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Role of ascorbic acid in the treatment of methemoglobinemia☆

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Dear Editor,

We read with great pleasure the recent article wrote by Toker et al in your esteemed journal.[1] We would like to share our experience of two similar cases on "Role of ascorbic acid in treating methemoglobinemia".

A-45 year old middle aged gentleman was diagnosed as a case of acute ITP 6 months back when he was evaluated for symptoms of epistaxis and melena. He was treated with pulse doses of methylprednisolone (1000 mg for 3 days) followed by oral steroid therapy (1 mg/kg). He responded dramatically with complete resolution of symptoms and recovery of platelet count. Later, steroids were tapered on follow up and he became drug free. Three months after completion of therapy, he relapsed with complaints of gum bleed and petechial spots all over the body. Laboratory evaluation revealed severe thrombocytopenia (6×10^6/L). In view of his past treatment history and good response to steroid therapy, he was again started on oral steroid therapy (1 mg/kg). However, unlike the previous episode there was a stunted response to steroids this time and hence alternative medications were considered.

Due to financial constraints, costlier immunosuppressive agents like azathioprine, mycophenolate, cyclosporine, immunoglobulins or rituximab could not be considered in this case. In view of poor finances and a normal G6PD status, he was started on Dapsone (300 mg/day) as a cheaper and possibly an effective alternative along with anti-fibrinolytic agents and platelet transfusions. Three days after starting Dapsone, patient complained of mild dyspnea on exertion. On examination, he was sitting comfortably with a RR of 22/min, with mild tachycardia (88/min) & subtle peripheral cyanosis. Pulse oximetry showed a decreased SpO_2 of 88% at room air. At the same time, arterial blood gas (ABG) analysis showed O_2 saturation of 99.5%. Chest auscultation findings and chest X-ray were normal. As the patient received tablet Dapsone for 3 days and there was mismatch of SpO_2 in ABG and pulse oximetery, possibility of Dapsone induced methemoglobinemia was kept. Co-oximetery showed MetHb level of 18.3%. Immediately, Dapsone was stopped and high flow O_2 inhalation was started. Due to unavailability of methylene blue, patient was treated with intravenous infusion of vitamin C (dose of 2 g/day). The mismatch of SpO_2 gradually improved, 4 days later SpO_2 by pulse oximetry was 98% at room air and 97.5% in ABG thereby suggesting resolution of acute insult. MetHb level was repeated on day 4 and day 7 of the vitamin C therapy which was 2.4% and 1.7% respectively confirming successful therapy with ascorbic acid. Patient is being planned for splenectomy for definitive therapy of ITP. Fig. 1

Similarly, we have recently published another case treated successfully with ascorbic acid.[2] Table 1 briefly describes details of all the cases plus another case recently reported by Reeves et al.[3] In the case reported by Reeves et al, oncologists gave rasburicase as an emergency drug without knowing G6PD status of patient thereby leading to methemoglobinemia.[3] Basic principle of screening tests for G6PD deficiency is the inability of cells from deficient individuals to convert an oxidised substrate to a reduced state. Results of this test is usually available within couple of hours and hence decision of using oxidising agents like rasburicase should be taken accordingly. Case of Toker et al is similar to ours in terms of same inciting agent (Dapsone) and unavailability of methylene blue during initial phase of therapy thereby relying on other alternative agents like ascorbic acid and hyperbaric O_2 therapy.[1] While author could arrange

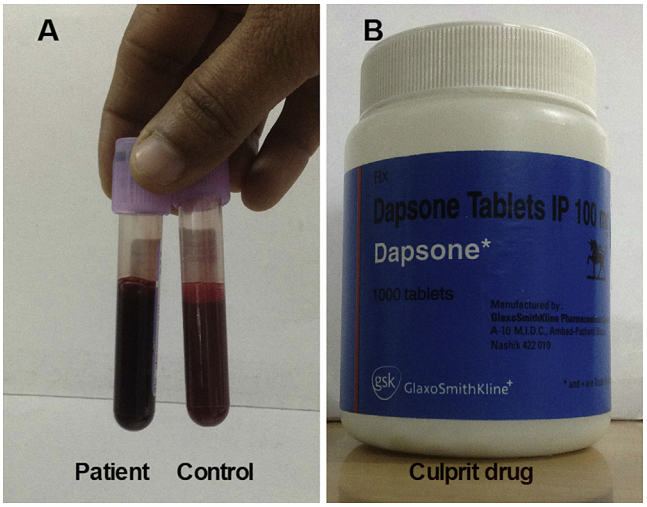

Fig. 1. A. EDTA vial showing chocolate brown colour of patient as compared to fresh red colour of a control sample. **B**. Inciting drug- Dapsone that caused methemoglobinemia.

☆ **Original article in response to which this letter to editor is being sent** – *Methemoglobinemia caused by dapsone overdose: Which treatment is best? Toker I1, Yesilaras M1, Tur FC1, Toktas R1: Turk J Emerg Med. 2016 Mar 9; 15 (4):182-4.* http://dx.doi.org/10.1016/j.tjem.2014.09.002. *eCollection 2015.*

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Table 1
Recent cases of methemoglobinemia managed with ascorbic acid.

Author	Age (Years)/ sex	Race	Baseline disease	Inciting drug	G6PD status	MetHb (%)	Dose of ascorbic acid used	Total dose of ascorbic acid used
Tokar et al[1]	34/M	–	Lichen Planus	Dapsone	NA	28.2	2 g × 1 dose	2 g
Reeves DJ et al[3]	46/M	African-American	Multiple myeloma	Rasburicase	Deficient	14.5	5 gm q 6 hrly (× 6 doses)	30 g
Deo P et al[2]	15/M	Asian (Indian)	Napthalene ball poisoning	Moth ball	Deficient	25.3	0.5 gm q 12 hrly (× 16 doses)	8 g
Present case	45/M	Asian (Indian)	Immune thrombocytopenia	Dapsone	Negative	18.3	1 gm q 12 hrly (× 14 doses)	14 g

methylene blue later from neighbouring city, we continued our patient on ascorbic acid and found good results in both of our cases.[1,2]

Purpose of writing this letter is to sensitise haematologists and oncologists regarding the importance of getting G6PD levels in cases where rasburicase and other similar drugs are planned to be used. Secondly, successful management of both the cases (present case and Toker et al case) suggests ascorbic acid as an alternative, cheap and easily available drug which can be used either as a bridging therapy till the time methylene blue could be arranged or as a sole agent when later is unavailable.

Ethical statement

The article doesn't contain participation of any human being and animal.

Conflict of interest

Authors have no conflicts of interest to declare.

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