

# Drug-induced Diffuse Hair Loss in Females: An Observational Study

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## Abstract

**Introduction:** A large number of drugs may interfere with hair cycle and produce diffuse hair loss (DHL). This needs to be identified, as it may lead to poor compliance with the drug regimen. **Material and Methods:** History of drug intake in the recent past was taken from 255 females presenting with DHL. Sixty-seven patients (26.2%) revealed a history of drug intake. Out of these, a detailed history about nature and duration of drugs was taken from 57 patients (22.3%) who had a history of drug intake preceding the onset of DHL or had a history of aggravation in preexisting hair loss following drug intake. **Results:** Duration of DHL ranged from 1 month to 5 years with a mean duration of  $9.8 \pm 13.1$  months. The mean duration of drug intake was  $49.1 \pm 80.8$  months. History of intake of 100 suspected drugs was available, most common group being antihypertensives (23%), followed by hormones (12%), nonsteroidal antiinflammatory drugs (11%), antidiabetic (8%), oral contraceptive pills (6%), antitubercular treatment (5%), tricyclic antidepressants (4%), and vitamin supplements (4%). Among individual drugs, thyroxine (10%) was the most commonly implicated agent followed by amlodipine (5%), Amitriptyline (4%), atorvastatin, aspirin, metformin, ibuprofen, and vitamin B complex (3% each). **Conclusions:** Drugs should be suspected as a cause of DHL in females and a detailed history about the nature and duration of drug intake should be taken in such patients.

**Key words:** Diffuse hair loss, drug induced, alopecia, telogen effluvium

## INTRODUCTION

Drug-induced hair loss is commonly associated with chemotherapeutic agents. It can be either telogen effluvium or anagen effluvium. Rarely drugs can be the cause of cicatricial alopecia. Telogen effluvium is common and caused by a long list of drugs. Anagen effluvium is almost exclusively caused by cytotoxic drugs. The extent and severity of alopecia depend on the drug as well as on the individual's predisposition.<sup>[1]</sup> Drugs that have been reported to induce hair loss include lipid modifying agents, anticoagulants, antineoplastic agents, antiretrovirals, oral contraceptives, GnRH agonists, antidepressants, anxiolytics, retinoids, antiepileptics, antithyroid drugs, beta blockers, serotonin uptake inhibitors, interferons, etc.<sup>[1]</sup> Diagnosis of the drug-induced alopecia remains difficult. The only way to confirm this is to observe whether or not any improvement occurs after discontinuation of the suspected drug. However, the list of drugs suspected of causing diffuse hair loss (DHL) is long. Owing to this lacuna, only few drugs have been confirmed to cause hair

loss. Telogen effluvium usually resolves spontaneously, but discontinuing the causative drug may not improve hair thinning. Finasteride or topical minoxidil have been used for hair regrowth, with variable results.<sup>[1]</sup> The list of drugs causing DHL is ever increasing. No studies are available to determine the list in our population.

## MATERIALS AND METHODS

History of drug intake in the recent past was taken from 255 females presenting with DHL. Sixty-seven patients (26.2%) revealed a history of drug intake. Candidates fulfilling the following inclusion criteria were included in the study:

- History of drug intake preceding the onset of DHL.
- History of aggravation in preexisting hair loss following drug intake.

Patients with female pattern hair loss, cicatricial alopecia, and with any other known cause of hair loss were excluded. Clinical examination was done to look for patchy or diffuse alopecia. Hair loss at other sites was also looked for. Finally, 57 patients (22.3%) were enrolled and a detailed history about nature and duration of drug intake was taken subsequent to their informed consent.

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## RESULTS

Duration of DHL ranged from 1 month to 5 years with a mean duration of  $9.8 \pm 13.1$  months. The mean duration of drug intake was  $49.1 \pm 80.8$  months. History of intake of 100 suspected drugs was available, most common group being antihypertensives (23%), followed by hormones (12%), nonsteroidal antiinflammatory drugs (NSAIDs; 11%), antidiabetic (8%), oral contraceptive pills (OCPs) (6%), antitubercular treatment (5%), tricyclic antidepressants (4%), and vitamin supplements (4%) [Table 1]. Among individual drugs, thyroxine (10%) was the most commonly implicated agent followed by amlodipine (5%), Amitriptyline (4%), atorvastatin, aspirin, metformin, ibuprofen, and vitamin B complex (3% each) [Table 2].

Acute hair loss was defined as hair loss lasting up to 6 months or less. Eleven drugs caused acute hair loss. Hair loss which lasted more than 6 months was defined as chronic hair loss. Eighty-nine drugs caused chronic hair loss.

## DISCUSSION

Among the various known causes of hair loss in females, drug-induced hair loss is one of the most neglected cause. It may be worrisome for the patient and may also lead to poor compliance with the treatment. Drug-induced hair loss is usually reversible.<sup>[2]</sup>

Anagen effluvium is almost exclusively seen after intake of cytotoxic drugs. Hair shedding is usually acute and severe and may produce loss of most of the scalp hair, eyebrows, and eyelashes. We did not encounter such patients in our study. Telogen effluvium is the most common form of hair loss induced by drugs and is characterized by excessive shedding of telogen hairs. Drugs can induce telogen effluvium through three different mechanisms:

1. By precipitating the follicle into premature rest.
2. As a consequence of discontinuation of drugs that prolong the duration of anagen, for example, topical minoxidil and oral contraceptives.

3. Premature detachment of the club hair from the follicles with shortening of the normal telogen phase, for example, retinoids.

Drug-induced diffuse telogen hair loss usually starts 6–12 weeks after the start of treatment and is progressive while the drug is continued.<sup>[3,4]</sup> It is most commonly a result of immediate anagen release.<sup>[5]</sup> Patients complain of increased hair shedding, which may be associated with scalp paresthesia or pain (trychodinia). Daily hair shedding is variable, but usually ranges between 100 and 150. The diagnosis of drug-induced telogen hair loss is made by demonstrating compatible chronology of drug exposure and the onset of the hair loss, and exclusion of the other causes of alopecia. Shedding can recur with drugs that are chemically unrelated, suggesting that true cross-reactivity is rare, and individual susceptibility exists to drug-induced telogen effluvium. Chronic telogen effluvium and androgenetic alopecia are important differential diagnoses. In our study we observed this type of hair loss as patients reported hair loss 2–3 months after intake of drugs.

The most common group of drugs responsible for hair loss in our study was antihypertensives. Atenolol and metoprolol were implicated in 2% patients each in our study. Propranolol and nebivolol were implicated in 1% patients each. Propranolol<sup>[6-8]</sup> and metoprolol<sup>[9]</sup> may produce diffuse alopecia by causing telogen effluvium. Atenolol and nebivolol, are from the same group, can lead to hair loss by similar mechanism, although in literature we could not find any report of hair loss due to these drugs. Similarly for thiazide diuretics we did not find any evidence, while in our study thiazide diuretics were implicated in 2% and hydrochlorthiazide in 2% patients. One patient was on ramipril. Captopril<sup>[3,10]</sup> and ramipril<sup>[11]</sup> have also been implicated for causing hair loss. Five patients in the present study were on amlodipine.

DHL has been described in females taking OCP.<sup>[12]</sup> In some cases, transient hair loss is seen 3–5 months after beginning of treatment with oral contraceptives. Interruption of oral

**Table 1: Class of Drugs Responsible for Diffuse Hair Loss**

Drugs	Number of patients (n=100)	Percentage	Drugs	Number of patients (n=100)	Percentage
Antiandrogen	1	1.0	Immunosuppressives	2	2.0
Antianxiety	1	1.0	Laxative	1	1.0
Antibiotics	2	2.0	LT antagonist	1	1.0
Antidiabetic	8	8.0	Mineral supplement	1	1.0
Antihypertensive	23	23.0	NSAIDS	11	11.0
Antispasmodic	1	1.0	OCP	6	6.0
ATT	5	5.0	Phenothiazine	1	1.0
Benzodiazepine	1	1.0	PPI	3	3.0
Betahistine	1	1.0	Retinoids	1	1.0
CCB	1	1.0	Treatment for asthma	1	1.0
CNS depressant	1	1.0	Treatment for gout	1	1.0
H1 antihistamines	2	2.0	SSRI	1	1.0
Homeopathic med	1	1.0	TCA	4	4.0
Hormone	12	12.0	Vitamin supplement	4	4.0
Hypolipidemic	2	2.0	Total	100	100.0

**Table 2: Individual Drugs Responsible for Diffuse Hair Loss**

Drug	Number of patients (n=100)	Percentage	Drug	Number of patients (n=100)	Percentage
Unknown	9	9.0	Metformin	3	3.0
Alprazolam	1	1.0	Metoprolol	2	2.0
Amitriptyline	4	4.0	Metronidazole	1	1.0
Amlodipine	5	5.0	Monteleukast	1	1.0
Aspirin	3	3.0	Nebivolol	1	1.0
Atenolol	2	2.0	Nimesulide	1	1.0
Atorvastatin	3	3.0	OCP	5	5.0
ATT	5	5.0	Olmesartan	1	1.0
Clonazepam	1	1.0	Ormeloxifene	1	1.0
Clopidogrel	1	1.0	Pioglitazone	1	1.0
Cyclosporine	1	1.0	Prednisolone	1	1.0
Diclofenac	1	1.0	Prochlorperazine	1	1.0
Doxycycline	1	1.0	Progesterone	1	1.0
Esomeprazole	1	1.0	Propranolol	1	1.0
Fenofibrate	1	1.0	Rabeprazole	2	2.0
Finasteride	1	1.0	Ramipril	1	1.0
Flunarizine	1	1.0	Ranitidine	2	2.0
Fluoxetine	1	1.0	Sodium picosulphate	1	1.0
FSH	1	1.0	Telmisartan	1	1.0
Glimipiride	1	1.0	Thiazide	1	1.0
Hydrochlorothiazide	2	2.0	Thyroxine	10	10.0
Hyoscine	1	1.0	Vertin	1	1.0
Ibuprofen	3	3.0	Vitamin D	1	1.0
Iron	1	1.0	Multivitamin	3	3.0
Isosorbide dinitrate	2	2.0	Zolpidem	1	1.0
Isotretinoin	1	1.0	Total	100	100.0
Losartan	1	1.0			

contraceptive therapy is also frequently followed by telogen effluvium. This is because the estrogens contained in oral contraceptives prolong anagen duration and synchronize the hair cycle, which is followed by a transition into telogen of a large number of follicles after estrogen interruption.<sup>[13]</sup> In our study, five patients had a history of OCP intake. A total of 12% patients had diffuse hair fall due to other hormones. Ten patients in the present study had a history of thyroxine intake, however, in the literature it has rarely been reported to cause DHL.<sup>[1]</sup>

Chronic high dose aspirin ingestion may cause iron deficiency anemia, which may result in hair loss.<sup>[14]</sup> Ibuprofen,<sup>[15]</sup> naproxen, and indomethacin may also cause hair loss.<sup>[16]</sup> In our study, 11 patients were on NSAIDs. Three patients were on aspirin and ibuprofen each. One patient was on diclofenac.

Metformin has been associated with DHL.<sup>[17]</sup> Other antidiabetics have not been associated with DHL. In the present study, eight patients were on antidiabetics, three patients were on metformin, one patient was on glimepride and pioglitazone each.

Antitubercular therapy (ATT) can cause DHL.<sup>[18]</sup> Five patients in our study were on ATT. Isoniazid has been known to cause DHL occurring a month after the initiation of therapy.<sup>[19]</sup>

Antibiotics though uncommonly implicated drugs for hair loss;<sup>[20]</sup> in our study, seven patients related it to antibiotics. Mild

hair loss is frequent in patients taking vitamin supplements containing vitamin A.<sup>[1]</sup> In the present study, three patients were on multivitamins and one patient on vitamin D. A dose-related diffuse telogen hair loss is common with etretinate<sup>[21]</sup> and acitretin, but less common with isotretinoin. The retinoids appear to cause a telogen anchorage defect and reduce the duration of anagen. One patient in the present study who was on isotretinoin reported hair loss. Atorvastatin can cause DHL.<sup>[22]</sup> It can induce diffuse alopecia probably because of a defect in keratinisation.<sup>[23]</sup> Three patients in our study were on atorvastatin and one patient was on fenofibrate. Fluoxetine, which is the most commonly implicated antidepressant for telogen effluvium, was implicated for DHL in one patient in our study.<sup>[24]</sup> Tricyclic antidepressants are uncommonly reported to cause DHL.<sup>[1,20,25]</sup> Four patients in our study had a history of Amitriptyline intake. Cimetidine is an uncommonly reported cause of DHL.<sup>[20]</sup> In our study, two patients were on ranitidine.

The diagnosis of drug-induced hair loss is difficult to prove. Since, it is not always possible to discontinue the implicated drug and follow up the patient for adequate period of time (2–3 months) to see for normalization of hair loss. The literature features a large list of probable drugs but lacks proper studies to confirm these findings precisely because of this reason. Our study was an attempt to search for a list of drugs that can be looked for in cases of suspected drug-induced hair loss. But,

our study also suffers for this inherent drawback of lacking any confirmation. It is important to identify the drugs that cause hair loss. Hair loss following the drug intake may cause anxiety to the patient and may lead to cessation of therapy. A proper counseling of the patient of the likely possibility of hair loss following the drug intake and the reversibility in most of the cases may produce better compliance with the regimen.

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