

## Correspondence

### A hemolysis trigger in glucose-6-phosphate dehydrogenase enzyme deficiency. *Vicia sativa* (vetch)

To the Editor

I read the interesting case report by Bicakci<sup>1</sup> on a hemolysis trigger in glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency: *Vicia sativa* (vetch). I have 3 comments regarding the aforementioned case report. First, Turkey is situated within the belt of geographical distribution of G6PD deficiency. Various epidemiological, clinical, and molecular characteristics of G6PD deficiency in Turkey have been delineated. Clinically, the precipitating factors of hemolysis were found to be variable. Rather than antimalarial and antipyretic-analgesic drugs, infections seemed to be the main hemolytic factor.<sup>2</sup> The aforementioned case report is interesting in that, it is the first reported case of vetch induced hemolytic episode in G6PD deficiency despite the vetch seeds being a popular dietary item in Turkey. I presume that many cases of vetch induced hemolytic episodes in patients with G6PD deficiency have occurred, but they were overlooked. This might be due to the following possibilities: 1) The diverse genetic variants of G6PD deficiency might entail different susceptibility to the hemolytic risk from various offending agents.<sup>3</sup> Thus, one agent might be safe in some G6PD deficient subjects but harmful in others. This might be applicable to vetch too. 2) It was demonstrated that co-inheritance of 2 or more abnormal red blood cell (RBC) genes in the same individual might modify the severity of clinical response to various inflicting agents.<sup>4</sup> Since the Turkish population has a substantial occurrence of abnormal RBC genes like sickle cell gene, G6PD, and ( $\alpha$  and  $\beta$ ) thalassemia,<sup>5</sup> such abnormal RBC gene interactions might determine the hemolytic response to vetch exposure. 3) The clinical severity of hemolysis might be so mild that it did not attract medical attention. 4) The common trend of attribution of hemolysis to the well-known triggering factors apart from vetch.

Second, the author stated that the hemolytic episode in the studied patient occurred after ingestion of a large quantity of vetch and postulated the effect to be dose-related. This seems questionable as drug induced hemolytic episode was found to exhibit the dose-related effect. Moreover, the available studies on the roles of vicine, divicine, convicine, beta-cyanoalanine glycosides, and isouramil, the main oxidants in the fava beans and vetch seeds, in inducing hemolytic episodes have not yet revealed a clear cut dose-related effect.

Therefore, additional studies are needed to determine whether vetch induces hemolytic episodes in patients with G6PD deficiency through a dose-related effect or idiosyncratic reaction.

Third, vetch (*Vicia sativa*) seeds can be certainly added to the plants list of fava beans (*Vicia faba*),<sup>6</sup> Henna (*Lawsonia inermis* Linn.),<sup>7</sup> herbal broth of Sinhala (*Acalypha indica*),<sup>8</sup> Sumac (*Rhus coriaria* L.),<sup>9</sup> and unripe peaches,<sup>10</sup> that were previously documented to be prohibited in patients with G6PD deficiency. In addition, pediatricians and internists need to consider regional plants as potential hemolytic triggers causing sudden onset of pallor or jaundice in those with both occult and overt G6PD deficiency.

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#### Reply from the Author

I agree with the opinion regarding the frequency of G6PD deficiency in our country, and that the lack of any report of hemolysis related with vetch may be due to the probabilities mentioned by Al-Mendalawi. However, vetch agriculture is most commonly performed in the underdeveloped rural areas. Research hospitals are generally found in developed regions where there is little vetch agriculture. Other reasons for the unreported hemolysis due to vetch include difficulty of transportation for rural people who suffer from vetch-related hemolysis and decreased admissions due to the disappearance of the symptoms of hemolytic anemia after some time. It is obvious that differentiation of the exact dose-effect relation with one case is very difficult. However, data regarding large consumption of the broad bean, which is a good oxidant, have shown that the levels of vicine and convicine that trigger hemolysis exposure, are increased. For this reason, increased hemolysis with increased bean intake suggests the probable relation between dose and hemolysis.<sup>11</sup> It is thought that vetch consumption can lead to hemolysis in patients with G6PD deficiency, just as bean consumption does, since vicine and convicine are found in equal amounts in vetch and beans, and the degree of hemolysis could be directly proportionally related to the amount of consumed vetch.<sup>12,13</sup> The amount of vicine, convicine, beta-cyanoalanine, divicine, and isouramil, which are found in the bean and vetch as oxidants, that would lead to hemolysis are unknown. Further investigations should be performed. For this reason, I agree with

the opinions of Al-Mendalawi. *Vicia sativa* should be added to the hemolysis triggerers' list in patients with G6PD deficiency, as Al-Mendalawi has mentioned. Furthermore, I completely agree with the suggestions and comments of Al-Mendalawi, and I thank him.

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