Exchange Transfusion: An Extra Therapeutic Tool for Severe Pertussis

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Abstract

Background: *Bordetella pertussis* is a common, under-recognized, and vaccine-preventable cause of critical illness with a high mortality in infants worldwide. Severe pertussis is characterized by refractory hypoxemia, pneumonia, cardiogenic shock and requires intensive care. When pertussis is associated with hyperleukocytosis, mortality rate approaches to 80% with the degree of leukocytosis consisting an independent predictor of death. It is proposed that severe leukocytosis may contribute to pulmonary hypertension by blocking pulmonary capillaries and restricting blood flow.

Aims: To describe the use of exchange transfusion in pertussis as a safe and useful technique for reducing leukocyte mass.

Methods: A 2.5 month-old girl admitted to PICU due to an apnoeic cyanotic episode. Prior symptoms were cough, rhinitis and poor feeding for 10 days and *B. pertussis* had been detected by PCR on nasal secretions. She presented a second apnoeic cyanotic episode with bradycardia and was intubated. Due to severe and persistent hypercapnoea, she was ventilated in high frequency oscillatory ventilation with no amelioration. As she presented leukocytosis and hemodynamic instability with tachycardia, she underwent a double volume exchange transfusion through a central line, and white blood cells reduced from 72,000/μL to 19,000/μL. The benefits of the procedure were clear and immediate, as the respiratory parameters improved and the heart rate stabilized in normal range in less than 24 hours. Although the course of the infant was prolonged, the outcome was favorable.

Results: The patient was discharged without any neurological sequelae.

Conclusions: Exchange transfusion should be considered as a useful therapeutic tool in children with severe pertussis and severe leukocytosis before shock has occurred.

Keywords: Severe Pertussis; Exchange Transfusion; Hyperleukocytosis

Introduction

Pertussis (whooping cough) is an infection of the respiratory tract caused by *Bordetella pertussis*, a Gram-negative bacterial pathogen. Its main characteristic is severe and prolonged coughing [1] and it’s the fifth leading cause of vaccine-preventable deaths in children under 5 years of age [2]. Adolescent and adult patients are frequently not diagnosed, allowing them to spread disease to the healthy community (American academy of pediatrics). As a result, half of the infant cases were infected by parents or siblings whose immunity had waned 5 - 10 yrs after vaccination [3]. Estimates from WHO suggest that, in 2008, about 16 million cases of pertussis occurred worldwide, 95% of which were in developing countries, and that about 195,000 children died from the disease. The major risk factors for high mortality in whooping cough are (a) high white blood cell count, (b) severe pulmonary hypertension, (c) age less than 6 months, (d) prematurity, and (e) incomplete immunization (Thielen., *et al.* 2008).

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Severe pertussis, also known as critical pertussis, is characterized by refractory hypoxemia, cardiogenic shock and pneumonia associated with extreme leukocytosis, requiring intensive care treatment [4]. Mortality risk has been correlated with the degree of leukocytosis, a clear manifestation of pertussis toxin [5].

These findings, as well as the strongly established benefit of exchange transfusion in acute leukemia, another leukocytosis disease, have led Romano., et al to perform leukoreduction as an adjunctive therapy with favorable results, in 2004 [6]. Since then, this technique has been used in a few cases. In this article, we present a case of severe pertussis in which exchange transfusion was part of the treatment approach.

Case Report

A 2.5 month-old, 4.6 kg, white female infant, presented cough, rhinitis and poor feeding, 10 days before admission. Upon the onset of symptoms, she was prescribed inhaled salbutamol, fluticasone and a 2-day course of dexamethasone, all with minimal improvement. The patient was admitted to a local hospital with mild respiratory distress. Her physical examination was unremarkable. She had a WBC count of 49530/mm³, with 56.8% lymphocytes and 34.5% neutrophiles. A chest x-ray had no abnormalities. Due to persistent cough and lymphocytosis, pertussis was suspected and the patient was treated with per os clarithromycin (15 mg/Kg/day) and intravenous fluids. B. pertussis was detected by PCR on nasal secretions. Oxygen saturation was > 96% using an oxygen hood. The labor and delivery were uneventful, she had no surgical history and was not taking medication.

The patient’s condition rapidly worsened, and on day 2 of hospitalization she had an apnoeic cyanotic episode during which, oxygen saturation fell < 82%. She was supported with bag-valve mask ventilation based on the ABC algorithm. The patient was transferred to the pediatric intensive care unit (PICU). On admission she was tachypneic (44/min) and tachycardic (180/min), and oxygen saturation was 98% using an oxygen hood (6 lt/min). Peripheral perfusion, blood pressure, and temperature were within normal limits. She had a gradually deteriorating course over the next 3 days, requiring high concentration of oxygen. Antibiotics changed to teicoplanin-piperacillin-tazobactam and clarithromycin. On day 3 she presented an apnoeic episode with severe bradycardia (< 40 bpm) so intubation was performed and she was placed on pressure-control mode on ventilator set at PIP = 22 cm of water, end expiratory pressure of 5 cm of water, with a rate of 35 breath/min and FiO₂ 0.85. Sedation with midazolam and morphine in order to maintain ventilation was used. Due to severe and persistent hypercapnoea, she switched to high frequency oscillatory ventilation (HFOV). Despite the mechanical support, her respiratory function continued to deteriorate and she was led to hemodynamic instability with tachycardia (> 220 bpm).

Faced with the rapid progression of respiratory failure and the literature data about poor outcome once hypotension and shock occurs in this specific patient group, a leukocyte mass reduction was suggested. An exchange transfusion was used, rather than leukopheresis, based on rapid availability within our institution. Parental consent was obtained. The patient underwent an 600-mL double volume exchange transfusion through a central venous catheter (double-lumen) which was inserted in left femoral vein, in 20-mL aliquots, using cytomegalovirus-negative, leukophor-filtered, irradiated packed red blood cells reconstituted to an estimated hematocrit of 45%. The blood injection was timely programmised by electric pump so as to maintain her hemodynamic stability. The main clinical and laboratory values before and after exchange transfusion are seen in table 1. The procedure completed with no adverse effects. The benefit of exchange transfusion on cardiorespiratory function was clear and immediate as heart rate decreased to 165 and PO₂/FiO₂ increased to 203 in 24 hours after ET.

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<table>
<thead>
<tr>
<th>Variable</th>
<th>Before ET</th>
<th>After ET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse (bpm)</td>
<td>225</td>
<td>165</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td>135/75</td>
<td>120/50</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>36</td>
<td>38.3</td>
</tr>
<tr>
<td>Respiratory rate per minute (ventilated)</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Fraction of inspired oxygen</td>
<td>90/69 (HFO)</td>
<td>70</td>
</tr>
<tr>
<td>PO$_2$/FiO$_2$</td>
<td>89</td>
<td>203</td>
</tr>
<tr>
<td>WBC count (x10$^9$ cells/L)</td>
<td>71,59</td>
<td>19</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>11,6</td>
<td>15,5</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>36</td>
<td>48,1</td>
</tr>
<tr>
<td>Platelets (x10$^9$ cells/L)</td>
<td>579</td>
<td>122</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>43</td>
<td>45</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>140,8</td>
<td>138</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>3,9</td>
<td>138</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9,4</td>
<td>8,1</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>101</td>
<td></td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dL)</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0,4</td>
<td>0,5</td>
</tr>
<tr>
<td>pH (mg/dL)</td>
<td>6.93/7.11</td>
<td>7.42</td>
</tr>
<tr>
<td>pO$_2$ (mmHg)</td>
<td>128.6/61.3</td>
<td>142.1</td>
</tr>
<tr>
<td>Saturation O$_2$ (%)</td>
<td>96/81.4</td>
<td>98.8</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>27.9/27.4</td>
<td>24.9</td>
</tr>
<tr>
<td>pCO$_2$ (mmHg)</td>
<td>140.1/89.3</td>
<td>38.2</td>
</tr>
</tbody>
</table>

The patient had a prolonged ventilator course characterized by episodes of atelectasis, cyanosis when sedation was lifted. Her course was complicated by *Acinetobacter baumannii* infection treated by colistin. She weaned off HFOV on hospital day 30 and she was extubated successfully 2 days later through conventional ventilation. After the extubation, patient continued to present episodes of recurrent cough. The infant was discharged on hospital day 59, with normal respiratory function and normal blood gases as well as without any apparent neurologic deficit.

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Discussion

Pertussis remains an important cause of infant death worldwide and continues to be a public health concern even in countries with high vaccination cover. Its incidence has been steadily increasing in children during the past decades, especially those not vaccinated. Severe pertussis affects only a small proportion of children infected with *B. pertussis* and is associated with up to 80% mortality [7].

Reducing leukocyte mass can be accomplished by few techniques. Exchange transfusion (ET) is equally effective with automated leukapheresis but probably safer. With few complications the procedure can rapidly reduce an excessive leukocyte burden and improve associated metabolic abnormalities [8]. ET has been suggested to ameliorate the outcome by having dual effect: firstly, the leukoreduction reduces the leukocyte mass that obstructs pulmonary microcirculation, leading to pulmonary hypertension with heart failure and hypoxemia and secondly, plasma exchange reduces circulating pertussis toxins which have a combination of effects on leukocyte surface adhesion molecules and chemokine receptor signaling to cause further leukocytosis and tissue damages [9,10].

In 2004 Romano, et al. [6] reported the first use of exchange transfusion with clinical improvement in a child with pertussis complicated by pulmonary hypertension and cardiogenic shock. There have been few case-reports since 2004. The largest case-control series has been presented by Rowlands, et al. [11], confirming the significant benefit in mortality reduction.

According to proposed algorithm urgent double-volume exchange transfusion is suggested in the following situations:

1. If the patient has no severe cardiorespiratory failure nonresponsive to medical therapy but WBC count is above 100,000/mm$^3$
2. If WBC count is above 70,000/mm$^3$ but the patient has cardiac and respiratory failure
3. If WBC count is above 70,000/mm$^3$ and the patient has cardiac or respiratory failure and echocardiographic evidence of PHT
4. If WBC count is above 50,000/mm$^3$ and the patient has deteriorating cardiac or respiratory function.

Our patient belonged to the fourth category as her WBC were 71,590/mm$^3$ and she continued to be deteriorated.

Another parameter that has to be considered, is the early intervention as proposed by Nieves, et al [12]. The decision for ET should be based on the early appearance of pneumonia, the presence of pulmonary hypertension and the rapidity in the rise of the WBC count. This requires that WBC counts to be performed every 12 to 24 hours. Rapidly rising counts that reach 30,000 cells/mm³ should prompt immediate consideration of ET. Also rising pulse and respiratory rates should also be considered as indicators for performing ET. As a result, if ET is planned in an infant it should be done before organ failure occurs.

In our case the decision to perform ET was made on 3rd day of hospitalization in PICU before cardiac failure. The infant had normal blood pressure without requiring inotropic support. ECHO with normal injection fracture and no regurgitation of the heart valves.

Conclusion

In conclusion, we described a favorable outcome in an infant treated with ET for severe pertussis and leukocytosis admitted to the PICU. We strongly believe that the intervention with ET was crucial for patient prognosis. A deeper understanding of the molecular base of pertussis infections could be crucial in understanding the pathophysiologic mechanisms of complications as well as in the development of new strategy therapies. But, even the best treatment approach could not reach the paramount importance of parental adherence to the routine immunization schedule because as Hippocrates said <prevention is better than treatment>.

Conflict of Interest

The authors report no conflicts of interest or funding sources.

Bibliography


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