

# Clofazimine induced methemoglobinemia – Points to be focussed

Sir,

We read with great interest regarding a case report of clofazimine-induced methemoglobinemia: A rare incidence by Ahmed Asif *et al.*<sup>[1]</sup> The authors have very nicely pictured out the case with the utmost management that prevent the patient to recover from the dangerous situation. The authors have managed the acute ingestion of several tablets of suspected clofazimine capsules that have resulted in methemoglobinemia. This case report is an important signal regarding the suspected clofazimine overdosage that was not even documented in the drug information sources available with the manufacturer.<sup>[2]</sup> Being a country harboring 60% of leprosy cases globally<sup>[3]</sup> and getting treated with multibacillary blister pack, this type of adverse event should be carefully notified as clofazimine is the major component of the blister calendar pack.

Regarding this case, we try to add some valuable point that will help the reader to get insight regarding the leprosy problem and also this case scenario.

Regarding the ingestion of many tablets or quantity of drug is important in this case. Since, in the management of leprosy, we prescribe 300 mg capsule clofazimine once a month followed by 28 days with a dose of 50 mg of clofazimine for an adult case.<sup>[4]</sup> However, in the management of lepra reaction especially erythema nodosum leprosum, it is 300 mg per day in a divided dose of 100 mg tds for maximum of 12 months is the approved protocol.<sup>[5]</sup> Because in this case, the patient was also on prescribed prednisolone making a possible diagnosis of leprosy with reaction.

Because it is drug suspected case, a few emphases has to be made regarding the antihypertensive drugs and antidiabetic drugs also. Because the antidiabetic drug commonly prescribed in women is metformin as some derivative comes under sulphonamides.

Here, high-level suspicion of clofazimine is made. Generally, in country like India, managing leprosy case is mostly done at the government hospital set up only. Hence, if the patient got treated in government hospital, she might or should have been provided with blister calendar pack containing both dapsone and clofazimine and rifampicin. Only a few private practitioner in some parts of the country prescribing dapsone, rifampicin, and clofazimine separately in their routine practices. Hence, it

is difficult to know whether the patient have only consumed clofazimine or along with dapsone as there were lots of literature commenting on dapsone and methemoglobinemia.

The other important point suggesting the possibility of methemoglobinemia is the half-life of two drugs. Dapsone has a half-life of 20 to 30 h.<sup>[6]</sup> Hence, in this case, it corresponds more or less to the effect of dapsone as per the symptoms and its improvement with intervention. However, in the case of clofazimine, the half-life is 70 days.<sup>[7]</sup> Hence, if we suspect the event due to clofazimine, there will be also the additional risk of developing this abnormality frequently in the blood for the possible next 1 year as the drug may remain in the body because total elimination time takes around five half-life pharmacologically.

Further direction in this case or like this case in future is to calculate the concentration of clofazimine in blood and/or if possible in tissues because its half-life is in several days. This will definitely be helpful as this is the first case being reported and can be nicely correlated out.

Finally, another important thing that a physician should follow according to this case is the reporting of adverse drug reaction/event. Here, it is more thought as the reaction. Hence, it should be notified to the India pharmacopoeia commission (IPC Ghaziabad).<sup>[8]</sup>

In addition, from the Naranjo probability scale,<sup>[9]</sup> we are getting a score of 2 interfering “possible” causation. This should be reported, as the review of the literature in the past failed to reveal any publication of acute methemoglobinemia with the current situation.

This case report will definitely create awareness about the possibility of methemoglobinemia by clofazimine, and this will definitely help the primary care physician as they treat leprosy cases and treating emergency physician to suspect early in any stigmatized leprosy patients presenting with a history of unknown or suspected drug overdose and to manage successfully. Acute excessive ingestion of suspected clofazimine leading to methemoglobinemia should be borne in mind of Primary Health Centre (PHC) doctors when dealing with patients of unknown drug poisoning, especially something relevant with leprosy.

To conclude, if possible in future this patient needs a psychological and psychiatric opinion as we strongly suspect the patient may also tried for suicide because of her stigmatized illness.

### Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## Pugazhenthana Thangaraju<sup>1</sup>, Sajitha Venkatesan<sup>2</sup>

<sup>1</sup>Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), Raipur, Chhattisgarh, <sup>2</sup>Department of Clinical Division, Central Leprosy Teaching and Research Institute, Chengalpattu, Tamil Nadu, India

**Address for correspondence:** Dr. Pugazhenthana Thangaraju,  
Department of Pharmacology, All India Institutes of Medical  
Sciences (AIIMS), Raipur, Chhattisgarh, India.  
E-mail: drpugal23@gmail.com

## References

1. Asif A, Preetham C, Mahajyoti C, Nibedita M. Clofazimine-induced methemoglobinemia: A rare incidence. *J Family Med Prim Care* 2018;7:1573-5.
2. Overdosage information on lamprone. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2003/19500slr010\\_lamprone\\_lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2003/19500slr010_lamprone_lbl.pdf). Retrieved on 24/02/2019.
3. India contributes 60% of global leprosy cases. [https://www.who.int/neglected\\_diseases/news/India\\_massive\\_leprosy\\_case\\_detection\\_campaign\\_reaches\\_320\\_mill/en/](https://www.who.int/neglected_diseases/news/India_massive_leprosy_case_detection_campaign_reaches_320_mill/en/). Retrieved on 24/02/2019.
4. Multibacillary drug therapy Adult (MDT-A). <https://www.who.int/lep/mdt/regimens/en/>. Retrieved on 24/02/2019.
5. Clofazimine in Erythema Nodosum Leprosum. <https://www.who.int/lep/research/WHOenlguide.pdf?ua=1>.

Retrieved on 24/02/2019.

6. Zuidema J, Hilbers-Modderman ES, Merkus FW. Clinical pharmacokinetics of dapsone. *Clin Pharmacokinet* 1986;11:299-315.
7. Half life of clofazimine. <http://apps.who.int/medicinedocs/en/d/Js5511e/3.1.html>. Retrieved on 24/02/2019.
8. Adverse drug reaction reporting. <https://ipc.gov.in/PvPI/adr.html>. Retrieved on 24/02/2019.
9. Naranjo probability scale in adverse reactions. <https://livertox.nih.gov/Naranjoassessment.pdf>. Retrieved on 24/02/2019.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

### Access this article online

#### Quick Response Code:



#### Website:

[www.jfmpc.com](http://www.jfmpc.com)

#### DOI:

10.4103/jfmpc.jfmpc\_165\_19

**How to cite this article:** Thangaraju P, Venkatesan S. Clofazimine induced methemoglobinemia –Points to be focussed. *J Family Med Prim Care* 2019;8:1517-8.

© 2019 Journal of Family Medicine and Primary Care | Published by Wolters Kluwer - Medknow