Henna causes life threatening haemolysis in glucose-6-phosphate dehydrogenase deficiency

P Raupp, J Ali Hassan, M Varughese, B Kristiansson

Abstract
Haemolytic crisis in glucose-6-phosphate dehydrogenase deficient individuals following topical application of henna occurred in four children: a female neonate (haemoglobin 50 g/l, serum bilirubin 700 µmol/l), who recovered after exchange transfusion; a male infant (haemoglobin 28 g/l) who died despite transfusion; and two preschool children (haemoglobin 40 and 41 g/l respectively).

Keywords: henna; lawsone; glucose-6-phosphate dehydrogenase deficiency; haemolysis

Case 1
A term baby girl, with family history of glucose-6-phosphate dehydrogenase deficiency (G6PD) deficiency and negative direct Coombs test required phototherapy for one day during the first week. G6PD screening (modified Beutler method; Sigma Diagnostics, St Louis, USA, procedure no. 203) was equivocal. At 20 days the mother applied henna to the baby's whole body. Lethargy and jaundice developed within 24 hours: haemoglobin (Hb) was 69 g/l, serum bilirubin (SBR) 455 µmol/l on admission. The Hb fell further to 50 g/l, and SBR increased to 700 µmol/l (conjugated 25 µmol/l) despite phototherapy. Intensive phototherapy and repeated exchange transfusions resulted in a Hb of 101 g/l, and an SBR of 296 µmol/l. Subsequently Hb stabilised, and SBR fell gradually. Phototherapy was discontinued 24 hours after the second exchange transfusion, and she was discharged the following day. Follow up (Hb was then 124 g/l).

Case 2
A term male neonate required phototherapy and was found to be G6PD deficient on screening. Although the parents had been instructed to avoid henna, the mother applied it to his palms and soles when he was 2 months old. Within 48 hours he passed red urine, became pale and jaundiced, and vomited; he was brought to hospital after two further days. He was in shock: arterial pH was 6.64, PaCO$_2$ 12 mm Hg, Hb 28 g/l, haematocrit 8.9%, leucocytes 31 200/µl, platelets 657 000/µl, reticulocytes 18%, lactate dehydrogenase (LDH) 2322 U/l, SBR 231 µmol/l, conjugated 1 µmol/l; liver enzymes were unremarkable. Blood and urine cultures remained sterile, thin and thick blood film for malaria were negative. Despite transfusions he remained anuric, developed notable uraemia with disseminated intravascular coagulation and cerebral seizures, and died two days after admission.

Case 3
A 3 year old boy with unremarkable family and past medical history had his soles soaked in henna. Three days later he started to vomit and became anaemic (Hb 71 g/l) and mildly jaundiced (total SBR 132 µmol/l, conjugated 7 µmol/l), without fever. Leucocytes, platelet count, and liver enzymes were normal. Within 24 hours he developed increasing pallor (Hb 41 g/l, haematocrit 12.4%, SBR 98 µmol/l, LDH 827 U/l), tachycardia, and poor peripheral perfusion. After transfusion his jaundice subsided, and his Hb remained stable. G6PD screening revealed deficiency, taken at the time of maximal haemolysis and after six weeks follow up (Hb was then 124 g/l).

Case 4
A 4 year old girl with unremarkable family history and past medical history had henna applied to palms and soles. Two days later she developed pallor (Hb 40 g/l, haematocrit 11.8%), jaundice (SBR 168 µmol/l), lethargy, and vomiting, without fever. Liver enzymes were normal and thin and thick film for malaria were negative. G6PD screening revealed deficiency, taken at the time of maximal haemolysis and after six weeks follow up (Hb was then 124 g/l).

Discussion
Ingestion of hazardous foods or drugs by the patients or their breast feeding mothers was denied, and it appears highly unlikely that unreported first exposure to other trigger substances coincided with first henna exposure. Fever or other evidence of acute infection was not observed. Naphthalene, usually inhaled from moth balls, has been identified as a frequent cause of haemolytic episodes in neonates, potentially fatal even for G6PD deficient adults. An important chemical ingredient of henna—a traditional cosmetic agent—is
lawsone (2-hydroxy-1,4 naphthoquinone). Its structure and redox potential is similar to 1,4 naphthoquinone, a metabolite of naphthalene and potent oxidant of G6PD deficient cells. Unexplained hyperbilirubinaemia observed in neonates exposed to henna led to the in vitro demonstration that lawsone is capable of causing oxidative haemolysis. G6PD deficient newborns admitted for hyperbilirubinaemia in Kuwait had significantly higher SBR and reticulocyte counts after exposure to henna. However, their haemoglobin concentrations were neither critical nor different from G6PD deficient babies without henna exposure. Life threatening consequences of henna application have only been described in Sudan, namely angioneurotic oedema associated with admixture of para-phenylenediamine to henna—not with haemolysis, and with a clearly different pathophysiological basis.

Our cases, collected over one year, suggest a life threatening potential of henna causing acute haemolysis in G6PD deficient children. Case 1 was presumably heterozygous with borderline G6PD activity and massive exposure to henna; this X linked disorder is not uncommon in girls, as a result of homozygosity, and heterozygosity with unequal inactivation of the X chromosomes. Furthermore, one third of all cases of haemolysis caused by naphthalene inhalation were seen in G6PD non-deficient neonates. The use of henna should be discouraged in infants in general, and in known G6PD deficient individuals of any age. Given the local popularity of henna and the failure of G6PD screening to detect most of the (equally susceptible) heterozygous neonates, public health education and universal G6PD screening will not prevent all cases of acute haemolysis caused by henna.

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