than using gallium nitrate alone. The pooled estimate showed a comparable duration in the LED and non-LED phototherapy groups (mean difference (MD) (IV, fixed-effect) -0.43 hours, 95% CI -1.91 to 1.05). However, statistical heterogeneity was noted to be high ($I^2 = 78\%$). The significant reduction in duration of phototherapy observed by Martin et al could have contributed to the high statistical heterogeneity in the meta-analysis.

Rate of fall of serum bilirubin (Outcome 1.2)

Rate of decline of serum total bilirubin was reported in four studies (511 neonates) (Seidman 2000; Seidman 2003; Maisels 2007; Kumar 2010) and the pooled estimate showed a comparable decline (MD (IV, fixed effect) 0.01 mg/dL/hour, 95% CI -0.02 to 0.04).

Treatment failure (need for exchange blood transfusion or additional phototherapy) (Outcome 1.3)

Treatment failure, defined as need for additional phototherapy or exchange transfusion, was reported in two studies (360 neonates) (Martins 2007; Kumar 2010). Although the effect estimate was com-

parable (RR (M-H, fixed-effect) 1.83, 95% CI 0.47 to 7.17), neonates meeting the criteria of treatment failure belonged to one study only (Kumar 2010), were small in number, and there were more in the LED group (6/142 versus 3/130).

Side effects (Outcomes 1.4 to 1.6)

Side effects of phototherapy like hypothermia (RR (M-H, fixed-effect) 6.41, 95% CI 0.33 to 122.97), hyperthermia (RR (M-H, fixed-effect) 0.61, 95% CI 0.18 to 2.11) and skin rash (RR (M-H, fixed-effect) 1.83, 95% CI 0.17 to 19.96) were rare in the two groups. Although the estimates for the side effects are not statistically significant, the very wide confidence intervals may be due to a paucity of evidence and there could be large undetected differences between LED and non-LED phototherapy. These estimates are from two studies (360 neonates) (Martins 2007; Kumar 2010) of which one (Martins 2007) reported a complete absence of temperature instability and skin rash in both the study groups.

Nursing staff and parents comfort or satisfaction

Numerical estimates of nursing staff and parents comfort or satisfaction were not reported by any study. One study (Seidman 2003) reported that nurses taking care of babies under phototherapy did not complain of nausea or dizziness. However, both nurses and parents noted that the use of blue-green lights gave a more disturbing hue to the newborn's skin than blue lights or halogen lamps.

Comparison 2: phototherapy with LED versus halogen light source

Four studies (Seidman 2000; Seidman 2003; Martins 2007; Bertini 2008) compared LED phototherapy with a halogen light source. The mean duration of phototherapy was significantly shorter with LED phototherapy versus a halogen light source (MD (IV, fixed-effect) -5.00 hours 95% CI -9.03 to -0.98) with the presence of significant statistical heterogeneity ($I^2 = 79\%$) (Outcome 2.1). However, the rate of decline of serum total bilirubin was similar with the two devices (MD (IV, fixed-effect) 0.02 mg/dL/hour, 95% CI -0.03 to 0.07) (Outcome 2.2).

Comparison 3: phototherapy with LED versus compact fluorescent light source

Two studies (Maisels 2007; Kumar 2010) compared LED phototherapy with a compact fluorescent lamp (CFL) light source. LED and CFL light sources were comparable in pooled estimates of duration of phototherapy (MD (IV, fixed-effect) 0.29 hours, 95% CI -1.31 to 1.88; $I^2 = 71\%$) (Outcome 3.1) as well as the rate of decline of serum total bilirubin (MD (IV, fixed-effect) 0.01 mg/dL/hour, 95% CI -0.03 to 0.04) (Outcome 3.2).

Comparison 4: phototherapy with LED versus non-LED light source and irradiance matched

In another predefined subgroup analysis of four studies (Seidman 2000; Seidman 2003; Maisels 2007; Martins 2007) in which irradiance was matched in LED and non-LED phototherapy groups, pooled estimates for duration of phototherapy (MD (IV, fixed-effect) 0.43 hours 95% CI -1.28 to 2.14) (Outcome 4.1) and rate of decline of serum total bilirubin were similar (MD (IV, fixed-effect) 0.03 mg/dL/hour, 95% CI -0.02 to 0.07) (Outcome 4.2).

Comparison 5: phototherapy with LED versus non-LED light source and distance matched

Duration of phototherapy was significantly shorter (MD (IV, fixed-effect) -2.99 hours 95% CI -5.95 to -0.03) (Outcome 5.1) (Figure 13) with LED phototherapy for two studies (Bertini 2008; Kumar 2010) in which the distance between baby and light source was kept similar in the two experimental groups, though the rate of decline of serum total bilirubin was similar (MD (IV, fixed-effect) 0.00 mg/dL/hour, 95% CI -0.03 to 0.03) (Outcome 5.2).

Comparisons 6 and 7: phototherapy with LED versus non-LED light source in term and preterm neonates

Two studies enrolled only term neonates (Seidman 2000; Seidman 2003) and two only preterm neonates (Martins 2007; Bertini 2008). Separate data (unpublished) for term and preterm neonates were made available from another study (Kumar 2010) which enrolled term and late-preterm neonates. On subgroup analysis including term neonates alone, pooled estimates of duration of phototherapy (MD (IV, fixed-effect) -1.72 hours, 95% CI -4.89 to 1.44) and rate of decline of serum bilirubin (MD (IV, fixed-effect) 0.01 mg/dL/hour, 95% CI -0.02 to 0.04) were similar in the two groups (Outcome 6.1). In preterm neonates, the duration of phototherapy was significantly shorter in the LED phototherapy group (MD (IV, fixed-effect) -7.22 hours, 95% CI -11.69 to -2.76). However, the rate of decline of serum bilirubin was similar (MD 0.01 mg/dL/hour, 95% CI -0.05 to 0.07).

Comparison 8: phototherapy with LED versus non-LED light source in different underlying causes of jaundice

No data were available for subgroup analysis based on underlying cause of jaundice.

DISCUSSION

Summary of main results

Six randomised controlled trials were included in this systematic review comparing the efficacy of LED and non-LED light sources for providing phototherapy to neonates with hyperbilirubinaemia. Phototherapy based on LED and non-LED light sources had similar clinical efficacy as measured by duration of phototherapy, rate of decline of serum total bilirubin and rate of treatment failure. Side effects of phototherapy were rare and similar among the two types of light sources.

Overall completeness and applicability of evidence

The efficacy of phototherapy depends on characteristics of the light source such as emission peak wavelength, emission range and irradiance, apart from various clinical factors like presence of haemolysis and adequacy of enteral feeding. There is no 'standard' recommended method of administering phototherapy and a variety of strategies have been followed by different researchers. Among studies included in this review, four (Seidman 2000; Seidman 2003; Martins 2007; Bertini 2008) compared LED phototherapy with a halogen light source and two (Maisels 2007; Kumar 2010) compared LED phototherapy with a compact fluorescent light source. In four studies (Seidman 2000; Seidman 2003; Maisels 2007; Martins 2007) the investigators made efforts to match irradiance between the LED and non-LED phototherapy groups and in two studies (Bertini 2008; Kumar 2010) the distance between baby and light source was kept similar in the two experimental groups. On predefined subgroup analysis, duration of phototherapy was shorter with LED

phototherapy when the comparison was restricted to halogen light source phototherapy or to studies in which the distance between baby and light source was kept similar in the two experimental groups. One study (Martins 2007) used LED phototherapy with a different physical and chemical composition (indium gallium nitrate). This was the only study which reported a significant reduction in duration of phototherapy and was the probable cause of significant heterogeneity noted in the meta-analysis.

The endogenous rate of production of bilirubin and severity of hyperbilirubinaemia may influence the efficacy of phototherapy. Neonates with haemolytic jaundice were included in three studies (Seidman 2000; Seidman 2003; Maisels 2007). However, the proportion of neonates with haemolytic jaundice was either very small (two out of 66 in Maisels 2007) or not mentioned in the study reports (Seidman 2003; Seidman 2000). In addition, probably due to close follow-up during the hospital stay and after discharge from hospital, the mean peak serum bilirubin levels in all studies were below 15 to 17 mg/dL. Therefore, further studies are warranted for evaluating the efficacy of LED phototherapy in neonates with haemolytic jaundice or in the presence of severe hyperbilirubinaemia (STB $\geq$ 20 mg/dL).

The main advantages of a LED light source include low energy consumption and the ability to emit high intensity light of narrow wavelength spectrum with the production of minimal heat. LEDs have been reported to have a life span nearly 20 times longer than other light sources and may be more cost-effective in the long run. However, none of studies have actually investigated the cost-effectiveness of LED phototherapy. Due to minimal heat production, theoretically LED light sources can be placed very close to the neonate without any untoward effect. This approach has the potential to further increase the efficacy of phototherapy by increasing spectral power. Further studies are needed to investigate the efficacy of LED phototherapy kept very close to the skin of the infant, for example embedded in clothing or a blanket.

The side effects like hypothermia and hyperthermia were rare and comparable in the two groups. This may partly be because the enrolled neonates were treated in temperature controlled environments (Martins 2007; Kumar 2010) with regular monitoring of body temperature. Since LEDs do not produce much heat, hypothermia may be a problem when used in small and sick babies, and in environments without temperature control. In such situations, closer monitoring and an external heat source may be required.

Quality of the evidence

All six studies included in this systematic review used a randomisation process for treatment group allocation. However, only four studies adequately described the process of allocation sequence generation. Three studies reported measures to ensure concealment of allocation sequence. None of the studies reported blinding of research personnel measuring the outcome (clinician decid-

ing to start or stop phototherapy or laboratory personnel measuring serum bilirubin). However, predefined thresholds were used to start and stop phototherapy in all the studies. Overall, studies included in the review are of moderate to good quality.

One difficulty in comparing different phototherapy devices is lack of a composite measure of efficacy. Clinical efficacy of phototherapy is determined by patient characteristics (severity of hyperbilirubinaemia, body surface area, skin perfusion, skin thickness and presence of haemolysis) and phototherapy characteristics (emission peak wavelength, spectral emission range, irradiance and age of light source, body surface area covered) (Vreman 2008). Measurement and comparison of phototherapy characteristics like irradiance and coverage of body surface area across different devices is not standardized or possible with a unique measuring device. This could have led to clinical 'intervention' heterogeneity while pooling data from different studies.

Potential biases in the review process

The review authors are also authors of one of the study included in this review.

Agreements and disagreements with other studies or reviews

To our knowledge there is no other published review comparing the efficacy of LED and non-LED light sources for phototherapy.

AUTHORS' CONCLUSIONS

Implications for practice

LED light source phototherapy is efficacious in bringing down levels of serum total bilirubin at rates similar to phototherapy with conventional (CFL or halogen) light sources. Although side effects are reported to be as uncommon as with other type of light sources, the limited amount of data warrants careful monitoring of babies.

Implications for research

Further studies are warranted for evaluating the efficacy of LED phototherapy in neonates with haemolytic jaundice or in the presence of severe hyperbilirubinaemia (STB $\geq$ 20 mg/dL). Studies are also needed to investigate the efficacy of LED phototherapy kept very close to the skin of the infant for example embedded in clothing or a blanket.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Bertini 2008

Methods	Randomised controlled trial.
Participants	31 preterm neonates admitted in neonatal intensive care unit enrolled if born at less than 34 weeks of gestational age, did not require respiratory support, and were clinically stable. Neonates with malformations, perinatal asphyxia, respiratory distress, patent ductus arteriosus, intracranial haemorrhage, hypo- or hypertension, infection, anaemia (venous Hb<10 g/dL), polycythaemia (venous Hb>22 g/dL), or neonates receiving cardiovascular drugs (i.e., dopamine, dobutamine) excluded.
Interventions	Experimental group (n=17) received phototherapy with a commercial LED device with special blue light emitting diodes. Control group (n=14) received phototherapy with a device incorporating a metal vapour discharge blue lamp with two filters. Phototherapy was started when serum total bilirubin was more than 171.0 µmol/L [>10 mg/dL]) and discontinued when serum total bilirubin declined below 145 µmol/L (<8.5 mg/dL).
Outcomes	Main outcomes were trans-epidermal water loss and change in cerebral haemodynamics. Also reported duration of phototherapy.
Notes	In both study groups distance between the infants and the light sources kept similar at 30 cm.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	".....selected to enter either of the two groups randomly"
Allocation concealment (selection bias)	Low risk	Using sealed envelopes technique.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding of intervention or ascertainment of outcome has not been mentioned and are unlikely due to nature of the intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Relevant clinical outcomes for all enrolled neonates have been reported.
Selective reporting (reporting bias)	Low risk	Study protocol not available in public domain. However, authors have reported the clinically relevant outcomes. Risk of bias due to selective reporting is unlikely.
Other bias	Low risk	Risk of bias due to other reasons is unlikely.

Kumar 2010

Methods	Multi-centre randomised controlled trial.
Participants	272 newborn infants born at 35 or more completed weeks of gestation with hyperbilirubinaemia needing phototherapy within first 7 days of life. Infants with perinatal asphyxia (Apgar score <4 at 1 minute or <7 at 5 minute), onset of jaundice within 24 h of age, evidence of haemolysis (positive direct Coombs

Kumar 2010 (Continued)

test), rhesus haemolytic disease, culture-positive or clinical sepsis, need for exchange transfusion at the time of enrolment, and major congenital malformations excluded.

Interventions	Experimental group (n=142) received phototherapy with a prototype device having multiple LED bulbs arranged in an area of about 20×15 cm. Control group (n=130) received phototherapy with a commercial device having 6 special blue compact fluorescent tubes. Distance kept similar in the two groups. Phototherapy was started on the basis of the age of the baby in hours and serum total bilirubin (STB) levels, as per American Academy of Pediatrics guidelines. Phototherapy was stopped when two consecutive STB levels, measured 6 hours apart were less than 15 mg/dL.
Outcomes	Duration of phototherapy, failure of phototherapy (serum total bilirubin rising or becoming more than 20 mg/dL during phototherapy, which required either use of double surface phototherapy or exchange transfusion), rate of decrease in serum total bilirubin over total duration of phototherapy and incidence of hypothermia.
Notes	Distance of 25-30 cm was maintained between the baby and the bulb/lamp surface for both type of units.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A web-based random number generator was used for block randomisation stratified for each centre.
Allocation concealment (selection bias)	Low risk	Using sealed envelopes technique.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding of intervention or ascertainment of outcome has not been mentioned and are unlikely due to nature of the intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Relevant clinical outcomes for all enrolled neonates have been reported.
Selective reporting (reporting bias)	Low risk	Study protocol is available from Clinical Trial Registry of India (clinical trial registration number: CTRI/2008/091/000072). All relevant clinical outcomes have been reported.
Other bias	Low risk	"The prototype LED phototherapy units at all sites were provided by Srichakra Scientifics, Hyderabad, India free of cost." Unpublished information: Srichakra Scientifics, Hyderabad, India were not involved in planning, conducting, analysis or decision to publish the study.

Maisels 2007

Methods	Randomised controlled trial.
Participants	Newborn infants born at 35 or more completed weeks of gestation were eligible for enrolment if decision to start phototherapy was made by attending paediatrician. Among 66 infants enrolled, 30 received phototherapy during birth hospitalisation and 36 during readmission.
Interventions	For infants receiving phototherapy during birth hospitalisation: LED group (n=14) received phototherapy using a prototype device. Control group (n=16) received phototherapy using eight 2-feet long special blue fluorescent tubes. In both groups a fiberoptic blanket was kept underneath the infant.

Light-emitting diode phototherapy for unconjugated hyperbilirubinaemia in neonates (Review)

Maisels 2007 (Continued)

For infants receiving phototherapy during readmission: LED group (n=19) received phototherapy using a commercially available device. Control group (n=17) received phototherapy using two phototherapy units above the infant with each unit containing four special blue fluorescent tubes. In both groups additional phototherapy provided from underneath the infant using four fluorescent special blue tubes. Decision to start phototherapy was made by the attending paediatrician.

Outcomes	Primary outcome: rate of decline of serum total bilirubin over total duration of phototherapy.
Notes	The distance between the lights and the infants was adjusted to provide an irradiance of approximately 40 $\mu\text{W}/\text{cm}^2/\text{nm}$.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated set of random numbers.
Allocation concealment (selection bias)	Low risk	Sealed enveloped used.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding of intervention or ascertainment of outcome has not been mentioned and are unlikely due to nature of the intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Relevant clinical outcomes for all enrolled neonates have been reported.
Selective reporting (reporting bias)	Low risk	Study protocol not available in public domain. However, authors have reported the clinically relevant outcomes. Risk of bias due to selective reporting is unlikely.
Other bias	Unclear risk	Supported by a grant from Natus Medical Inc.

Martins 2007

Methods	Randomised controlled trial.
Participants	88 preterm neonates weighing more than 1000 gm admitted to neonatal intensive care unit. Neonates with direct bilirubin greater than 2 mg%, haemolytic jaundice (positive Coombs test), ecchymosis, malformations or congenital infection were excluded.
Interventions	Experimental group (n=44) given treatment with blue LED phototherapy system positioned 30 cm from the patient and illuminating an elliptical area of 38 cm x 27 cm diameter. Control group (n=44) given treatment with a halogen phototherapy system equipped with a single quartz-halogen lamp with a dichroic reflector, positioned 50 cm from the patient and illuminating a circle of 18 cm diameter. To match surface area exposed in two groups, two halogen light phototherapy systems used for each patient in control group. Criteria to start phototherapy were based on serum bilirubin concentration for different birth weight ranges published in literature (Bhutani 2004). Phototherapy was stopped when serum bilirubin values reached 30% below the initial values.
Outcomes	Rate of decrease of serum total bilirubin (TB) concentration in the first 24 hours of treatment and duration of treatment (hours).

Light-emitting diode phototherapy for unconjugated hyperbilirubinaemia in neonates (Review)

Martins 2007 (Continued)

Notes Two halogen phototherapy systems used for each patient in the control group so that surface area exposed to phototherapy is similar in control and experimental group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"performed stratified randomisation in blocks of 4" method of sequence generation not mentioned.
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding of intervention or ascertainment of outcome has not been mentioned and are unlikely due to nature of the intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Relevant clinical outcomes for all enrolled neonates have been reported
Selective reporting (reporting bias)	Low risk	Study protocol not available in public domain. However, authors have reported the clinically relevant outcomes. Risk of bias due to selective reporting is unlikely.
Other bias	Low risk	Risk of bias due to other reasons is unlikely.

Seidman 2000

Methods	Randomised controlled trial.
Participants	69 healthy term neonates with hyperbilirubinaemia.
Interventions	Experimental group (n=34) received LED phototherapy with a prototype device consisting of 6 focused arrays, each with 100 3-mm blue LEDs. Control group (n=35) received phototherapy with three halogen-quartz bulbs. Distance adjusted to provide similar irradiance. Phototherapy was started and stopped based on American Academy of Pediatrics practice parameters.
Outcomes	Rate of decrease in serum total bilirubin over total duration of phototherapy, duration of phototherapy.
Notes	LED phototherapy device placed at a distance that provided light intensity within the measured limits of conventional phototherapy device.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random table.
Allocation concealment (selection bias)	Unclear risk	Not described.

Seidman 2000 (Continued)

Blinding (performance bias and detection bias) All outcomes	High risk	Blinding of intervention or ascertainment of outcome has not been mentioned and are unlikely due to nature of the intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Relevant clinical outcomes for all enrolled neonates have been reported.
Selective reporting (reporting bias)	Low risk	Study protocol not available in public domain. However, authors have reported the clinically relevant outcomes. Risk of bias due to selective reporting is unlikely.
Other bias	Low risk	Risk of bias due to other reasons is unlikely.

Seidman 2003

Methods	Randomised controlled trial.
Participants	114 health term neonates with hyperbilirubinaemia.
Interventions	Experimental group (n=47) received LED phototherapy and was further randomised to either blue or blue-green LED phototherapy. Control group (n=57) received phototherapy with three halogen-quartz bulbs. Phototherapy was started and stopped based on American Academy of Pediatrics practice parameters.
Outcomes	Rate of decrease in serum total bilirubin over total duration of phototherapy, duration of phototherapy.
Notes	LED phototherapy device placed at a distance that provided light intensity within the measured limits of conventional phototherapy device.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random table.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding of intervention or ascertainment of outcome has not been mentioned and are unlikely due to nature of the intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Relevant clinical outcomes for all enrolled neonates have been reported.
Selective reporting (reporting bias)	Low risk	Study protocol not available in public domain. However, authors have reported the clinically relevant outcomes. Risk of bias due to selective reporting is unlikely.
Other bias	Low risk	Risk of bias due to other reasons is unlikely.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Chang 2005	Compared efficacy of prototype blue gallium nitride LED phototherapy unit with commercially used halogen quartz phototherapy device by measuring both in vitro and in vivo (in Gunn rats) bilirubin photodegradation.
Karadag 2009	An observational study which compared chromosomal effects caused by conventional phototherapy and intensive (LED) phototherapy in jaundiced newborns. Study also reported rate of decline of serum total bilirubin.
Vreman 1998	Compared efficacy of a prototype LED device with that of conventional phototherapy devices by measuring the in vitro photodegradation of BR in human serum albumin.

Characteristics of studies awaiting assessment *[ordered by study ID]*

[Morris 2008](#)

Methods	Multi-centre randomised controlled trial
Participants	1974 infants with extremely low birth weight (501-1000 g) at 12 to 36 hours of age
Interventions	Subjects were randomised to aggressive or conservative phototherapy groups. Aggressive-phototherapy was initiated at enrolment or whenever bilirubin level was more than 5-7 mg/dL). Conservative phototherapy was initiated, continued, or restarted whenever the bilirubin level was more than 8-10 mg/dL.
Outcomes	Primary outcome was death or neurodevelopmental impairment at 18 to 22 months of corrected age
Notes	Data from subgroup of neonates who received LED phototherapy is not yet published

DATA AND ANALYSES

Comparison 1. Phototherapy with LED versus non-LED light source

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Duration of phototherapy	6	630	Mean Difference (IV, Fixed, 95% CI)	-0.43 [-1.91, 1.05]
1.1 LED versus halogen light source	4	292	Mean Difference (IV, Fixed, 95% CI)	-5.00 [-9.03, -0.98]
1.2 LED versus compact fluorescent light source	2	338	Mean Difference (IV, Fixed, 95% CI)	0.29 [-1.31, 1.88]
2 Rate of decline of serum total bilirubin	4	511	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.02, 0.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 LED versus halogen light source	2	173	Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.03, 0.07]
2.2 LED versus compact fluorescent light source	2	338	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.03, 0.04]
3 Treatment failure (need of additional phototherapy or exchange transfusion)	2	360	Risk Ratio (M-H, Fixed, 95% CI)	1.83 [0.47, 7.17]
4 Hypothermia	2	360	Risk Ratio (M-H, Fixed, 95% CI)	6.41 [0.33, 122.97]
5 Hyperthermia	2	360	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.18, 2.11]
6 Skin rash	2	360	Risk Ratio (M-H, Fixed, 95% CI)	1.83 [0.17, 19.96]

Analysis 1.1. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 1 Duration of phototherapy.

Analysis 1.2. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 2 Rate of decline of serum total bilirubin.

Analysis 1.3. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 3 Treatment failure (need of additional phototherapy or exchange transfusion).

Analysis 1.4. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 4 Hypothermia.

Analysis 1.5. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 5 Hyperthermia.

Analysis 1.6. Comparison 1 Phototherapy with LED versus non-LED light source, Outcome 6 Skin rash.

Comparison 2. Phototherapy with LED versus halogen light source

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Duration of phototherapy	4	292	Mean Difference (IV, Fixed, 95% CI)	-5.00 [-9.03, -0.98]
2 Rate of decline of serum total bilirubin	2	173	Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.03, 0.07]

Analysis 2.1. Comparison 2 Phototherapy with LED versus halogen light source, Outcome 1 Duration of phototherapy.

Analysis 2.2. Comparison 2 Phototherapy with LED versus halogen light source, Outcome 2 Rate of decline of serum total bilirubin.

Comparison 3. Phototherapy with LED versus compact fluorescent light source

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Duration of phototherapy	2	338	Mean Difference (IV, Fixed, 95% CI)	0.29 [-1.31, 1.88]
2 Rate of decline of serum total bilirubin	2	338	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.03, 0.04]

Analysis 3.1. Comparison 3 Phototherapy with LED versus compact fluorescent light source, Outcome 1 Duration of phototherapy.

Analysis 3.2. Comparison 3 Phototherapy with LED versus compact fluorescent light source, Outcome 2 Rate of decline of serum total bilirubin.

Comparison 4. Phototherapy with LED versus non-LED light source and irradiance matched

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Duration of phototherapy	4	327	Mean Difference (IV, Fixed, 95% CI)	0.43 [-1.28, 2.14]
2 Rate of decline of serum total bilirubin	3	239	Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.02, 0.07]

Analysis 4.1. Comparison 4 Phototherapy with LED versus non-LED light source and irradiance matched, Outcome 1 Duration of phototherapy.

Analysis 4.2. Comparison 4 Phototherapy with LED versus non-LED light source and irradiance matched, Outcome 2 Rate of decline of serum total bilirubin.

Comparison 5. Phototherapy with LED versus non-LED light source and distance matched

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Duration of phototherapy	2	303	Mean Difference (IV, Fixed, 95% CI)	-2.99 [-5.95, -0.03]
2 Rate of decline of serum total bilirubin	1	272	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.03, 0.03]

Analysis 5.1. Comparison 5 Phototherapy with LED versus non-LED light source and distance matched, Outcome 1 Duration of phototherapy.

Analysis 5.2. Comparison 5 Phototherapy with LED versus non-LED light source and distance matched, Outcome 2 Rate of decline of serum total bilirubin.

Comparison 6. Phototherapy with LED versus non-LED light source in term neonates

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Duration of phototherapy	3	382	Mean Difference (IV, Fixed, 95% CI)	-1.72 [-4.89, 1.44]
2 Rate of decline of serum bilirubin	3	382	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.02, 0.04]

Analysis 6.1. Comparison 6 Phototherapy with LED versus non-LED light source in term neonates, Outcome 1 Duration of phototherapy.

Analysis 6.2. Comparison 6 Phototherapy with LED versus non-LED light source in term neonates, Outcome 2 Rate of decline of serum bilirubin.

Comparison 7. Phototherapy with LED versus non-LED light source in preterm neonates

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Duration of phototherapy	3	182	Mean Difference (IV, Fixed, 95% CI)	-7.22 [-11.69, -2.76]
2 Rate of decline of serum bilirubin	1	61	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.05, 0.07]

Analysis 7.1. Comparison 7 Phototherapy with LED versus non-LED light source in preterm neonates, Outcome 1 Duration of phototherapy.

Analysis 7.2. Comparison 7 Phototherapy with LED versus non-LED light source in preterm neonates, Outcome 2 Rate of decline of serum bilirubin.

CONTRIBUTIONS OF AUTHORS

PK and DC searched the literature with the help of the Cochrane Neonatal Review Group search coordinator. PK and DC independently extracted data. All three authors independently assessed included studies for risk of bias. Data analysis was conducted by DC with inputs from PK and AD.

DECLARATIONS OF INTEREST

All the authors declare that they have no conflict of interest.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None

INDEX TERMS

Medical Subject Headings (MeSH)

Hyperbilirubinemia, Neonatal [*therapy]; Jaundice, Neonatal [therapy]; Phototherapy [adverse effects] [instrumentation] [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans; Infant, Newborn