

## A Case Report on Alprazolam Induced Pedal Edema

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### Abstract

Alprazolam induced pedal edema is a rare entity. Alprazolam acts at several sites within the central nervous system, including the limbic system and reticular formation effects which may be mediated through GABA (A) sub unit receptor system where by leading to increase in neuronal membrane permeability to chloride ions enhances the inhibitory effects of GABA. We report a case of a 70 year-old-female patient with complaint of difficulty in breathing, tiredness and palpitations. She was later diagnosed with congestive heart failure. On the third day patient had complaint of difficult in sleeping and was prescribed alprazolam.

The following day, during the ward round, odema was reported and alprazolam was stopped and reported as an ADR through spontaneous reporting form of an adverse drug reaction. During Hospitalization the Prognosis of the patient to withdrawal of the causative agent was done and the Patient her swollen left leg, managed with loop diuretic. Hence forth we report a rarely incidence of alprazolam inducing pedal edema.

**Keywords:** Incidence; Alprazolam; Pedal edema; Adverse Drug Reaction

### Introduction

Alprazolam induced pedal edema is a rare entity. Alprazolam acts at several sites within the central nervous system, including the limbic system and reticular formation effects which may be mediated through GABA (A) sub unit receptor system where by leading to increase in neuronal membrane permeability to chloride ions enhances the inhibitory effects of GABA.

### Case Report

A 70-year-old female Patient was admitted to Female Medical ward at Government Hospital with complaints of difficult in breathing, tiredness and chest pain.

However, her medication history were not identified.

The patient was diagnosed with congestive heart failure. On the first day patient was prescribed with tablet digoxin 0.25 mg,

injection cefotaxime, injection gentamycin. On the second day patient was added up with injection deriphyllin for her complaint of breathlessness. On the third day patient had complaint of difficult in sleeping and was prescribed with alprazolam, initially the patient pedal edema was not present on the time of the admission the following day during the ward rounds, patient had aggravating severe pedal edema and because she was class II stage diagnosed heart failure, her left leg presenting with pedal edema as shown in figure 1 and the main cause was ruled out and suspected drug for her pedal edema was detected.



**Figure 1:** Presentation of Left foot with pedal edema.

Alprazolam was stopped and reported as an ADR through spontaneous reporting form of an adverse drug reaction. During hospitalization the prognosis of patient to withdrawal of the causative agent was done and patient her swollen left leg was managed with combination of loop diuretic as well with the potassium sparing diuretic.

## Discussion

Drug induced edema is presently clinical manifestation caused by variously medication prescribed in patients [1]. Majority of

medication prescribed are NSAIDs medications, antihypertensive drugs, anticancer drugs and so on. Alprazolam is a benzodiazepine which is used for the management of anxiety including panic disorder, Alprazolam act by the binding to GABA sub unit A receptor which associate with binding into receptors at several sites within Central Nervous System including the limbic system and reticular formation effects may be mediated through GABA receptor system increasing in neuronal membrane permeability to chloride ions enhances the inhibitory effects of GABA the shift in chloride ions causes hyperpolarization and stabilization of the neuronal membrane [2].

Inspite of that some of the drug causing pedal edema have been reported with recently few literatures. However, researchers noted that this adverse event appeared to be dose dependent but also idiosyncratic as no predisposing features were identified in patients who did develop edema following drug induced edema. Furthermore, researchers concluded that development of edema resulted in extensive medical evaluation in some patients and was only minimal responsive to diuretic therapy [3]. Alprazolam acts at several sites within the CNS, including the limbic system and reticular formation effects which may be mediated through GABA (A) sub unit receptor system increase in neuronal membrane permeability to chloride ions enhances the inhibitory effects of GABA.

Despite of that there are few studies of the case report which has elaborated of the drug induced pedal edema for example on the use of dihydropyridine calcium blockers to cause pedal edema it is well to be known [4]. In our case study left leg pedal edema has been observed as an adverse drug reaction to a noticeable point of Alprazolam administration which is used for management of insomnia and inspite of that it is well documented with Food and Drug Administration to cause peripheral edema [5]. However mechanism of Alprazolam induced pedal edema it is not well understood, Although Leg edema might occur in systemic circulation and to local types as well. Systemic edema could be caused by congestive cardiac failure, renal failure, hypoalbuminemia or proteinuria [6].

There are many factors could cause above mentioned adverse drug reaction, into our patient we suggest that an incidence of edema due to alprazolam administration into her prescription which led to aggravating her pedal edema, despite the use of diuretics

which were prescribed later on after reporting the incidence. The probability assessment scale of adverse drug reaction was done according to Naranjo Scale Probability for assessment of Adverse drug Reaction (ADR) was found to be possible with the average score of +4 [7].

Naranjo Adverse Drug Reaction Probability Scale					
	Question	Yes	No	Do Not Know	Score
1.	Are there previous conclusive reports on this reaction?	+1	0	0	+1
2.	Did the adverse event appear after the suspected drug was administered?	+2	-1	0	0
3.	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4.	Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5.	Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	
6.	Did the reaction reappear when a placebo was given?	-1	+1	0	0
7.	Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8.	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9.	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10.	Was the adverse event confirmed by any objective evidence?	+1	0	0	+1
	Total Score				+4

**Table 1:** Scoring for Naranjo algorithm: >9 = definite ADR; 5–8 = probable ADR; 1–4 = possible ADR; 0 = doubtful ADR.

vention of drug induced pedal edema especially towards diagnosed patient with class two congestive heart failure. The main stay treatment of patient presented with pedal edema due to the drug induced is discontinuation of responsible drug. However, patient may be treated with combination therapy of diuretics as to improve the overall patient prognosis of drug induced pedal edema.

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