Reviewer's report

Title: Benzocaine and Lidocaine Induced Methemoglobinemia After Bronchoscopy

Version: 2 Date: 30 September 2007

Reviewer: Melinda J Throm

I am familiar with the literature and believe that this case meets one of the 7 criteria for evaluation in the journal: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Comments to authors:

In general, this case report illustrates likely topical anesthetic or ‘caine’-induced methemoglobinemia. It is well written and flows logically. The discussion provides an adequate review of the pathophysiology, diagnosis, and treatment of methemoglobinemia.

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Although cases of moderate and severe cases of methemoglobinemia treated with methylene blue are well published in the literature, cases of mild methemoglobinemia not requiring treatment with methylene blue are less published in the literature and limited or no reports are reviewed in the Journal of Medical Case Reports. If the authors are able to better highlight what is unique about this case report, it may be more suitable for publication in the Journal of Medical Case Reports. In the discussion, the authors could focus on how to differentiate when to administer methylene blue vs. not.

The following comments may assist with the revision process:

Background section:
1) It is stated that methemoglobinemia is “uncommon” and “most often reported …when topical anesthetics are used during bronchoscopy…” Provide statistics/references supporting these statements. What is the incidence of methemoglobinemia with lidocaine vs. benzocaine?

Patient case section:

2) The 1st paragraph describes the patient. Include the patient’s race, weight, and baseline H/H. As certain ethnicities may be more predisposed to inherited vs. acquired methemoglobinemia and patient’s with baseline anemia are at a higher risk of developing more severe symptoms of methemoglobinemia, the author needs to establish risk factors for development of methemoglobinemia. As gold standard dosing of methylene blue is weight-based, include baseline weight. Although patient did not require methylene blue, still include weight.

3) 2nd paragraph, 3rd line: suggest change “done” to “performed.” 2nd paragraph, 6th line: Per JCAHO, #g is an unapproved abbreviation in the healthcare/hospital setting. If this patient was in the hospital, consider using microgram or mcg. 2nd paragraph, 7th line: consider adding “non-metered dose” Hurricaine (double check spelling) as newer topical anesthetics with metered dosing, have less risk of methemoglobinemia. As there are other medications that may cause methemoglobinemia, it is important to include other concomitant medications that the patient was receiving in order to establish the likelihood of caine-induced disorder. Author reviews other medications that may cause methemoglobinemia in the discussion section, so need to tie back to presented patient.

4) 3rd paragraph, clarify whether the oxygen saturation was via pulse oximetry, co-oximetry, or ABG. 3 paragraph, 3rd line, add ‘beats/minutes’ for heart rate units. Clarify why “uncomfortable” is in quotations.

5) 4th paragraph, oxygen administration rates should read 10 (add space) L/minutes. Change throughout patient case. Clarify if the oxygen saturation, methemoglobin level, and pH/PCO2, were obtained via pulse oximetry, co-oximetry, or ABG. Both co-oximetry (used to measure methemoglobin levels) and ABG require an arterial blood sample, whereas pulse ox is non-invasive. When the methemoglobin level is > 10%, pulse ox and ABG are inaccurate. Include what the color of the blood sample was since a ‘chocolate’ brown blood is characteristic of methemoglobinemia. If the color of blood was not noted for this patient, then state this.

6) 5th paragraph, state if the patient’s cyanosis resolved (ie. What was his coloring?). Also, clarify how the methemoglobinemia level was obtained (via co-oximetry?).

Discussion section:

7) 2nd paragraph, incorporate the incidence of inherited methemoglobinemia.

8) 3rd paragraph, incorporate the incidence of acquired methemoglobinemia. In Table 1, consider adding celecoxib and EMLA.

9) 4th paragraph, discuss the differences in the incidence of methemoglobinemia with lidocaine (only a handful of case reports) vs. benzocaine (numerous case
reports). Also, discuss pharmacologic differences between the two agents (benzocaine more lipophilic; therefore, may require repeat doses of methylene blue, prolonged duration). Define what is considered an elderly patient (age > x years). Is this patient truly elderly at age 62 years? Discuss other risk factors for methemoglobinemia ie. Anemia at baseline/concomitant disease states/concomitant medications/metered dose vs. non-metered dose topical anesthetics. This would be a good place to discuss the probability of caine-induced methemoglobinemia utilizing the Naranjo adverse drug event scale (Clin Pharmacol Ther 1981;30(20):239-45). Authors need to better establish the likelihood of caine-induced methemoglobinemia.

10) 5th paragraph, define what methemoglobin level/signs and symptoms are defined as mild methemoglobinemia.

11) 6th paragraph, discuss in more depth the tests used to diagnosis and monitor methemoglobinemia (pulse oximetry, co-oximetry, or ABG).

12) 7th paragraph, put more emphasis on how to differentiate when to administer methylene blue vs. not to administer. What is mild methemoglobinemia defined as? Are there any risks (side effects, contraindications) to administering methylene blue to patients with mild methemoglobinemia? This patient did not require the antidote, further justify why. State route of administration of methylene blue (slow IV push); at low doses acts as a reducing agent, at high doses (> 7 mg/kg) can act as an oxidizer and cause methemoglobinemia (Table 1).

13) 8th paragraph (conclusion), state if caine-induced methemoglobinemia is rare or common. Clarify if this patient is elderly.

If the authors are better able to illustrate the uniqueness of this case report, it would be more suited for publication.

What next?: Revise and resubmit

Quality of written English: Acceptable