Transfusion Requirements of Patients with Enzyme Deficient Red Blood Cells

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ABSTRACT

Red cell enzyme deficiency disease states are reviewed to outline the requirements for transfusion therapy in the neonatal period, during spontaneous crises, drug or infection-induced crises and chronic anemia.

Transfusion of normally functioning red blood cells to replace red cell volume lost owing to hemolytic crises induced in patients with enzyme deficient red blood cells is frequently the only life-saving therapy available. The need for prompt diagnoses followed by appropriate therapy is best illustrated by the case history of such a patient.

Case History

B. R., a 24-year old, previously healthy, white male, was admitted with second and third degree burns on the face and neck covering an estimated 15 percent of his body. Prior to admission, sulfonamides were administered to ward off infection. In Table I are summarized laboratory findings during hospitalization. Abnormally-shaped red cells and intense hemoglobin staining of the serum associated with a fall in hemoglobin, were reported on the second hospital day.

The absence of red cell glucose-6-phosphate dehydrogenase (G-6-PD) was not appreciated. infection induced further hemolysis and renal failure ensued. Transfusion therapy, late in the patient's clinical course, could not reverse the fatal course lasting only five days.

This case illustrates the most serious complication of renal shut-down, following sudden, massive hemolysis. If the hemoglobin can be removed, there is still the need for red cell replacement by transfusion. G-6-PD deficiency has been predominantly found in Negroes where the usual outcome of hemolytic crises is spontaneous recovery. Caucasians are more severely affected and require more intense therapy.

Spontaneous recovery from hemolytic crises probably accounts for the lack of information in the literature pertaining to the effects of blood transfusions in patients with enzyme-deficient red cells. In red cell enzyme deficiency states, the administration of blood is determined by certain considerations. In the neonatal period, exchange transfusions are necessary for removal of excess bilirubin in an effort to prevent brain damage. Children and adults may need red cell mass restitution to assure adequate oxygen supply for tissue respiration. During hemolytic crises, shock may be treated by transfusion to prevent a fatal outcome. Chronic hemolytic states may result in bone marrow failure requiring transfusions to combat the ensuing anemia.
TABLE I
B.R. 24-Year Old White Male
15 Percent Burns Face and Neck
Glucose-6-phosphate dehydrogenase Deficiency

<table>
<thead>
<tr>
<th>Date</th>
<th>HB</th>
<th>HCT</th>
<th>WBC</th>
<th>FTR</th>
<th>PC</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-23</td>
<td>15.6</td>
<td>45.6</td>
<td>28.4</td>
<td>Dec</td>
<td>2</td>
<td>Run 19</td>
</tr>
<tr>
<td>12-23</td>
<td>15.7</td>
<td>46.7</td>
<td>26.6</td>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-25</td>
<td>11.9</td>
<td>32.1</td>
<td>9.8</td>
<td>Dec</td>
<td>2</td>
<td>Gross hemolysis</td>
</tr>
<tr>
<td>12-26</td>
<td>9.8</td>
<td>29.3</td>
<td>9.8</td>
<td>Dec</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-27</td>
<td>9.8</td>
<td>23.2</td>
<td>19.9</td>
<td>Dec</td>
<td>2</td>
<td>Marked Nuc. RBC's</td>
</tr>
<tr>
<td>12-29</td>
<td>9.3</td>
<td>28.0</td>
<td>20.6</td>
<td>Dec</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>12-28</td>
<td>9.3</td>
<td>28.0</td>
<td>20.6</td>
<td>Dec</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Fibrin split products - Negative
Haptoglobin = 30 mg per dl 12-28

No matter how beneficial transfusions are, much thought has to be given to the complications associated with this form of treatment modality. Known disadvantages have to be delicately balanced with their therapeutic effectiveness. More detailed discussion requires grouping of the enzyme abnormality.¹

Aerobic Enzyme Deficiencies

Aerobic enzyme deficiencies affecting the hexose monophosphate shunt (Table II) most likely encountered in clinical practice include G-6-PD, glutathione reductase (GSSG-R) and glutathione peroxidase (GSH-Px).¹,²,³,⁴,⁷,⁸,¹₀-¹⁵,¹⁶,¹⁷,¹⁸,¹⁹,²¹,²²,²³ Patients with both G-6-PD and GSH-Px deficiencies present with neonatal jaundice, leading to exchange transfusions. In a jaundiced infant where no blood group incompatibility can be demonstrated, red cell enzyme defects must be diligently searched for in order to explain the abnormal hemolysis and to plan future therapy. GSH-Px deficient infants require more frequently exchange transfusions than those with G-6-PD. In those geographic areas with populations of Mediterranean origin, severe neonatal jaundice of G-6-PD deficiency is encountered.¹⁹,²⁰

Adult hemolytic crises are seen in G-6-PD, GSSG-R and GSH-Px deficiencies having in common their induction by drugs and infections as the only mechanism. The study of red cell enzymes was initiated because of drug-related hemolytic crises during malarial prophylaxis and therapy. GSH-Px deficiency may present with spontaneous crises. Chronic hemolysis is seen in deficiencies of both GSSG-R and GSH-Px.

The little known association of serious crises and infection challenges the transfusionist. During childhood, respiratory infections are probably the most common illnesses inducing crises. In later years, illnesses range from Rickettsial²³ infections to the fairly common urinary tract infections or hepatitis.¹⁵ Since renal failure owing to the sudden hemolysis may be a major complication, early recognition of the disease and adequate normal transfusions is necessary. Table II is a summary of the transfusion requirements in red cell enzyme deficiencies.

TABLE II
Transfusion Requirements in Red Cell Enzyme Deficiencies Aerobic Enzymes (Hexose Monophosphate Shunt)

<table>
<thead>
<tr>
<th>Deficient Enzyme</th>
<th>Type of Hemolysis</th>
<th>Induced Crises</th>
<th>Transfusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose-6-phosphate dehydrogenase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutathione reductase</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Glutathione peroxidase</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Exchange + during adult life</td>
</tr>
</tbody>
</table>
red cell replacement by transfusion are
life-saving measures.

Enzyme deficiencies of the anaerobic
pathway (Table III) are pyruvate kinase
(PK), phosphohexose isomerase (PHI),
hexokinase (HK), triosephosphate isomerase
(TPI) and 2-3-diphosphoglycerate
mutase (2-3-DPGM).4,5,6,9,13,14,16,20,24
TPI and 2-3-DPGM do not present as
neonatal jaundice. Chronic hemolysis
necessitates continuous transfusion
therapy, even though death during in-
fancy is the usual outcome. PK, PHI and
HK require exchange transfusions. Dur-
ing childhood, the chronic hemolytic
state is especially severe in patients with
PK.4,6,9 The need to maintain adequate
hemoglobin levels by transfusion in-
duces iron overload. This secondary
complication must be considered, par-
ticularly in children before irreparable
tissue damage leads to liver cirrhosis.
Determinations of severe iron levels and
iron binding capacity are helpful in the
evaluation of the state of iron saturation.
Splenectomy has been shown to decrease
transfusion requirements, although the
mechanism involved is unclear.
Anaerobic enzyme deficient red cells
are not drug sensitive. Spontaneous
crises are only seen in PI which also
presents with crises following infec-
tion.5,13,14

Summary

Hemolytic states which are due to red
cells with enzyme deficiency may re-
quire transfusions. A thorough knowl-
edge of the clinical course of the disease
states caused by the enzyme defect is
necessary to initiate the most effective
red cell replacement with the least dam-
age to the patient.

References

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fi ciency in patients with non-spherocytic

Table III

<table>
<thead>
<tr>
<th>Deficient Enzyme</th>
<th>Type of Hemolysis</th>
<th>Induced Crises</th>
<th>Transfusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyruvate kinase</td>
<td>Yes</td>
<td>No</td>
<td>Exchange decrease after splenectomy</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Exchange + extensive Exchange</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>Exchange Yes</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>Exchange Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>Exchange Yes</td>
</tr>
<tr>
<td>Triosephosphate isomerase</td>
<td>No</td>
<td>Yes</td>
<td>Most patients die in childhood</td>
</tr>
<tr>
<td>2-3 DPG mutase</td>
<td>No</td>
<td>Yes</td>
<td>Die in childhood Yes</td>
</tr>
</tbody>
</table>


