Increased Electronic Mean Corpuscular Volume Induced by Marked Hyperglycemia

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ABSTRACT

A very high glucose level in a diabetic was associated with an increased electronic mean corpuscular volume (MCV). The hematocrit was falsely high and the mean corpuscular hemoglobin concentration (MCHC) falsely low, while the mean corpuscular hemoglobin (MCH) was normal. Blood smears failed to corroborate the abnormal indices. Correct values could be obtained by predilution of the blood in isotonic medium and allowing 10 to 15 minutes for equilibration. It is suggested that glucose in the cell produces a hyperosmolar state which results in the rapid diffusion of water into the cells in the counter. The phenomenon is dependent on the concentration of glucose to which the red cell is exposed. It is temperature dependent and it is rapidly reversible.

Introduction

The shape of the red cell is dependent upon a number of factors including the contractile forces within the membrane and the osmotic milieu. The mean corpuscular volume as measured electronically by the Coulter Counter is influenced by several phenomena. Cells as they enter the aperture of the counter displace sodium and chloride ions and create an electronic impedance proportional to the size of the cell. If cold agglutinins are present, pairs of cells or clumps of cells may pass through together producing a single count with a high MCV. If blood from an anemic patient with a high white count and large immature forms is counted, the large white cells will influence the MCV. In these cases, the finding of the agglutination in the blood tube as it cools to room temperature or examination of a smear for agglutination or large white cells will provide obvious clues to the artifact affecting the MCV. Recently, another phenomenon affecting the MCV came to our attention when a patient presented to the Emergency Department with an extremely high serum glucose.
Case Report

A 52 year old white male with a history of heavy ethanol intake for two to three weeks presented in a somnolent state. He had experienced nausea, vomiting, and diarrhea for two days and polyuria, polydipsia, tremulousness and somnolence for one day. Physical examination showed a dehydrated middle aged male with a pulse of 88 and a blood pressure of 180/100 (mm Hg). His liver was palpable 15 cm below the costal margin and he showed generalized muscle wasting.

Laboratory examination showed a serum glucose of 2250 mg per dl, a serum urea nitrogen of 25 mg per dl, a sodium of 127 mEq per liter, a potassium of 4.4 mEq per liter, a CO₂ of 28 mEq per liter and a chloride of 79 mEq per liter. Hematologic values showed a white count of 6900 per cu mm, a platelet count of 98,000, a hemoglobin of 11.7 g per dl, and a red cell count of 3.55 ml per cu mm with an MCV of 128 pi. The MCHC was 26 g per dl and the MCH was 33 pg per rbc. In spite of the indices showing an increased cell size and a low mean corpuscular hemoglobin concentration, examination of the blood smear showed no macrocytosis or hypochromia. Neither were agglutination nor large white cells observed. A microhematocrit, performed because of the discrepancies, was 37 percent.

The patient’s course (table I) was one of rapid improvement with the administration of sodium chloride infusion and insulin. As the serum glucose returned toward normal over the next few days, the MCV also returned toward normal and the electronic hematocrit decreased to match the microhematocrit on day nine.

To examine this phenomenon more closely, several experiments were performed using normal blood in EDTA.

Materials and Methods

Blood was obtained in EDTA vacutainers containing ethylene diamine tetraacetic acid from normal laboratory personnel or from patient samples with normal parameters. Pure glucose in powder form* was added to blood in various concentrations. Similarly, pure sucrose in pow-

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TABLE I

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<thead>
<tr>
<th>Patient Course</th>
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<tr>
<td>Day</td>
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<tr>
<td>Glucose</td>
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<td>MCV</td>
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<tr>
<td>Electronic hematocrit</td>
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<td>Manual hematocrit</td>
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MCV = Mean corpuscular volume

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* (Reagent Grade) Baker Chemical Co., Philadelphia, NJ.
† Coulter Industries, Hialeah, FL.
other parameters. Glucose was measured by kinetic method using hexokinase on the Dupont ACA.†

† Dupont Instruments, Wilmington, DE.

Results

Incubation of normal red blood cells with glucose 20 mg per ml (2000 mg per dl) for one hour produced an increase in MCV from 93 to 114. Longer incubations produced little change thereafter. Incubation of normal red blood cells with sucrose in equimolar concentrations 40 mg per ml (4000 mg per dl) for one hour or more produced no change in MCV (figure 1). The effect was easily reversed by diluting the glucose containing blood 1 to 200 in isotonic saline diluent* for 10 to 15 minutes (figure 2).

The increase in MCV was related to the concentration of glucose in which the cells were incubated from 500 to 2000 mg per dl (figure 3), and a greater increase in MCV was observed at higher temperatures (figure 4).

Discussion

These results demonstrate that an increase in electronically measured MCV is produced by a high ambient glucose level

* Isoton, Coulter Industries, Hialeah, FL. (Actual proportions 44.7 to 10 ml isoton using of Coulter S.)
either in vivo or in vitro, which is readily reversed by reducing the glucose concentration. Patients with serum glucose concentrations in the range of 1000 to 3000 mg per dl probably have red blood cells with a high intracellular glucose and a hyperosmolar state.2,8 Our studies suggest the MCV changes are directly related to the concentration of glucose in the serum, are temperature and time dependent, and are easily reversible.

The mechanism is not entirely dependent upon metabolic activity since it is not completely inhibited by cooling to 4°C. It is not yet certain whether the change in the electronic MCV is due to intracellular glucose causing rapid uptake of water during dilution and counting in the Coulter S or due to membrane bound glucose excluding ions from the vicinity of the membrane or some combination of both.

A number of studies have shown that glucose and water are rapidly taken up by the red blood cell.2,3,6,12 Rapid loss of glucose and water from the hyperosmolar intracellular space has been well documented.2 The rapid reversal of this phenomenon when red cells are diluted in isotonic medium indicates an easy leak of glucose from or through the cell membrane must occur.

The recent evidence that membrane proteins can be non-enzymatically glycosylated in diabetics9 and that specific receptors exist4,5 suggest that some glucose may bind to the external membrane of the cell displacing sodium and chloride ions in the immediate environment of the cells. Such displacement could possibly give the appearance of a large cell (increased MCV) in a measuring device dependent upon electronic impedance.

High serum glucose in diabetics must be added to the growing list of causes for an elevated MCV as determined by Coulter Counter. The computerized hematocrit will be falsely high, and the MCHC falsely low, while the MCH will be normal in patients with serum glucose around 1000 mg per dl. Correct values can be determined by manual methods or by diluting in isotonic medium for 10 to 15 minutes prior to determining the values electronically. Further work is necessary to define this phenomenon more accurately.

References

11. Unpublished observations by authors.