# Hemopure: A Potential Option for Anemia in Jehovah's Witnesses

Anh Vu Le; Mohan S. Dhariwal, DO
Medical College of Wisconsin, Milwaukee, WI

## Learning Objectives

Learn about Hemopure, recognize its side effects, and examine its potential as an option for anemia in Jehovah's Witness unable to accept allogeneic blood transfusions.

## Case

A 70 year old Jehovah's Witness male with a history of HTN, T2DM, dyslipidemia, and peptic ulcer disease presents with a 3 week history of lightheadedness, malaise, dark urine, and scleral icterus. He was worked up by his PCP, found to be anemic and instructed to come to ED as soon as possible.

Exam

- Only remarkable for scleral icterus and jaundiced skin with no abdominal pain or tenderness

Pertinent Laboratory & Diagnostic Findings

- ED Workup on 3/19/15:
  - WBC 18.7, Hb/Hct of 5.1/18, total bilirubin 4.7
    - Hb 6.0 g/dL on 3/18/15
    - Hb 9.5 g/dL on 3/16/15
    - Hb 14.5 g/dL in Dec 2014
  - Positive DAT (Coombs) and IAT (antibody and serum) tests found to be consistent with warm antibody autoimmune hemolytic anemia
  - CT abd & pelvis: no evidence of malignancy, 3.0 cm AAA

Hospital Course - Highlights

- Hb continued to decrease from 5.1 to 4.8 g/dL over 10 hours and lactic acid increased from 1.2 to 3.1 over 24 hours. Patient declined blood transfusions given his religious beliefs. IV steroids, folic acid, iron EPO were started
- Hemopure was recommended and clearance was obtained through the manufacturer and FDA for "compassionate use." Patient consented after discussing with religious leaders
- Splenectomy was considered but not viable given patient's severe anemia
- After one week of Hemopure infusions, patient's hemoglobin improved but he developed progressively worsening dysphagia of unclear etiology
- Esophagram #1 showed a "bird's beak" appearance suggesting achalasia as a cause of his dysphagia (see Fig. 1a-b), and this was later confirmed by esophageal manometry.
- Bone marrow biopsy: hypercellular bone marrow, no evidence of hematologic malignancy
- Hemopure infusion was stopped after Hb/Hct had stabilized and it appeared maximal benefit had been achieved.
- Patient's dysphagia gradually improved after stopping his Hemopure infusion
- He underwent successful partial splenic artery embolization
- Repeat esophagram 11 days after stopping infusion showed resolution of the previously seen achalasia (see Fig. 2c-d)

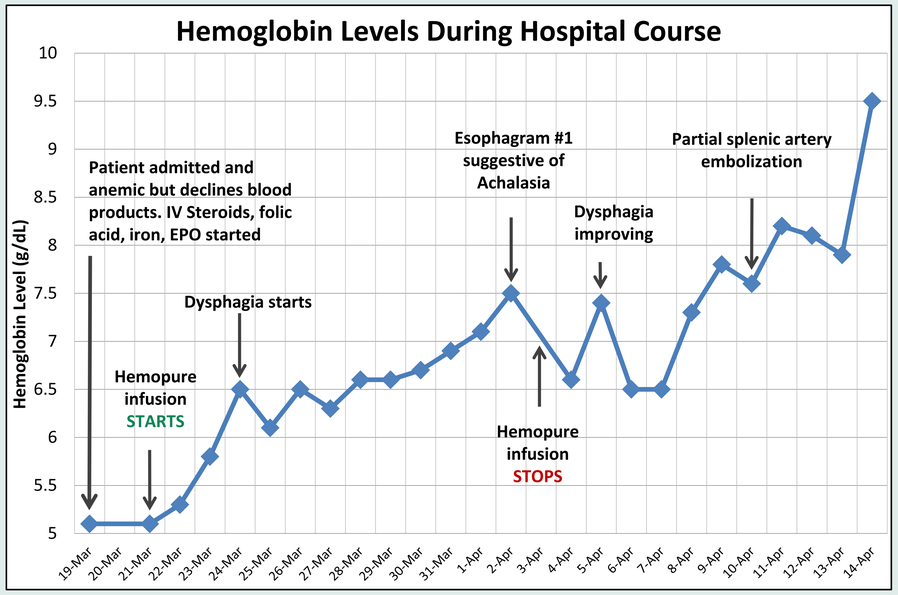



**Fig. 1a-b Esophagram 12 days after STARTING Hemopure infusion**

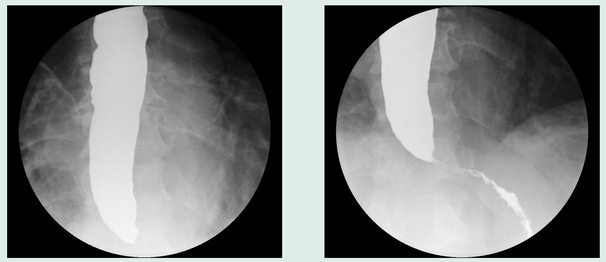
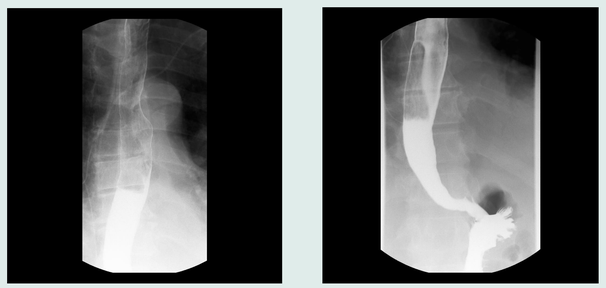


**Fig. 2c-d Esophagram 11 days after STOPPING Hemopure infusion**



Patient Follow Up:

| | 4/21 | 5/8 | 6/1 | 6/15 | 7/15 | 8/19 |
|---|---|---|---|---|---|---|
| **Hb** (g/dL) | 9.6 | 10.7 | 13.5 | 13.5 | 13.5 | 13.7 |

## References

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2. Gannon CJ, Napolitano LM. Severe anemia after gastrointestinal hemorrhage in a Jehovah's Witness: new treatment strategies. Crit Care Med 2002; 30:1893.
3. Cothren CC, Moore EE, Long JS, et al. Large volume polymerized haemoglobin solution in a Jehovah's Witness following abruptio placentae. Transfus Med 2004; 14:241.
4. Lanzkron S, Moliterno AR, Norris EJ, et al. Polymerized human Hb use in acute chest syndrome: a case report. Transfusion 2002; 42:1422.
5. Agrawal YP, Freedman M, Szczepiorkowski ZM. Long-term transfusion of polymerized bovine hemoglobin in a Jehovah's Witness following chemotherapy for myeloid leukemia: a case report. Transfusion 2005; 45:1735.
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## Discussion

**Hemopure (HBOC-201)**

Background information

- Hemopure is a bovine-derived hemoglobin-based oxygen carrier (HBOC) that is manufactured in the United States but not approved for use by the FDA. It is only available in South Africa and Russia. However, it is available for "compassionate use" for treatment of life-threatening anemia through an expanded access program which involves clearance through the manufacturer and FDA under an emergency investigational new drug (EIND).

Mechanism

- Bovine hemoglobin that has undergone polymerization binds and releases oxygen like human Hb but does not require 2,3-DPG. Instead, a chloride shift is used to right shift $O_2$ dissociation curve to ↑$O_2$ delivery to tissues [1].
  - Hemopure has Hb concentration 13 g/dL and half life 19 hours.

Side effects

- Methemoglobinemia, nitric oxide (NO) scavenging, vasoconstriction
- Interference with lab tests (e.g., albumin, bilirubin, LFTs)
- GI side effects (nausea, vomiting, diarrhea, dysphagia) – reported GI symptoms were mild to moderate and often did not require treatment
  - **Achalasia review**: Lower esophageal sphincter tone is normally regulated by the balance between excitatory (acetylcholine) and inhibitory (NO) neurotransmitters. Pathophysiology of achalasia involves the loss of inhibitory, NO-producing neurons
  - It is hypothesized that NO scavenging from Hemopure contributed to achalasia in this patient

Literature Review

- Reported cases where patients were successfully treated with a HBOC include: GI hemorrhage [2], abruptio placenta [3], acute chest syndrome [4], and chemotherapy-induced anemia [5]
- Most recently, a 19 y.o. female Jehovah's Witness with WAIHA and Hb 2.8 g/dL was successful transfused with 2 units of Hemopure to improved Hb of 8.7 g/dL 10 days later [6]

Future direction

- An expanded access study for HBOC-201 for the treatment of life-threatening anemia has been initiated in the United States, with completion of enrollment planned for December 2016 [7]

## Take Home Points

- Hemopure may serve as a potential bridging option in emergency situations for Jehovah's Witnesses who are unable to obtain human blood products
- The decision to use this product requires close monitoring of its potential GI side effects such as dysphagia and achalasia
- Each Jehovah's Witness patient should be treated on an individual basis without making any assumptions about their position on blood transfusions. They present unique but not impossible medical challenges.