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Low-dose oral minoxidil improves global hair density and length in children with loose anagen hair syndrome

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Loose anagen hair syndrome (LAHS) is a sporadic or autosomal dominant hair disorder which typically affects girls aged 2-6 years.¹ It is characterised by increased hair shedding, non-scarring alopecia, inability to grow long hair, dull and lustreless hair. Premature and defective keratinisation of the inner root sheath (IRS), and impaired anchorage of anagen

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hairs underlie the pathogenesis.¹ A favourable response has been demonstrated in three patients with LAHS treated with topical minoxidil.¹⁻³ Low-dose oral minoxidil (LDM) has been shown to be effective in adult androgenetic alopecia, alopecia areata and telogen effluvium.⁴ Herein we describe the efficacy and safety of LDM in LAHS.

We retrospectively reviewed records of patients with LAHS treated with LDM in an Australian specialist hair clinic between March 2016 and October 2019. Diagnosis was based on typical clinical features, a positive hair pull test and characteristic findings on light microscopy (anagen hairs with misshapen bulbs, ruffled cuticles and absent IRS).¹ Patients with known hepatic, cardiac or renal dysfunction were ineligible for treatment. LDM was initiated in patients who had failed topical minoxidil or whose condition was associated with significant psychosocial distress. Dosing of oral minoxidil (OM) was based on body weight (≤ 0.02 mg/kg/day). Patients were screened for adverse effects, and their heart rate and blood pressure monitored every 1-3 months. Changes in global hair density and length were evaluated by two independent dermatologists, comparing standardised photographs and using a 3-point scale: improvement, unchanged or worsening.

Eight females with a median age of 7 years (range 2-10) were included (Table 1). LDM was prescribed at a mean dose of 0.24 mg, equivalent to 0.01 mg/kg/day (range 0.10-0.50 mg; 0.005-0.02 mg/kg/day) for a mean duration of 12.5 months (range 7-26 months). Hair length improved in all cases, and global hair density improved in seven cases (figures available on request). All patients noted a subjective reduction in hair shedding. One patient developed mild hypertrichosis of the legs but continued treatment. None of the patients reported cardiac or respiratory symptoms, had abnormal vital signs, or abnormal weight gain. Interestingly, two patients experienced a change in hair colour during treatment (from reddish/dark-brown to light-brown). Seven to 18 months after initiation, LDM was discontinued in six patients whose hair was visibly denser and longer. Two patients are on ongoing treatment.

Our findings suggest that LDOM is a promising treatment for LAHS, particularly in children at the more severe end of the spectrum. Given the natural history of LAHS and the fact that our patients were very young (mean age 5.75 years), it is likely that the improvement in hair length and density seen in our patients after an average of 12.5 months of treatment was attributable to LDOM rather than spontaneous improvement, which is usually seen by adolescence. Chandran *et al.* hypothesised that topical minoxidil promotes DNA synthesis and cell proliferation, thereby correcting the defective keratinisation of the IRS and improving anchorage of anagen hairs.³ The change in hair colour seen in two of our patients, one of whom has previously been described,⁵ is of unclear significance.

In children, side effects of topical minoxidil include contact dermatitis, transient hair shedding and generalised hypertrichosis,⁶ but the safety of LDOM in children has not been systematically evaluated. It was generally well tolerated in our patients, with hypertrichosis representing the only adverse effect. In our experience, generalised hypertrichosis is the most frequent, albeit still uncommonly, reported side effect in paediatric patients. The tachycardia, pedal oedema and postural hypotension reported in adults⁷ is rarely seen at the doses used in children in our clinic (unpublished data). The recommended starting dose of OM for paediatric hypertension is 0.2mg/kg/day (20 times the mean dose in our patients). However, OM exerts minimal hypotensive effects in normotensive subjects.⁶ A 2-year-old boy who accidentally ingested OM 100mg in a single dose recovered fully after developing a transient reflex tachycardia.⁶ While the above observations are reassuring, close monitoring is essential and LDOM should be reserved for patients who are psychologically affected by the appearance of their hair, and/or fail to respond to topical minoxidil or improve spontaneously with age. Treatment should be initiated and monitored by a dermatologist or paediatric dermatologist.

Limitations of our study include the retrospective design and small sample size. Our study shows that, when dosed appropriately, LDOM may be an effective and safe treatment for LAHS in children. Future prospective studies are needed to confirm these findings.

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Table 1: Clinical and epidemiologic data of eight patients with loose anagen hair syndrome treated with low-dose oral minoxidil.

Patient no.	Weight (kg)	Sex	Age at diagnosis, y	Hair colour	Dose of LDOM*, mg	Dosage of LDOM, mg/kg	Treatment duration, mo	Clinical response		Adverse effects
								Global Hair density^	Estimated increase in hair length (cm)	
1	14.5	F	2	Blonde	0.10	0.007	7	2	4	Hypertrichosis on legs
2	23.8	F	7	Black	0.25	0.010	26	1	NR	None
3	40	F	10	Blonde	0.25	0.006	10	2	3	None
4	22	F	7	Dark brown	0.10	0.005	7	2	2	None
5	26	F	7	Brown	0.50	0.020	18	2	10	None
6	15	F	3	Blonde	0.10	0.007	9	2	10	None
7	37	F	6	Reddish-brown	0.50	0.014	12	2	10	None
8	14.5	F	4	Brown	0.15	0.010	11	2	NR	None
Mean	24.1	N/A	5.75	N/A	0.24	0.010	12.5	N/A	6.5	N/A

*Minoxidil 0.1 mg/mL suspension was compounded extemporaneously. The dose of LDOM titrated according to response to a maximum of 0.02 mg/kg. The maximum dose is reported.

^ Global hair density was graded using a 3-point scale where 0 = worsening; 1 = no change ; 2 = improvement.

Abbreviations: cm, centimetres; kg, kilograms; LDOM, Low-dose oral minoxidil; mg, milligrams; mo, months; y, years

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