

Base Rate, Occam's Razor, and Hypoglycemia

Sir,

Recently, we encountered a patient with recurrent hypoglycemia. She was a middle-aged Punjabi woman, tall and hefty, who had presented elsewhere with seizure-like activity. The venous blood glucose during seizure was 40 mg/dl. On probing, the patient recounted several episodes of hypoglycemia for the last few months. Most of them occurred in the postprandial period, but a few were in the fasting state. The patient was diagnosed to have Sjogren's syndrome 2 years back. On examination, she had mild acanthosis nigricans. Her hemoglobin A1C was 6.1%.

Our initial differentials were autoimmune hypoglycemia and reactive hypoglycemia of prediabetes. Since hypoglycemia was recurrent, was severe, and happened in a patient with a known systemic autoimmune disease, we considered autoimmune hypoglycemia as the chief possibility. We subjected the patient to a standard 72-h supervised fast. The patient did not develop hypoglycemia during the first 48 h. Even more puzzling was the absence of ketonuria even after 48 h of fasting. Since this finding defied basic biochemistry, we reconfirmed the absence of surreptitious calorie intake.

As the supervised fast did not allow us to exclude endogenous hyperinsulinism, we did an extended glucose tolerance test with 100 g of glucose. Four hours after ingesting glucose, the patient developed hypoglycemia. The critical sample showed endogenous hyperinsulinism and absence of anti-insulin antibodies. Thus, we made the diagnosis of prediabetes leading to reactive hypoglycemia. The insulin resistance and the resultant "endogenous hyperinsulinism" perhaps explain the lack of ketonuria during fasting.

In the evaluation of hypoglycemia, the order of testing-supervised fast versus meal challenge is not emphasized.^[1] Of the causes

of postprandial hypoglycemia, reactive hypoglycemia is most common because of the sheer number of prediabetes patients. In our attempt to abide by the dictum of Occam's razor in medicine – of eschewing a double diagnosis when one would suffice (autoimmunity and reactive hypoglycemia vs. autoimmunity alone), we committed the fallacy of base rate neglect.

We ignored prior probabilities (of reactive hypoglycemia) when confronted with specific details about the patient (with a systemic autoimmune disease). As Tversky and Kahneman show in their seminal paper,^[2] this bias is common and has profound implications for medicine – common problems are more common even in patients with rare diseases. As an extension, a test that teases out the more common problem should be done first. Thus, in obese patients with hypoglycemia, it is preferable to do an extended glucose tolerance test first before the 72 h fast. This also has several practical advantages: glucose tolerance test is easier to do, does not require admission, and is well "tolerated" by the patients.

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Conflicts of interest

There are no conflicts of interest.

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