

Topical N-acetylcysteine treatment in neonatal ichthyosis

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Unpredictable transcutaneous absorption of topically administered drugs and potential teratogenicity and toxicity of systemic drugs would make it mandatory to innovate more efficacious and less toxic drugs for the treatment of ichthyosis, which is not a fully curable disease in the neonatal period. In this article the clinical efficacy of 10% N-acetylcysteine emulsion in the topical treatment of congenital ichthyosis in a newborn was assessed, comparing simultaneously with 4% urea emulsion. After treating the skin of the left and right halves of the body with topical N-acetylcysteine and 4% urea, respectively, for nine days, the improvement was much more outstanding on the skin of the left half of the body when compared to the right half of the body. Topical N-acetylcysteine, to our knowledge, has not been used in a newborn with ichthyosis before, and this is the first report of a case of neonatal ichthyosis successfully treated with topical N-acetylcysteine. We conclude that 10% N-acetylcysteine emulsion, as a non-toxic and hypoallergic amino acid derivative, can be safely and efficaciously used in the topical treatment of neonatal ichthyosis, although the permanent cure may not always be possible.

Key words: ichthyosis, N-acetylcysteine, newborn, topical, treatment.

Ichthyoses (disorders of cornification) are a primary group of inherited conditions that are characterized clinically by patterns of generalized intense dryness and a variable scaling, and histopathologically by hyperkeratosis. There are at least four distinct forms of ichthyoses that present in the neonatal period, and of these, congenital nonbullous ichthyosiform erythrodermal/lamellar ichthyosis is a difficult diagnostic and management problem since it is not fully curable, and is thus a chronic disease¹.

Topical treatment of ichthyosis has classically included generous and frequent applications of emollients and keratolytic agents such as retinoic acid (0.1% cream) lactic acid², urea³, a mixture of lactic acid and propylene glycol⁴, and calcipotriol⁵. Unpredictable transcutaneous absorption of topically administered drugs and potential teratogenicity and toxicity of systemic drugs would therefore make it mandatory to innovate more efficacious and less toxic drugs for the treatment of ichthyosis. We assessed the clinical efficacy of 10% N-acetylcysteine emulsion in the topical treatment of congenital ichthyosis, and hereby report the successful treatment of this disease in a newborn without

any side effects.

Case Report

A male infant born at 38 weeks' gestation to a 34-year-old gravida 7, para 3 mother by spontaneous vaginal route was transferred to our neonatology unit immediately after birth because of striking grotesque appearance. The parents were first-degree relatives and there was no family history. Birth weight was 2,950 g. Physical examination on admission revealed a thick taut membrane resembling oiled parchment and covering the body of the baby, ectropion, flattening of the ears and nose, and eclabium and fixation of the lips in an O-shaped configuration (Fig. 1). The diagnosis of lamellar ichthyosis was made on the basis of clinical appearance and findings.

The baby was placed in an incubator and fed enterally. After written informed consent was obtained from both parents, a water-in-oil emulsion containing 10% N-acetylcysteine was prepared and applied twice daily on the skin of the left half of the body, whereas 4% urea emulsion was applied to the skin of the right half of the body twice daily. After shedding of the parchment-like membrane and

a nine-day-long treatment, improvement was much more outstanding on the left half of the body, with improvement best in scaling and dryness, while minimal changes were noted in the right half of the body (Fig. 2). The N-acetylcysteine emulsion was applied to the whole skin for an additional duration of eight days, and recovery was observed on the whole skin of the body thereafter. Ectropion and eclabium

disappeared. On the 18th postnatal day the baby was discharged in good condition.

Discussion

Topical treatment of ichthyosis consists of emollient creams, ointments, keratolytic agents, and bath oils. However, any topically applied agent will be transcutaneously absorbed to a much higher degree than through normal



Fig. 1. The newborn with ichthyosis exhibiting a thick taut membrane, ectropion, eclabium, and fixation of the lips in an O-shaped configuration before treatment and shortly after birth.



Fig. 2. Outstanding improvement in the skin of the left half of the body after a nine-day-long treatment with topical N-acetylcysteine.

skin, requiring careful monitorization of dosing. Treatment with systemic retinoids has had variable success⁶; however, the long-term risks of these compounds (teratogenicity and toxicity to bone) limit their usefulness. Newborns are more vulnerable to toxic and harmful effects of topical drugs due to their relatively greater body surface area compared to body weight. Thus there is a need for new, efficacious and safer innovations for treatment of ichthyosis in the newborn.

N-acetylcysteine is a thiol derivative that has traditionally been used as a mucolytic agent and as an antidote for acetaminophen toxicity⁷. The inhibitory effect of this drug on proliferation of NIH3T3 fibroblast cells has recently been demonstrated⁸, and its antiproliferative effect is mediated by reversible blocking cell-cycle progression in G₁ phase⁸, but not by its cytotoxic effect⁹. The inhibition of keratinocyte proliferation by N-acetylcysteine has raised the idea of the dermatological usefulness of this drug in treatment of diseases with increased epidermopoiesis, and recently a 33-year-old woman with lamellar ichthyosis was satisfactorily treated with topical N-acetylcysteine⁹. To our knowledge, topical N-acetylcysteine has not been used previously in a newborn with ichthyosis, and thus this is the first report of a case of neonatal ichthyosis successfully treated with topical N-

acetylcysteine.

We conclude that 10% N-acetylcysteine emulsion, as a non-toxic and hypoallergic amino acid derivative, can be safely and efficaciously used in the topical treatment of neonatal ichthyosis, although the permanent cure may not always be possible.

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