

# Skin science to advance emollient therapy in the care and health of preterm infants

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For the first time, the World Health Organization (WHO) made a recommendation in 2022 to consider a skin treatment—“application of topical oils to the body of preterm or LBW infants”, based primarily on evidence from studies with sunflower seed oil (SSO)—in the management of preterm or LBW infants.<sup>1</sup> Moreover, the WHO called for additional research on emollient effects, composition, dosing and mode of application.<sup>2</sup>

Russell et al.<sup>3</sup> are to be congratulated for investigating the role of treatments (SSO and chlorhexidine) to the skin on measures related to the health of LBW infants in the NeoCHG trial. The choice of oil (SSO containing >60% linoleic acid) and the mode of application appear to be appropriate for use in newborn infants, although important information on oil processing (e.g., cold pressed) and storage (given the propensity for oxidation) and the precise manner in which the oil was applied (given the risk of injuring the skin during emollient applications) was not specified. SSO comes in two primary forms: one comprised of high oleic and low linoleic acid content for use in cooking. The other less frequently available form used in the NeoCHG study is high in linoleic and low in oleic acid content and is the type of SSO desired for examination of potential health benefits. Linoleic acid is a key ingredient, as it binds to peroxisome proliferator activated receptor activator- $\alpha$  and stimulates corneocyte formation (upregulating involucrin in corneocyte scaffolding of the skin barrier in the stratum corneum), lipid production and assembly (forming the permeability barrier) and cationic antimicrobial peptide production (bolstering innate immunity).<sup>4</sup>

In the NeoCHG study, Russell et al. did not find significant effects of SSO treatment on skin condition scores based on unaided visual assessment of the skin for degree and extent of skin dryness, erythema and breakdown.<sup>3</sup> They also did not detect effects of SSO treatment on the density of the skin flora based on colony counts from cultures of skin swabs. Arguing that no evidence was found for safety concerns, the authors concluded that “... further trials examining clinical outcomes are warranted.”

In proceeding with further examination of SSO (and chlorhexidine) effects on the skin of newborn infants,

improvements to study design may aid learning. Skin condition scores may correlate with risk for systemic infection,<sup>5</sup> and typically they worsen over the first several days after birth into a terrestrial environment. Treatment of preterm infant skin with SSO has been shown to improve skin condition scores relative to untreated control infants, although early initiation of treatment within 24 h of birth, which could not be achieved in the NeoCHG study, appears to be critical for maintaining skin integrity and reducing risk for sepsis.<sup>5</sup> Little variation was found in skin condition scores over time, even in the control group, or with treatment in NeoCHG; thus, a more sensitive measure of skin barrier integrity may be needed. The most accessible and sensitive measure of epidermal permeability barrier function is the rate of trans-epidermal water loss (TEWL).<sup>6</sup> Aims of topical therapy are to reduce TEWL and accelerate recovery of baseline TEWL rates following skin injury—while not becoming overly occlusive and adversely impacting epidermal metabolism—and to improve skin hydration and acidify the skin surface. SSO treatment in neat oil form can become occlusive and disruptive to the metabolism, formation and function of the skin barrier; thus, it is critical to measure its specific effects on the barrier, as even high linoleate forms of SSO can have detrimental effects.<sup>7</sup>

Prior research has shown that a SSO product that improved skin barrier function in a mouse model of infant skin<sup>6</sup> also reduced risks for sepsis and mortality in preterm infants in Bangladesh.<sup>8</sup> However, no effect on skin flora density was observed using culture-based methods<sup>9</sup> similar to those utilized by Russell et al.<sup>3</sup> Rather, evidence was advanced to suggest that SSO treatment impeded the entry of pathogens from the skin surface into the bloodstream.<sup>9</sup> During 10 days of SSO treatment of young children with severe acute malnutrition in Bangladesh, using more advanced methods based on 16s rRNA gene amplicon sequence data and ecological statistics, increased beta-diversity of the skin microbiome was found, associated with reduced risk for infection.<sup>10</sup>

Leveraging advances in skin science will aid learning and accelerate improvements in care and health outcomes of preterm infants based on evidence of safety, efficacy and mode of action of well-defined topical treatments.

## Contributors

GLD is the sole contributor to the writing of this letter.



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## Declaration of interests

GLD declares no competing interests.

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