2,3-Diphosphoglycerate in acute asthma

P. J. GALLAGHER

From the Biochemical Section, John Bonnett Clinical Laboratories, Addenbrooke’s Hospital, Cambridge

SYNOPSIS The blood levels of 2,3-diphosphoglycerate have been studied in 16 acute asthmatics and a group of healthy controls. No significant difference was found, but asthmatics had higher haemoglobin concentrations.

2,3-Diphosphoglycerate (23DPG) is one of the chief products of glucose metabolism in the red cells of man and many other animals (Rapoport and Guest, 1941). This compound is now known to play a vital role in promoting oxygen release from the erythrocytes to the tissues. This effect is produced by the preferential binding of 23DPG to deoxy haemoglobin (Benesch and Benesch, 1969). A recent review (Bunn and Jandl, 1970) has summarized the information on the binding site of 23DPG to haemoglobin and its accessibility in relation to the state of oxygenation.

This hypothesis has now been supported by the finding of an increased concentration of 23DPG in erythrocytes in a variety of hypoxic conditions. They include acclimatization to high altitude (Lefant, Torrance, English, Finch, Reynafarje, Ramos, and Faura, 1968), cyanotic heart disease and respiratory disorders (Oski, Gottlieb, Devivoria-Papadopulas, and Miller, 1969), and red cell mass deficits (Valeri and Fortier, 1969).

The present investigation has been concerned with 23DPG levels in acute asthma.

Patients and Methods

Sixteen longstanding adult asthmatics were studied. They were an unselected group presenting in acute relapse to the Admission Unit of Addenbrooke’s Hospital in a four-month (summer) period. The mean duration of symptoms was six days (range 12 hr to 28 days). A control group consisted of healthy hospital personnel.

Venous or arterial blood was drawn into anticoagulant (sequestrene or heparin). Aliquots of 0.02 ml were deproteinized with 6% perchloric acid, and neutralized with 5 N potassium carbonate. The 23DPG levels of this extract were estimated by an enzymatic method (Krimsky, 1963). All extractions and estimations were performed in duplicate.

Arterial gas analyses used standard Astrup technique and Radiometer electrodes. Arterial samples were taken only when required for the clinical management of the patient.

Haemoglobin was estimated as cyanmethaemoglobin.

Results

The findings in the asthmatic and control groups are compared in Table I. There is no significant difference in 23DPG levels between the two groups (p < 0.8). The asthmatic group had significantly higher haemoglobin concentrations than the group of controls (p < 0.005).

<table>
<thead>
<tr>
<th></th>
<th>Asthmatics</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Mean age</td>
<td>37.5</td>
<td>28.0</td>
</tr>
<tr>
<td>Mean haemoglobin ± SD</td>
<td>16.4 ± 1.4</td>
<td>14.8 ± 1.3</td>
</tr>
<tr>
<td>Mean 23DPG ± SD</td>
<td>1.00 ± 0.15</td>
<td>0.98 ± 0.19</td>
</tr>
<tr>
<td>Range 23DPG</td>
<td>0.74 – 1.21</td>
<td>0.66 – 1.39</td>
</tr>
<tr>
<td>SD of duplicate estimations</td>
<td>0.10</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Table I Details of asthmatic and control groups

Erythrocyte 23DPG concentrations expressed as moles per mole of haemoglobin.

There was no relationship between the subjective duration of the relapse in the asthmatics and their level of 23DPG. In particular, higher levels were not associated with a longer relapse. Patients on long-term steroid therapy had similar levels to other asthmatics.

The results in the six patients whom arterial gas tensions were estimated are summarized in Table II. These are detailed separately because hypoxia was confirmed objectively. The level of 23DPG in this group does not differ significantly from the remainder of the asthmatics (p < 0.8).
2,3-Diphosphoglycerate in acute asthma

<table>
<thead>
<tr>
<th>pH</th>
<th>Mean Value ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.39 ± 0.02</td>
<td>7.37-7.41</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>61 ± 16</td>
<td>39-84</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>48 ± 9</td>
<td>37-58</td>
</tr>
<tr>
<td>% O₂ sat</td>
<td>86 ± 7.5</td>
<td>74-94</td>
</tr>
<tr>
<td>23DPG</td>
<td>1.02 ± 0.16</td>
<td>0.79-1.21</td>
</tr>
</tbody>
</table>

Table II Details of six patients giving arterial blood samples

1Erythrocyte 23DPG concentrations expressed as moles per mole of haemoglobin.

Discussion

No single factor is known to regulate red cell 23DPG concentration. An increase in the proportion of deoxygenated haemoglobin and a rise in erythrocyte pH are both thought to trigger off an elevation of 23DPG, but the biochemical mechanisms are still far from clear (Bunn and Jandl, 1970).

Acute asthma is associated with hypoxia, hypercarbia, and a tendency to respiratory acidosis, and at least one of these was noted in all patients in this series on whom arterial gas analyses were performed. If the primary physiological adjustment to hypoxia includes a rise in red cell 23DPG it is surprising that no such change occurred in these asthmatics. Inadequate duration of hypoxia can hardly be desirable, because Lenfant et al (1968) found that a 50% rise in red cell 23DPG could occur within 36 hours of ascent to high altitudes. Perhaps in the present series an increase in haemoglobin has been the inadequate attempt at compensation.

Perusal of the literature might suggest that hypoxia of any cause is compensated by an increase of 23DPG levels with a corresponding decrease in oxygen affinity of the blood. However, this work emphasizes that not all such patients will show an elevation of 23DPG in erythrocytes. Therefore, complacency about the 'buffering effect' of this compound in facilitating oxygen release to hypoxic tissues must not be allowed to develop, particularly in acute asthma.

When a safe method of artificially raising red cell 23DPG levels becomes available asthmatics would seem ideal candidates for a therapeutic trial.

I am grateful to Professor H. Lehmann for suggesting this study, and to Dr E. C. Gordon-Smith (Department of Haematology, Hammersmith Hospital) for his tuition in the analysis of 23DPG.

References


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