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# Low dose oral minoxidil and the conundrum of cardiovascular complications

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## Abstract

In recent months, the general public has become more cognizant of the potential of oral minoxidil to promote hair growth; this was promulgated, in part, by an article published in the *New York Times* entitled, "An Old Medicine Grows New Hair for Pennies a Day, Doctors Say." Minoxidil was added to the pharmacologic armamentarium as an antihypertensive nearly 60 years ago and was found to trigger hypertrichosis in many patients, but its use dropped sharply as cardiologists observed a number of adverse cardiovascular events including ischemic heart disease, left ventricular hypertrophy, pleural effusions, and pericardial effusions. Studies in the realm of dermatology have explored the utility and safety of low dose oral minoxidil (LDOM) for management of alopecia. This article highlights potential clinical conundrums posed by these rare but severe cardiovascular complications and the importance of collaboration between cardiologists and dermatologists when employing this agent in patients with cardiorenal or cardiovascular risk factors.

*Keywords: alopecia, cardiac, effusion, hypotension, minoxidil, renal*

## Introduction

We read with great interest an article recently published in *The New York Times* entitled, "An Old Medicine Grows New Hair for Pennies a Day, Doctors

Say." In this article, dermatologists highlight the role of oral minoxidil to promote hair growth. Since then, we have observed our alopecia patients having an increased interest in this medication. Although its mechanism remains unclear, minoxidil is converted to minoxidil sulphate and appears to shorten the telogen phase while lengthening the anagen phase, thereby promoting hair growth [1,2].

## Discussion

Oral minoxidil was first used in 1965, employed by cardiologists to manage treatment-resistant hypertension [3]. The most common side effect, hypertrichosis, prompted development of topical formulations in the 1980s to address alopecia [2]. Topical minoxidil has demonstrated a favorable side effect profile and is accessible over the counter. In contrast, oral minoxidil is associated with a number of cardiovascular events based on studies performed in the 1980s and 1990s, including ischemic heart disease, pulmonary hypertension, ST-segment and T wave abnormalities, left ventricular hypertrophy, cardiac tamponade, pleural effusion, and pericardial effusion. Peripheral edema arises due to sodium retention, whereas pleural and pericardial effusions are considered idiosyncratic reactions [4]. If prescribed, minoxidil carries a black box warning highlighting these side effects [4]. Absolute contraindications for oral minoxidil include pheochromocytoma and pericardial effusion, whereas caution should be used in patients with

renal failure, post-myocardial infarction, congestive heart failure, and tachycardia.

Studies conducted in the realm of dermatology depict a different picture of oral minoxidil's safety. Low-dose oral minoxidil (LDM), ranging from 0.25mg to 5mg daily, has been used to treat androgenetic alopecia, telogen effluvium, lichen planopilaris, and adult alopecia areata [1,2,5]. The most commonly reported side effect was hypertrichosis. Cardiovascular side effects rarely occurred, with some experiencing lower extremity edema, hypotension, or tachycardia [1,2,5]. If lower extremity edema develops on LDM, dosage reduction or treatment cessation should be considered while other potential causes are ruled out. Despite this wealth of data, a few case reports have been published recently that describe cases of pericardial effusions, one arising in a woman who was otherwise healthy placed on minoxidil 0.25mg daily and another in a man started on minoxidil 2.5mg daily with known history of idiopathic pericardial effusion; in both cases, the patients' conditions resolved after discontinuation of LDM [6,7].

Several factors may contribute to the variability of side effects documented in the literature. Notably, the treatment of treatment-resistant hypertension entails the use of minoxidil at 10-40mg daily, a far higher dose than what has been studied for treatment of alopecia. In addition, patients with treatment-resistant hypertension have a number of comorbidities such as chronic kidney disease (CKD), hypertensive cardiomyopathy, diabetes, and coronary artery disease, which places patients at greater risk of developing pericardial effusions, conduction abnormalities, or other cardiovascular issues while taking minoxidil [3,4]. These comorbidities may not be as commonplace among patients being seen for hair loss. Lastly, the duration of treatment with low dose oral minoxidil (LDM) in

prior studies has ranged between three to 30 months; in actual practice, treatment duration with LDM may be much longer, if not indefinite. Effusion may be idiosyncratic and it is unclear if treatment duration is associated. Despite this, prior studies have documented both development and spontaneous resolution of pericardial effusions while on minoxidil [1].

## Conclusion

Although the data in the dermatology literature demonstrates that LDM, is safe, effective, and well-tolerated, dermatologists must be aware of potential cardiovascular side effects. Shared decision-making between patient and provider and screening for patients with cardiovascular disease or other comorbidities may mitigate the risk of adverse cardiovascular events. Collaboration between cardiologists and dermatologists may help to risk stratify patients with cardiovascular disease for whom LDM's safety may be uncertain. If minoxidil is pursued, dermatologists should screen for symptoms such as dyspnea and edema; manifestation of these symptoms may prompt cardiovascular evaluation and either dose modification or discontinuation of minoxidil. Caution must be exercised when considering this agent for patients with CKD or end-stage renal disease, as there is a paucity of data illustrating LDM's safety in this patient population. Future larger scale studies can assist with quantification of the risks of these adverse events, creation of potential screening recommendations, and ultimately, with shared decision-making.

## Potential conflicts of interest

The authors declare no conflicts of interest.

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