Title

Characterizing Low-Dose Oral Minoxidil-Induced Peripheral Edema in Alopecia Patients

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Research letter

Characterizing low-dose oral minoxidil-induced peripheral edema in alopecia patients

To the Editor: Low-dose oral minoxidil (LDOM) has emerged as an effective adjunct therapy for various forms of alopecia. A notable adverse effect is peripheral LDOM-induced edema, reported in 2% to 3% of patients, attributed to its vasodilatory and sodium-retaining properties.[1,2] Understanding the specific features and risk factors associated with LDOM-induced edema is crucial for optimizing patient management.

A retrospective analysis of alopecia patients treated with LDOM (0.625-5 mg daily) at our institution between 2023 and March 2024 with approval from University of California, Irvine Institutional Review Board (HS# 2016-3076). Inclusion criteria included diagnosis of alopecia, at least 1 month of LDOM therapy, and a minimum of 2 visits within a 12-month period with reported peripheral swelling postmedication initiation. A total of 250 alopecia patients were included, with a predominance of females (78%) and a mean age of 51 years (SD, 19) (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/pbv8pdv3mj/1). Among them, 22 patients (8.8%) reported edema secondary to LDOM therapy, comprising 20 adults and 2 children. The affected population was primarily female (90.9%; age range 10-76 years), and predominantly comprised of White and Asian races.

Risk factors for edema were identified using multivariate logistic regression models adjusted for age, sex, race, and dose/weight (mg/kg/d) (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/pbv8pdv3mj/1). The most common sites for LDOM-induced edema were bilateral legs and feet ($n = 21$), face ($n = 9$), and hands ($n = 4$). Most cases presented as pitting edema ($n = 17$), typically developed within 3 months of LDOM dosing ($n = 21$). Treatment strategies included LDOM dose reduction ($n = 10$), discontinuation ($n = 4$), or diuretic use ($n = 1$), resulting in complete resolution of edema in 11/22 patients, within a median 1-2 weeks. Among patients who did not adjust LDOM regimen ($n = 7$), 3 had spontaneous resolution within 4 weeks, while remaining maintained LDOM dose despite edema ($n = 4$) (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/pbv8pdv3mj/1). Persistent, episodic LDOM-induced edema was observed in 8 patients, all with predisposing factors including prior history of peripheral edema ($n = 4$), cardiovascular disease ($n = 3$), kidney transplant ($n = 1$), and prednisone use for polymyalgia rheumatica ($n = 1$).

The overall incidence of LDOM edema of 8.8% in this study exceeds rates from previous trials.[1-3] This discrepancy may be attributed to higher initial and incremental LDOM dosing at our center (1.25-2.5 mg daily vs 0.25-0.625 mg daily in published studies).[1-3] The findings demonstrated a positive association between LDOM dose-weight and edema (odds ratio, 1.04; 95% CI, 1.02-1.06; $P = .001$), with dose-dependent relationship evident in the pediatric patients.

The mechanistic underpinnings of minoxidil-induced edema involve its direct arteriolar vasodilatory effects, facilitation of fluid extravasation, activation of the renin-angiotensin-aldosterone system leading to salt and water retention, and its role as a potassium channel opener potentially impairing lymphatic function.[4,5] These insights highlight the heightened vulnerability of patients with pre-existing conditions or those on medications affecting fluid balance to develop edema with LDOM therapy. The prescribing information recommends concurrent use of a diuretic to mitigate significant fluid accumulation.[4]

In summary, LDOM-induced edema represents a dose-dependent and mostly reversible complication. Dose adjustment or discontinuation typically improves edema within weeks, though it may persist intermittently in some patients, especially those with pre-existing risk factors. We underscore the importance of cautious, incremental dosing of LDOM, especially in patients with a history of peripheral edema.

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Conflicts of interest

None disclosed.

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