EFFECT OF URSODEOXYCHOLIC ACID ON INDIRECT HYPERBILIRUBINEMIA IN NEONATES TREATED WITH PHOTOTHERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Neonatal hyperbilirubinemia occurs in 60-70% of term, and in 80% of preterm infants. Approximately 0.14% lead to neuronal dysfunction and death. Usual management involving phototherapy and other treatment modalities is expensive with undesirable side-effects. Studies have emerged that ursodeoxycholic acid (UDCA) has benefit of reducing indirect hyperbilirubinemia in the neonatal period with fewer and tolerable complications.

Objective: To determine the benefit of UDCA to neonates with indirect hyperbilirubinemia treated with phototherapy in terms of bilirubin levels and duration of phototherapy.

Design: Meta-analysis

Participants: Neonates with indirect hyperbilirubinemia

Methodology: Studies selected were RCT's in neonates with indirect hyperbilirubinemia treated with UDCA and phototherapy for the experimental group, and phototherapy alone for the control group. Literature search was done in PubMed, Cochrane Library, and Google Scholar. Nine RCTs met the predefined inclusion criteria. Quality of evidence was assessed using the GRADE approach. RevMan Version 5.4 was used for data synthesis and meta-analysis.

Main Outcome Measures: Bilirubin levels and duration of phototherapy

Results: Mean differences with 95% confidence intervals were calculated for changes in bilirubin levels and duration of phototherapy. The use of UDCA with phototherapy shows a significant difference, with a P value<0.05, in bilirubin levels with a mean difference of -1.63[-2.51,-0.75] for 24hours; -1.24[-2.11,-0.36] for 48hours; and -1.35[-1.66,-1.03] for 72hour post-treatment. The decrease in the duration of phototherapy with the addition of UDCA was statistically significant, with a P value<0.000001, at a mean difference of -16.31[-24.38, -8.25] hours.

Conclusions:
In neonates with indirect hyperbilirubinemia, the use of UDCA with phototherapy at 24 and 48hours of treatment may result in a larger reduction in the bilirubin levels with low certainty of evidence, and with moderate certainty of evidence, will likely result in a larger reduction in the duration of phototherapy as opposed to using phototherapy alone.

***Keywords**: neonates, indirect hyperbilirubinemia, ursodeoxycholic acid, phototherapy*