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Oral minoxidil 7.5 mg for hair loss increases heart rate with no change in blood pressure in 24 h Holter and 24 h ambulatory blood pressure monitoring☆

Dear Editor,

Low-dose oral minoxidil (LDOM) has emerged as an important alternative for treating different causes of hair loss.[1] Nonetheless, its cardiovascular adverse effects, such as tachycardia, hypotension, and edema, remain a concern even at low doses.

The standard dose for the treatment of hypertension typically ranges from 10 to 40 mg/day, and there is no consensus about the ideal dosage for treating hair loss.[2]

A wide range of doses (from 0.25 to 5 mg/day) has been evaluated in clinical studies, but not exceeding 5 mg/day.[2] Recently, a metanalysis demonstrated a positive dose-dependent association of LDOM with an increase in hair density as well as adverse effects.[2]

We have recently assessed 30 adult males taking 5 mg oral minoxidil for androgenetic alopecia (AGA) with 24-h Holter monitoring and 24-h ambulatory blood pressure monitoring (ABPM) before and after 24 weeks of treatment. They presented no relevant alterations regarding 24-h Holter monitoring and ABPM.[3] These findings were reinforced by an evaluation of 10 men with ABPM at baseline and after the first dose of 5 mg oral minoxidil.[4]

Previous pharmacokinetics studies have shown a mild reduction in blood pressure and a slight increase in heart rate in normotensive patients using oral minoxidil at doses up to 10 mg/day.[5] To assess the potential cardiovascular adverse effects of higher doses of oral minoxidil for hair loss, we increased the dose from 5 to 7.5 mg/day in 11 of the 30 patients who had completed our prior study. After 6-weeks of taking the increased dose, we re-evaluated these patients using 24-h Holter monitoring and ABPM.

The main clinical and demographic data of the participants are presented in Table 1. The ABPM and Holter monitoring results are displayed in Table 2. Despite a subclinical increase in the heart rate, oral 7.5 mg/day minoxidil did not lead to hypotension, tachycardia, or impairment in the nighttime dip.

One participant referred to headache and nine hypertrichoses with oral minoxidil 5 mg/day which did not lead to treatment discontinuation. None of them presented any adverse effects like headache, tachycardia, dizziness, edema, or insomnia after increasing the dose to 7.5 mg/day.

These results reinforce the mild antihypertensive effects of oral minoxidil in normotensive individuals. However, we suggest that doses above 5 mg should not be considered the standard for hair loss treatment and should only be used in exceptional circumstances. In such cases, we recommend that clinicians increase the dose gradually rather than starting with higher doses. It is essential to consider that even very low doses (0.25 mg/day) of oral minoxidil have been associated with uncommon idiosyncratic but severe adverse effects, such as pericardial and pleural effusions.[6]

Table 1 Main clinical and demographic data from the 11 participants of the study.

Variables		Values
Age (years), mean (SD)		37.9 (7.7)
Weight (kg), mean (SD)		86.2 (13.7)
Ethnicity, n (%)	White	8 (73%)
	Brown	2 (18%)
	Black	1 (9%)
Concomitant use drugs, n (%)	Finasteride	2 (18%)

☆ Study conducted at the Clínica Sanabria, Campo Grande, MS, Brazil.

Table 2 Main results of 24 h Holter monitoring and 24 h ambulatory blood pressure monitoring of 11 adult males with androgenetic alopecia assessed before (T0), after 24 weeks (T24) of treatment with 5 mg/d oral minoxidil, and after 6-weeks (T30) of treatment with 7.5 mg/d oral minoxidil.

Variables	T0 (Pre-treatment)	T24 (5 mg/d)	T30 (7.5 mg/d)	p-value* (T0 × T30)	p-value* (T24 × T30)
Heart rate (24 h); bpm[a]					
Minimum	47.3 (7.4)	48.5 (6.4)	53.0 (5.5)	**0.009**	**0.024**
Average	72.6 (8.7)	75.7 (9.1)	81.3 (7.8)	**0.037**	0.067
Maximum	129.9 (15.8)	124.5 (11.1)	131.9 (17.5)	0.400	0.142
Extra-systoles (events per 24 h)[b]					
Supraventricular	3 (2–14)	4 (2–11)	2 (1–6)	0.300	0.302
Ventricular	0 (0–0)	0 (0–1)	0 (0–0)	0.416	0.330
Mean arterial pressure[#]; mmHg					
Daylong	90.4 (10.4)	87.0 (7.7)	89.9 (9.7)	0422	0.298
Awake	94.6 (11.2)	89.4 (8.6)	93.8 (9.8)	0.396	0.202
Sleep	77.8 (9.3)	76.9 (7.7)	80.0 (8.6)	0.337	0.338
Nighttime dip (%)	-15.6 (8.1)	-11.0 (6.3)	-14.9 (5.7)	0.372	0.136
≥ 10%	8 (73%)	3 (30%)	5 (50%)	0.096	0.016
Systolic blood pressure; mmHg[a]					
Daylong	124.1 (11.7)	121.4 (9.3)	124.9 (12.4)	0.416	0.377
Awake	127.9 (13.0)	123.5 (10.2)	128.9 (12.7)	0.368	0.268
Sleep	112.4 (11.1)	112.5 (9.3)	114.0 (10.8)	0.418	0.419
Diastolic blood pressure; mmHg[a]					
Daylong	73.6 (9.9)	69.8 (7.9)	72.4 (9.0)	0.335	0.301
Awake	77.9 (10.9)	72.4 (8.8)	76.3 (9.2)	0.291	0.202
Sleep	60.5 (8.9)	59.1 (8.4)	63.0 (8.7)	0.304	0.257

AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; LDL, Low-Density Lipoprotein; HDL, High-Density Lipoprotein.
[a] Mean (SD).
[b] Median (p25–p75).
[#] (2*diastolic pressure + systolic Pressure)/3.
[*] One-tailed p-value from generalized mixed model, corrected (post-hoc) by Šidák procedure.

This study provides additional follow-up data from a previous cohort. Although the sample size was modest, it did not hinder the detection of major cardiovascular trends among patients taking oral minoxidil 7.5 mg/day.

In conclusion, administration of minoxidil 7.5 mg/day for AGA in normotensive adults was well tolerated and resulted in a mild increase in heart rate, with no observed changes in blood pressure.

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Authors' contributions

Baltazar Dias Sanabria: Data collection, approval of the final version of the manuscript; manuscript planning; drafting and editing of the manuscript; critical review of the literature and critical review of the manuscript.

Yuri Chiarelli Perdomo: Data collection, approval of the final version of the manuscript; manuscript planning; drafting and editing of the manuscript; critical review of the literature and critical review of the manuscript.

Hélio Amante Miot: Approval of the final version of the manuscript; manuscript planning; drafting and editing of the manuscript; critical review of the literature and critical review of the manuscript.

Paulo Müller Ramos: Approval of the final version of the manuscript; manuscript planning; drafting and editing of the manuscript; critical review of the literature and critical review of the manuscript.

Conflicts of interest

None declared.

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The use of intravenous immunoglobulin as a rescue therapy for refractory parainfectious leprosy-related neuritis: a case series☆

Dear Editor,

Leprosy-related parainfectious immune-mediated damage to peripheral nerves can lead to permanent physical disabilities.[1] Leprosy Neuritis (LN) is an acute inflammation of the peripheral nerves that occurs in some cases of leprosy. The current treatment of choice is the use of immunosuppressive doses of corticosteroids. There is growing evidence that corticosteroids may not be sufficient for a considerable number of leprosy patients experiencing refractory LN.[2]

We report here a case series of patients diagnosed with LN refractory to systemic corticosteroids who were treated with Intravenous Immunoglobulin (IVIg) as a rescue therapy for recovering the function of peripheral nerves.

Patients were evaluated at the Dermatology Outpatient Clinic University Hospital of Brasília, Brazil from 2016 to 2022. All patients received IVIg for the treatment of refractory leprosy reactions. The study was approved by the Research Ethics Committee of the Faculty of Medicine of the University of Brasília (CEP-FM/UnB) (72312117.4.0000.5558).

All patients had a diagnosis of leprosy confirmed by 2 board-certified dermatologists following the World Health Organization (WHO) criteria supported by polymerase chain reaction as described elsewhere.[3] Prior to the prescription of IVIg, all patients were evaluated by a board-certified neurologist. Detailed clinical and laboratory evaluations were performed, including searches for tuberculosis, sexually transmitted infections and American trypanosomiasis. Those conditions represented exclusion criteria for the use of IVIg. We used the Universal Pain Assessment Tool (UPAT) for pain evaluation, which has a scale from 1 to 10, and the WHO Disability Grading System, which has a scale from 0 to 2. Sensitivity tests were performed using the Semmes-Weinstein monofilaments according to the recommendations of the Brazil Ministry of Health. Electroneuromyography was performed 1-week before and 1-month after the 5th infusion cycle of IVIg.

Six patients were enrolled (Table 1). In only two cases, slit skin smears and PCR results were both negative. Three patients were classified as having leprosy relapse (Table 1). All patients had a diagnosis of leprosy-related neuritis with acute nerve function deterioration diagnosed by serial simplified neurological evaluation and by specialized neurological evaluation.

All patients had received more than 3 cycles of prednisone for at least 6 months at a minimal starting dose of 1 mg/kg/day (Table 2). One patient also received high doses of IV methylprednisolone (N4). Four patients underwent surgical decompression of the affected peripheral nerves (neurolysis), and 3 also underwent transposition of the peripheral nerves. All surgical procedures occurred at least 2 months prior to the 1st IVIg infusion. They received adjuvant treatment with either pregabalin, gabapentin, duloxetine or opioids (codeine or methadone).

Despite therapy, the disease in all patients evolved with worsening pain complaints and sensitivity, and motor function impairment. All patients already had adverse events related to the use of corticosteroids, including Cushingoid facies and high blood pressure. Patient 3 experienced a rapid evolution of cataracts. One patient also presented with opioid use disorder.

The induction dose of IVIg (Gamunex, Grifols Therapeutics LLC, Los Angeles, USA) was 2 g/kg divided across five days for all infusion cycles. Infusions were repeated for 5 cycles at monthly intervals. Additional doses were prescribed depending on the clinical response. All patients started immunoglobulin infusions with adjuvant 1 mg/kg/day prednisone or equivalent doses, and dosages were tapered weekly according to the response.

The median time from diagnosis to the first IVIg infusion was 12 months (range = 6–60). All patients (including relapse cases) received the first multidrug therapy dose on the same day of leprosy diagnosis. All patients were followed up for at least 12 months after the first IVIg cycle.

☆ Study conducted at the Hospital Universitário de Brasília, Brasília, DF, Brazil.