

## Brief Report

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# Assessment of safety and tolerability of local application of DEBA cream in infants and children

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Mosquito-borne diseases such as malaria, filariasis, dengue fever, and leishmaniasis, are responsible for considerable morbidity, especially in children. Although, the world's most widely used mosquito-repellent DEET (N,N diethyl-m-toluamide or N,N-diethyl-3-methylbenzamide) is considered efficacious safe in adults [2, 9], opinion regarding its safety in infants and children is divided [1, 3, 5, 9, 12, 16]. DEBA (N,N-diethylbenzamide) is a structurally related compound that has equivalent mosquito-repellent efficacy [8, 14] and has been used in India for over 40 years. As its safety has not been formally evaluated, we undertook a randomized, placebo-controlled study to determine the safety of DEBA in infants and children after obtaining approval from the Institutional Ethics Committee. Children aged 1 mo–12 yr were enrolled after obtaining consent from parents, and assent from children (if aged above 7 yr). The study cream (DEBA 1.25 g, Glyceryl monostearate 0.75 g, glycerine 0.3 g, carbopol 0.05 g, perfume 0.05 g, water 7.6 g; per 10 g) and placebo cream were identical in all respects. Four age groups (with 50 participants each) viz. 7–12 years, 4–6 years, 1–3 years and 1 mo–1 year; were studied, beginning with the oldest children. No formal sample size calculations were made as the study was carried out to substantiate the safety of DEBA, marketed for several years. The study had two arms: Single and multiple-application: The latter arm was initiated only after determining that no serious adverse events (SAE) occurred with the former arm. The first 10 subjects in each arm received the study cream (open label), while the remaining 40 subjects were randomized to study- or placebo-cream in 3 : 1 ratio. The designated cream (0.4 g/100 cm<sup>2</sup>) [11] was applied to the exposed parts of the body, gently by rubbing (below elbow, below knee). Subjects were observed for two hours after application for any immediate local (rash, itching, etc.) or systemic reactions (rash, breathlessness, irritability, alteration of sensorium, convulsions, etc.). Subsequently they

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were examined at 24- and 48-hours and on Day 7. They were also told to report to investigators if any adverse event occurred. Fischer's test was used to analyze "between-group" differences in number of subjects developing adverse events at 5% significance. Research participants who dropped out of the study were considered as having developed adverse events (AEs) in an "intent-to-treat" analysis. Four hundred healthy subjects (192 boys) aged 1 mo–12 yr were enrolled in the study. There were two drop-outs in the single application and five in multiple-application arm ( $p > 0.05$ ). No local or systemic adverse events were reported by parents or participants, nor were any adverse events noted on examination of the study subjects at follow-up visits.

DEET is associated with local reactions such as erythema, urticaria, itching, burning sensation, blisters, angioedema and contact dermatitis [6, 15] and systemic events such as anaphylaxis, psychosis, bradycardia and hypotension [4, 6, 10] in adults, most of which are overdose related. A concern has been expressed regarding its safety in infants and children related to a few reports of toxic encephalopathy and seizures [13, 16]. The American Academy of Pediatrics has indicated that DEET should not be used in infants aged up to 2 mo [1]. A Canadian Advisory Committee recommends that other personal protection measures should be preferred over insectifugals in infants aged up to 6 months [5]. As children have greater surface area: Body mass ratio, it is believed that this could lead to percutaneous absorption of greater amounts rendering them susceptible to systemic toxicity [16]. DEBA has been used in India for over 40 years without any SAE reports. Our study has demonstrated that use of DEBA is safe in infants and children. However, clinicians should appreciate that even if we consider that no adverse events occurred in our study, the upper limit of 95% CI for an AE occurring following DEBA-use could be 0.94% [7]. Findings obtained in this study can be considered while drafting guidelines regarding use of mosquito repellents in infants and children.

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