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Research Article

A Comparative Study of Effect of Oral Myoinositol Plus Topical Lactic Acid versus Oral Alpha Lipoic Acid plus Topical Lactic Acid in Patients with Acanthosis Nigricans

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ABSTRACT
Background: Acanthosis nigricans (AN) is a cutaneous marker of insulin-resistant states. Alpha-lipoic acid (ALA) and myo-inositol (MI) both improve metabolic profiles, yet comparative evidence in AN is limited.
Objective: To compare the clinical efficacy of oral MI + topical lactic acid (LA) versus oral ALA + topical LA in patients with AN.
Methods: In this hospital-based, prospective, comparative study (July 2022–December 2023), 72 consecutive AN patients were alternately allocated to MI + LA (Group A) or ALA + LA (Group B) for six months. Primary outcome was change in neck-lesion severity grade (0–4 scale). Secondary endpoints included insulin resistance (HOMA-IR) and safety. Data were analysed with x^2, t-tests, and one-way ANOVA ($\alpha = 0.05$).
Results: Mean age was 31.5 ± 8.2 years; 70.8 % were male. Baseline characteristics, HOMA-IR (mean 1.68), and grade distribution were comparable between groups. After 6 months, 58.3 % of all patients achieved ≥1-grade reduction; 13.9 % achieved ≥2 grades. Mean grade reduction was 1.36 ± 0.79 (ALA + LA) versus 0.89 ± 0.71 (MI + LA); between-group difference 0.47, F = 0.40, p = 0.53. No serious adverse events occurred.
Conclusion: Both regimens significantly improved AN severity, with numerically greater—but statistically non-significant—improvement in the ALA + LA arm. Either combination may be chosen according to patient preference and tolerability. Larger randomized trials are warranted.

Keywords: Acanthosis Nigricans; Myo-Inositol; Alpha-Lipoic Acid; Lactic Acid; Insulin Resistance; Comparative Study.

Introduction

Acanthosis nigricans (AN) is characterised by hyperpigmented, papillomatous plaques, most frequently on the neck, axillae and other intertriginous zones [5]. Histologically, the disorder reflects epidermal hyperplasia driven by chronic hyperinsulinaemia; excess insulin cross-activates insulin-like growth-factor-1 receptors on keratinocytes and fibroblasts, accelerating proliferation [1]. The clinical importance of AN lies in its strong association with insulin-resistant states—nearly 60 % of Indian patients fulfil metabolic-syndrome criteria [7]. Quantifying that resistance with the homeostasis-model assessment for insulin resistance (HOMA-IR) provides a convenient surrogate for euglycaemic clamp studies [6], and the triglyceride-to-HDL-cholesterol ratio offers an additional, inexpensive proxy [4].

Therapeutically, improving insulin sensitivity often reduces lesion severity. Myo-inositol (MI), the most abundant stereoisomer of inositol, enhances phosphatidylinositol-3-kinase signalling and lowers circulating insulin; randomised trials in polycystic-ovary syndrome (PCOS) show concurrent cutaneous and metabolic benefits [3]. Alpha-lipoic acid (ALA), a mitochondrial co-factor with potent antioxidant properties, also decreases insulin requirements and has demonstrated efficacy in AN comparable with metformin [2]. Topical lactic acid (LA), an α-hydroxy acid, promotes stratum-corneum desquamation and pigment dispersion and is widely used as adjunctive therapy. "However, comparative data on MI- versus ALA-based regimens in AN remain limited, and second-line physical modalities such as alexandrite or fractional CO_2 lasers—while sometimes effective—are constrained by cost and access [9, 10].

We therefore undertook a prospective, hospital-based study to evaluate the effectiveness of

oral MI plus topical LA relative to oral ALA plus topical LA in patients with AN, and to examine how clinical response correlates with HOMA-IR levels. We hypothesised that both regimens would improve disease severity, with ALA producing equal or superior outcomes.

METHODS

Study Design and Participants

A hospital-based comparative study was conducted in the Dermatology outpatient department of Mahatma Gandhi Medical College & Hospital, Jaipur (July 2022–December 2023) . After ethics approval and written consent, all successive AN patients of any age or sex were screened. Exclusion criteria were pregnancy, malignancy, topical/systemic AN treatments within eight weeks, or drug-induced AN.

Allocation and Interventions

Odd-numbered recruits received **Group A:** MI 2 g daily + 10 % LA lotion once nightly; even-numbered recruits received **Group B:** ALA 300 mg daily + identical LA lotion. Concomitant lifestyle advice (diet, exercise) was provided. Compliance was reinforced at each monthly visit.

Outcomes

Neck-lesion severity was graded (0–4) at baseline and six months (primary outcome). HOMA-IR, TG/HDL-C, fasting/post-prandial insulin ratios, and anthropometry were assessed. Adverse events were recorded.

Statistics

Sample-size estimation (≥50) was based on anticipated medium effect (d = 0.65), 80 % power. Data were analysed using SPSS 26. Between-group differences employed independent-samples t-test (continuous) or χ^2 (categorical). Change scores were compared by one-way ANOVA; $p < 0.05$ was significant.

RESULTS

Baseline Profile

Characteristic	MI + LA (n = 36)	ALA + LA (n = 36)	Total (n = 72)
Age, years (mean ± SD)	31.1 ± 8.5	31.9 ± 7.8	31.5 ± 8.2
Male, n (%)	25 (69.4)	26 (72.2)	51 (70.8)
Urban residence, n (%)	29 (80.6)	29 (80.6)	58 (80.6)
Mean HOMA-IR	1.66 ± 0.32	1.70 ± 0.34	1.68 ± 0.33

No significant baseline differences were observed (all $p > 0.3$).

Treatment Response

Outcome	MI + LA	ALA + LA	p value
Mean grade reduction	0.89 ± 0.71	1.36 ± 0.79	0.08
≥1-grade reduction, n (%)	20 (55.6)	22 (61.1)	0.62
≥2-grade reduction, n (%)	3 (8.3)	7 (19.4)	0.17

ANOVA confirmed no statistically significant difference ($F = 0.40$, $p = 0.53$) . Both groups showed significant within-group improvement (paired t-test, $p < 0.001$).

Correlates of Response

Lower baseline HOMA-IR correlated with greater grade reduction ($r = –0.42$, $p = 0.001$). Age showed modest positive correlation with HOMA-IR ($r = 0.31$). No serious adverse events occurred; mild transient dyspepsia in 6 patients (ALA) and nausea in 4 (MI) resolved spontaneously.

DISCUSSION

The present study demonstrates that six months of either oral MI or oral ALA, each combined with nightly 10 % LA lotion, produced significant clinical improvement in cervical AN. A mean grade reduction of 0.89 ± 0.71 in the MI arm and 1.36 ± 0.79 in the ALA arm translated into ≥ 1-grade improvement for more than half of participants, corroborating the central role of insulin-sensitising therapy in disease control. Although the ALA regimen achieved numerically greater change, the between-group difference did not reach statistical significance, suggesting comparable therapeutic potential when topical keratolysis is standardised.

Our findings align with those of Arindam et al., who reported that 300 mg ALA daily matched metformin in reducing lesion thickness and pigmentation over 24 weeks [2]. The present study extends that evidence by using LA as a common topical backbone and by including a direct MI comparator. MI's performance is consistent with PCOS trials in which oral MI improved insulin indices and cutaneous hyperpigmentation scores [3], underscoring the mechanistic overlap between AN and

hyperandrogenic insulin-resistant states. The modest but significant inverse correlation we observed between baseline HOMA-IR and grade reduction ($r = -0.42$) reinforces the concept that lower baseline insulin resistance facilitates better cutaneous resolution, echoing the metabolic targets proposed by Matthews et al. [6]. Clinicians may therefore consider early metabolic screening and intervention, even in cosmetically driven consultations.

Biochemical profiling further highlighted a relatively mild insulin-resistance burden (mean HOMA-IR ≈ 1.7), similar to the Indian cohort described by Varthakavi et al. [7]. This contrasts with Western series, where HOMA-IR values often exceed 3, possibly reflecting ethnic and dietary differences. While TG/HDL-C ratio tracked HOMA-IR in our subset analysis, its clinical utility warrants confirmation, despite encouraging surrogate data [4]. Adjunctive energy-based treatments may further enhance outcomes in refractory plaques: alexandrite laser improved pigmentation and texture in early series [9], while a recent comparative study reported fractional CO_2 resurfacing to be superior to glycolic peels for recalcitrant AN [10].

Strengths of the study include prospective design, objective photographic grading, and a homogenous treatment protocol within a single tertiary centre. Nevertheless, limitations merit consideration: alternate (rather than random) allocation introduces potential selection bias; blinding was not feasible for oral agents; and lesion assessment was confined to the neck, possibly under-representing flexural disease. The sample size, calculated for medium effect detection, may still be under-powered for subtle inter-group differences. Finally, the six-month horizon does not inform long-term relapse rates.

Future research should adopt double-blind, randomised methodology with larger, multicentric cohorts and incorporate patient-reported outcomes, histological markers, and post-treatment follow-up. Exploring combination therapy—such as low-dose ALA plus MI, as suggested by metabolic synergy in obese PCOS patients [8]—could also optimise efficacy while minimising pill burden.

In conclusion, both MI + LA and ALA + LA regimens offer safe, clinically meaningful improvement in AN severity over six months. Given similar efficacy profiles, treatment selection can be guided by cost, availability, and individual tolerance. Addressing insulin resistance—whether with MI, ALA, or alternative agents—remains pivotal for durable cutaneous and metabolic benefit in acanthosis nigricans.

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