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SAFETY OF TOPICAL PERMETHRIN IN BREASTFEEDING

Question:
What is the safety of topical permethrin based products in pregnancy and during lactation?

Answer:
Toxicity:
Permethrin is a photostable synthetic pyrethroid possessing a broad spectrum of insecticidal activity and low mammalian toxicity[1]. Indeed, permethrin has been rated one of the safest insecticides due to its low toxicity[1,2].

Based on oral LD50 (lethal dose in 50%) data for rats, permethrin is three times less toxic than malathion, and 40 times less toxic than lindane (gamma benzene hexachloride)[3,4]. It should be noted however that LD50 values can vary depending on the cis:trans ratio of isomers and the vehicle used[1].

The low mammalian toxicity of permethrin is primarily due to rapid biotransformation by ester hydrolysis and/or hydroxylation[1]. Under normal circumstances, single applications would be used and therefore data from chronic and high dose animal toxicity studies are of limited value in the context of this enquiry.

Absorption:
The percentage absorption of topically administered drugs is dependant on many factors including quantity applied, surface area, duration of contact, the vehicle and the type of skin (eg. site, ethnicity, etc.). It is likely that the skin is a site of permethrin metabolism and metabolite conjugation, therefore, systemic exposure via this route is likely to be minimal[1].

Published pharmacokinetic data on the absorption of this agent is limited. However, an in vitro study of the percutaneous penetration of 14-carbon-labeled permethrin revealed that only 0.62% of the applied dose (200mcg/cm^{-2}) penetrated human skin over an 8-hour period[5].

As part of the regulatory process, the manufacturer (Burroughs Wellcome) undertook percutaneous absorption studies, ranging from single applications to weekly treatments, over 8 weeks[6]. In these studies (n= >100), no quantifiable concentrations of intact permethrin were found in plasma or urine following treatment[6]. In another study, plasma sampling following full-body application of 5% permethrin cream on two occasions (7 days apart), failed to detect permethrin (<5mcg/L). The lack of detectable permethrin following doses of between 150-660mg permethrim would suggest slow and low absorption[1].

One of the most extensive studies applied carbon-14-radiolabeled permethrin to the shaved backs of 6 healthy volunteers. Plasma, urine and faeces were collected for 5 days after treatment and washing was not allowed during this time. The percutaneous absorption from the 5% permethrin cream ranged from 0.3% to 2.08%, and was independent of dose[6]. The mean percentage absorbed was less than 1%[6].

Teratogenicity:
Studies of carbon-14-radioactively labeled permethrin have shown that the label reaches rat foetuses following oral dosing[1]. No teratogenic effects have been seen in single and/or multigenerational rabbit, rat and mice studies[1,7]. Furthermore, genotoxicity studies, including the Ames test, mouse lymphoma assay, host mediated assay and mouse dominant lethal assays were negative[1]. Due to the interspecies variation, care must be taken in extrapolating this data to humans.

Data on human exposure during pregnancy is limited[8,9]. Judge et al describe treatment of a 5-month pregnant woman with a whole body application of 5% permethrin cream (for 12 hours)[10]. This occurred on several occasions for control of crusted scabies. This woman gave birth to a healthy, term baby.

Lactation:
We note reference to product data sheets statements that permethrin has been shown to have carcinogenic potential in animal studies and that it should be avoided in lactating women[11]. However, permethrin is not carcinogenic in rats. Although a small increase in lung adenomas was reported in a high dose carcinogenicity study of female mice, this is not considered to indicate risk for humans[12].

Indeed, if this carcinogenic potential existed, one should be more concerned with maternal health. Ultimately, transfer of topical drugs into breast milk is a function of systemic dose. In this instance, it is likely to be minimal.

Conclusions:
Due to minimal topical absorption, low toxicity, rapid metabolism and a lack of an association with animal or human teratogenicity, we consider this agent to remain the treatment of choice of scabies or headlice in pregnancy and lactation.

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