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BRIEF REPORT

WILEY Pediatric Dermatology

Topical N-acetylcysteine in ichthyosis: Experience in 18 patients

Abstract

The treatment options for ichthyosis are limited. Successful treatment with topical N-acetylcysteine has been reported in a small number of patients, with generally good results. We report the finding of a retrospective chart review of 18 patients treated with N-acetylcysteine. Although topical N-acetylcysteine is an effective therapy for some patients with ichthyosis, problems with irritation, objectionable odor, and compounding costs limit its use.

1 | INTRODUCTION

The ichthyoses are a group of rare genetic skin diseases most commonly characterized by scaling and erythroderma. Current therapies include emollients, bathing, keratolytics, and retinoids. Available topical and oral medications have success in some, but side effects can limit their us.

Topical N-acetylcysteine (NAC) was first reported as a promising treatment for lamellar ichthyosis in 1999.[1] Twenty-one cases have been published in the literature,[1-5] of which 16 had good responses, 4 did not benefit, and 1 discontinued the medication because of the odor. This report reviews the experience of topical NAC for ichthyosis at Children's Hospital of Philadelphia.

2 | METHODS

A retrospective chart review of individuals with ichthyosis seen from January 1999 to March 2017 was performed. Patients selected for this study (Table 1) had a diagnosis of ichthyosis, began topical 5%-10% NAC treatment, and had follow-up evaluations. Eighteen of 65 patients met these criteria—13 with autosomal-recessive congenital ichthyosis; 1 each with Netherton syndrome; cerebral dysgenesis, neuropathy, ichthyosis, and palmoplantar keratoderma syndrome; X-linked ichthyosis; and ichthyosis with confetti; and 1 with likely ichthyosis vulgaris. NAC was initiated because of suboptimal response to current therapies or at the patient's request.

The responses to treatment were graded much improved, improved, worsened, no change, or unknown (because of early discontinuation for adverse effect) as assessed according to patient and physician estimates of reduction of scaling. All patients saw one of five experienced pediatric dermatologists. Adverse effects included irritation and erythema. Intolerance of the medicinal odor, if present, was noted. At the last patient contact, we recorded whether the patient continued to use the drug or discontinued use because of adverse effects cost.

3 | RESULTS

The majority of patients noted improvement after use of NAC for at least 2 weeks; 3 had marked improvement, 11 improvement, 1 no change, and 1 worsening, and 2 discontinued the drug because of irritation before any therapeutic effect could be assessed (Table 1). Ten patients found the drug to cause irritation or erythema. In these cases, the NAC strength or base ingredients were altered, or intermittent use was recommended (Table S1). Nonetheless, 6 patients discontinued NAC because of irritation. Seven patients found the odor unpleasant, but none discontinued the medication solely for this reason.

Because topical NAC is not available from pharmaceutical companies, the drug is individually compounded for patients. Although the bulk cost of NAC is low, the prices charged at U.S. compounding pharmacies are high (~$250/454 g). Many patients experienced difficulties in securing insurance coverage. One patient purchased a machine to compound the medication at home. One patient discontinued NAC despite favorable results because of lack of insurance coverage.

Of the 18 patients, 10 ultimately had improvement without significant adverse effects. Eight discontinued the drug—6 because of irritation or erythema, 1 because of worsening of scaling, and 1 because of drug cost.

4 | CONCLUSION

Topical NAC is an effective therapy for some patients with ichthyosis, but problems with irritation, objectionable odor, and compounding costs may limit its use. Further studies are needed to determine which patients in particular can benefit from NAC.

Keywords

genodermatoses, ichthyosis, therapy–topical

TABLE 1 Individuals with ichthyosis treated with topical N-acetylcysteine (NAC)

Age	Sex	Clinical diagnosis	Genetic mutation	Initial NAC formulation	Scale response	Adverse effect	Comment
14 y	Female	ARCI; likely LI	Homozygous ABCA12	10% NAC in 5% urea w/rosemary oil	Improvement	Disliked scent	
15 y	Female	ARCI; likely LI	Homozygous ABCA12	10% NAC in 5% urea w/rosemary oil	Improvement	Disliked scent	
16 y	Female	ARCI; likely LI	Homozygous ABCA12	10% NAC in 5% urea w/rosemary oil	Improvement	Disliked scent	
9 y	Female	ARCI; likely LI	Homozygous ABCA12	10% NAC in 5% urea w/rosemary oil	Improvement	Disliked scent	
9 y	Male	ARCI; HI	ABCA12	10% NAC in 5% urea	Improvement		Discontinued—insurance problems
5 y	Female	Ichthyosis with confetti	Keratin 10; ALOXE3 p.R689W (het)	10% NAC in 5% urea	Worsened		Discontinued—worsening of scale
15 y	Male	Likely ichthyosis vulgaris		10% NAC in 5% urea	Improvement		
5 y	Male	ARCI	Negative for TGM-1	10% NAC in 5% urea	Discontinued before adequate evaluation	Irritation	Discontinued—irritation
6 y	Male	ARCI; CIE	NIPAL4 p.A176D	10% NAC in 5% urea	Improvement	Irritation; disliked scent	
9 y	Male	CEDNIK-like Syndrome	22q del(777 kb) chr22:20471591-21607293	10% NAC in 5% urea	Improvement	Irritation	Discontinued—irritation
8 y	Male	ARCI		10% NAC in 5% urea	Marked improvement	Irritation	Discontinued—irritation
8 mo	Male	ARCI; LI	TGM-1 p.T491M (het) p.G278R (het)	5% NAC in Cerave	Marked improvement	Irritation	
13 y	Male	X-linked ichthyosis	Xp22.31 del (1.63 mb) Chrx.6428059-8101017	10% NAC in 5% urea	Improvement		
3 y	Female	ARCI; likely CIE		5% NAC in Cerave	Discontinued before adequate evaluation	Irritation; disliked scent	Discontinued—irritation
11 y	Female	ARCI; CIE	NIPAL4 p.A176D	10% NAC in 5% urea	Unchanged	Irritation	Discontinued—irritation
3 y	Female	ARCI; HI	ABCA12 p.R2204X	10% NAC in 4% urea	Improvement	Irritation; disliked scent	
16 y	Female	Netherton syndrome	SPINK5 p.C297T	5% NAC in 2.5% urea w/lavender oil	Improvement	Irritation	
11 mo	Female	ARCI		10% NAC in Cerave	Marked improvement	Irritation	Discontinued—irritation

ARCI, autosomal-recessive congenital ichthyosis; LI, lamellar ichthyosis; HI, harlequin ichthyosis; CIE, congenital ichthyosiform erythroderma; CEDNIK, cerebral dysgenesis, neuropathy, ichthyosis, and keratoderma syndrome; del, deletion; mb, megabase; kb, kilobase; het, heterozygous.

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SUPPORTING INFORMATION

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