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Letter to the Editor
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A Quantitative Approach to Dilutional Anemia

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To the Editor

Anemia amongst hospitalized patients is widespread, occurring in up to 75% of inpatients [1]. In addition to primary hematologic diseases, contributing factors include acute illness, phlebotomy and dilutional anemia [2]. In fact, intravenous fluids are given to a majority of inpatients at some point during their hospitalization [3], and studies on fluid resuscitation in sepsis highlight the significant effect of hemodilution on anemia [4, 5]. With increasing recognition of the risks of over-transfusion of red blood cells, properly identifying dilutional anemia is important for patient care [6, 7]. Clinicians may benefit from using a simple, quantitative approach to predict how much a patient's hemoglobin concentration will change from a given intravenous fluid load.

Consider the following scenario: a 44-year-old woman who weighs 60 kg with minimal past medical history is admitted with *Plasmodium falciparum* malaria. Her initial hemoglobin concentration is 12 g/dL. She is given 4 L of intravenous 0.9% normal saline and started on anti-malarial medications. The next morning, her hemoglobin has dropped to 9.8 g/dL. Is this a sign of hemolysis from severe malaria, or due to dilutional anemia from the fluid bolus?

The principle underlying this approach is that, in the absence of blood loss, total body hemoglobin is approximately constant over a 24-h period [8]. This fact can be used to account for changes in blood hemoglobin concentration following the steps outlined in Table 1 [9-12].

Thus, assuming no loss of blood, infusion of 4 L of normal saline into this patient would result in dilutional anemia to a hemoglobin concentration of approximately 9.6 g/dL. Her actual hemoglobin of 9.8 g/dL is well explained by dilutional anemia, and she does not appear to have had significant hemolysis from malaria.

This simple calculation can be applied to scenarios in which the clinician would like to quantitatively estimate what the hemoglobin concentration should be after an intravenous fluid bolus. A fundamental assumption of this calculation is that total body hemoglobin is constant; thus, true loss of hemoglobin would render it inaccurate. Additionally, the equation assumes typical distribution of intravenous fluids, which may be inaccurate in patients with increased capillary permeability and increased hydrostatic or decreased oncotic pressures. Significant isotonic urine or stool output leading to volume loss may attenuate this decrease in hemoglobin, which may be seen in those on high-dose diuretics or secretory diarrhea. Additionally, in patients with obesity or pregnancy, a weight-based calculation of total blood volume may be inaccurate and more nuanced calculations are recommended [11, 13, 14].

Applied in the correct clinical setting, this simple quantitative approach may help clinicians discern when a drop in hemoglobin concentration is related to intravenous fluids or a separate etiology.

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Not applicable.

Author Contributions

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Table 1. Four Steps for Quantitative Assessment of Dilutional Anemia

Step 1: Calculate initial total blood volume
Various calculations exist to estimate total blood volume in normal human subjects, without a clear gold standard. The simplest may be an estimation that blood volume equals 65 mL/kg of total body weight in women and 75 mL/kg in men [9-11].
Case: A 60-kg woman would be expected to have 60 kg × 65 mL/kg = 3,900 mL or 39 dL of total blood volume.
Step 2: Calculate total body hemoglobin
This is the provided hemoglobin concentration in g/dL multiplied by the total blood volume in dL
Case: Total body hemoglobin = 12 g/dL × 39 dL = 468 g hemoglobin
Step 3: Calculate expected post intravenous fluid bolus total blood volume
For every 1 L of normal saline, approximately one-fourth will stay in the intravascular space. For D5W, only one-twelfth will remain [12].
Case: 1) 4 L infusion of normal saline × 1/4 = 1.0 L increased intravascular volume; 2) New total intravascular volume = initial blood volume + intravascular volume from the infusion = 3.9 L + 1.0 L = 4.9 L or 49 dL
Step 4: Calculate the expected post-infusion hemoglobin concentration
Case: Expected post-infusion hemoglobin concentration = 468 g total body hemoglobin divided by 49 dL total blood volume = 9.6 g/dL

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References

1. Koch CG, Li L, Sun Z, Hixson ED, Tang A, Phillips SC, Blackstone EH, et al. Hospital-acquired anemia: prevalence, outcomes, and healthcare implications. J Hosp Med. 2013;8(9):506-512.
2. Thavendiranathan P, Bagai A, Ebidia A, Detsky AS, Choudhry NK. Do blood tests cause anemia in hospitalized patients? The effect of diagnostic phlebotomy on hemoglobin and hematocrit levels. J Gen Intern Med. 2005;20(6):520-524.
3. Lawson DH. Intravenous fluids in medical in-patients. Br J Clin Pharmacol. 1977;4(3):299-303.
4. Maiden MJ, Finnis ME, Peake S, McRae S, Delaney A, Bailey M, Bellomo R. Haemoglobin concentration and volume of intravenous fluids in septic shock in the ARISE trial. Crit Care. 2018;22(1):118.
5. Perel A. The relationship between the decrease in haemoglobin concentration and the volume of fluids administered during resuscitation from septic shock may not be so "weak". Crit Care. 2018;22(1):234.
6. Perel A. Iatrogenic hemodilution: a possible cause for avoidable blood transfusions? Crit Care. 2017;21(1):291.
7. Carson JL, Triulzi DJ, Ness PM. Indications for and adverse effects of red-cell transfusion. N Engl J Med. 2017;377(13):1261-1272.
8. Katchman BJ, Murphy JP, Offner KM, Fox JC. Measurement of total body hemoglobin by bloodless technic. Clin Chem. 1967;13(10):877-889.
9. Gibson JG, Evans WA. Clinical Studies of the Blood Volume. II. The relation of plasma and total blood volume to venous pressure, blood velocity rate, physical measurements, age and sex in ninety normal humans. J Clin Invest. 1937;16(3):317-328.
10. Feldschuh J, Enson Y. Prediction of the normal blood volume. Relation of blood volume to body habitus. Circulation. 1977;56(4 Pt 1):605-612.
11. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. Surgery. 1962;51(2):224-232.
12. Frost P. Intravenous fluid therapy in adult inpatients. BMJ. 2015;350:g7620.
13. Lemmens HJ, Bernstein DP, Brodsky JB. Estimating blood volume in obese and morbidly obese patients. Obes Surg. 2006;16(6):773-776.
14. Vricella LK, Louis JM, Chien E, Mercer BM. Blood volume determination in obese and normal-weight gravidas: the hydroxyethyl starch method. Am J Obstet Gynecol. 2015;213(3):408 e401-406.