CASE REPORT

Intensive phototherapy treatment for severe haemolytic disease of the newborn

Fernando P. Facchini¹, Maria Otília N. Bianchi², Beatriz A. Brasileiro Silva³

Abstract

Objective: to discuss the use of alternative treatment methods in hemolytic disease of newborn to replace common early exchange transfusion.

Methods: case report of newborn with intensive Rh incompatibility treated with intensive phototherapy, plus phenobarbital instead of traditional early exchange transfusion. Results: The neonate’s cord blood showed 9.2 mg/dL of total bilirubin and 39% hematocrit. He was medicated with phenobarbital and intensive phototherapy at once. There was a rapid growing hyperbilirubinemia followed by stabilization for almost 60 hours with little changes, but without levels that justified an exchange transfusion. He became progressively anemic and needed a concentrate transfusion. When he was five days old, he was discharged and returned to follow-up at the 7th week of life when his bone marrow was beginning to recover from anemia.

Conclusions: this case demonstrates that pharmacologic agents and intensive phototherapy can be as useful as advantageous in severe hemolytic disease of newborn. We should always try to use them before adopting more aggressive therapies.


Introduction

With the use of anti-Rh hyperimmune gammaglobulin, we significantly reduced the number of cases of severe hemolytic disease due to the Rh factor in countries with a well-organized perinatal care system.¹

The few remaining cases are born with a mild pathology, since they receive adequate perinatal care and fetal medicine. However, we still have the opportunity to observe cases of severe hemolytic disease of the newborn, mainly caused by the RhD factor, due to non-accomplished or misled prenatal examinations.

Since the end of the 40s and the beginning of the 50s, authors who dedicated themselves to the study of isoimmunization called the attention to the importance of the determination of hemoglobin and bilirubin performed in cord blood² on the survival prognosis for critically affected newborns. This determination was then accepted as a rule for the performance of early exchange transfusion,³ whose purpose was to avoid massive hemolysis with the accumulation of large bilirubin concentrations in blood and mainly in the tissues. Thus, exchange transfusion with still low levels of bilirubin was indicated whenever bilirubinemia levels increased more than 0.5 mg/dl/hour.⁴,⁵
It is important to stress that these procedures were adopted in a time in which exchange transfusion was the only available device for treating hyperbilirubinemia. Phototherapy, which appeared in 1958, with Cremer, was only starting to be used; its mechanism of action was little known, and the equipment in use were really precarious. Thus, regardless of rare contestations,6 this procedure was recommended for very long, until the day when neonatology textbooks stopped endorsing it.7 However, in Brazil, it still persists as a rule, and is used by great part of neonatologists.

The issuing of this study aims at discussing alternative forms of treatment for the severe hemolytic disease of the newborn, instead of the traditional early exchange transfusion.

Case report

Newborn, male, born in May 7, 1999, at 10:49 hrs at the Centro de Atenção Integral à Saúde da Mulher, Universidade Estadual de Campinas.

Maternal history: a 30-year old mother, married, white, G4P2A1. Her first son was Rh-, and the second was Rh+. She denies anemia or jaundice in both. Abortion occurred during the second gestation. She reports having received postdelivery “vaccine”. She denies any vices. Prenatal was initiated in the 8th month (two appointments). Mother A Rh-. Indirect Coombs: 1:128. Echography in April: 34 weeks and 5 days. On June 5: 36/37 weeks. Venereal disease research laboratory: negative. Cesarean section was indicated because she was in the IA zone of Liley’s graph. Epidural anesthesia.


Evolution: a cord-blood sample was picked presenting total bilirubin = 9.2 mg/dl, and micro-hematocrit = 39%. Phenobarbital 10 mg/day/3 days and double phototherapy were initiated. Besides that, we also performed a glycemia monitoring, collected complete hemogram and reticulocyte count. He presented hypoglycemia corrected intravenously. The hemogram results showed: hemoglobin, 9.57 g/dl; hematocrits, 29%; leukocytes, 13,400/mm³ (metamyelocytes, 2%; rods, 10%; segmented, 54.5%; lymphocytes, 27.4%; monocytes, 4%; eosinophils, 0%; basophils, 1%); platelets, 113,000/mm³; and reticulocytes, 30%. The evolution of bilirubin and hematocrit dosages is reported in Table 1 and Figure 1. Bilirubin dosages were performed through plasmatic spectrophotometry, and sporadically compared to total and direct-fraction bilirubin dosages, performed through the Jendrassik method. The correlation of values between the two methods was always good and, there were no significant increases in direct-reacting bilirubinemia. When the hematocrits fell to 16%, a transfusion was indicated, and within 77 hours, about 60% of the planned correction had already been made, bilirubin had fallen to 11.3 mg/dl, and the hematocrits had raised to 35%. At the end of this transfusion, the hematocrits had raised to 46%. Within 100 hours of life, we suspended double phototherapy. With 125 hours of life (5th day) he was discharged from hospital after total bilirubin and ferritin dosage, which was of 1,090 ng/ml. Another appointment was scheduled with a specialized clinic. In that occasion, the neurological examination resulted totally normal.

<table>
<thead>
<tr>
<th>Hours of life</th>
<th>Bilirubins (mg/dl)</th>
<th>Hematocrits (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9.2</td>
<td>39</td>
</tr>
<tr>
<td>5</td>
<td>17.8</td>
<td>36</td>
</tr>
<tr>
<td>11</td>
<td>15.4</td>
<td>30</td>
</tr>
<tr>
<td>15</td>
<td>16.0</td>
<td>30</td>
</tr>
<tr>
<td>21</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>34</td>
<td>18.2</td>
<td>28</td>
</tr>
<tr>
<td>39</td>
<td>15</td>
<td>28</td>
</tr>
<tr>
<td>51</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>73</td>
<td>13</td>
<td>16*</td>
</tr>
<tr>
<td>77</td>
<td>11.3</td>
<td>35**</td>
</tr>
<tr>
<td>100</td>
<td>08.6</td>
<td>51</td>
</tr>
<tr>
<td>125</td>
<td>9.5</td>
<td>51</td>
</tr>
</tbody>
</table>

* Beginning of transfusion
** 60% of transfusion concluded

Figure 1 - Evolution of the levels of bilirubins and hematocrits
He returned on June 22, 1999 to the unit in great general status, with weight = 4,275 g, height = 55 cm, exclusively breastfed. We performed dosages of: ferritin, 912 ng/ml; reticulocytes, 6.3%; micro-hematocrit, 22%; and erythrocytes, 2,480,000/mm³.

Discussion

The possibility of performing exchange transfusions changed significantly the gloomy panorama of hemolytic diseases of the newborn. Mortality, which until 1941 was at 35.8%, fell to 8.9% soon after its adoption. Although the mortality rates mentioned are progressively decreasing, the values are quite variable, oscillating from 1 to 8%. Much lower indexes, of 0.6%, were mentioned in recently published books. Unfortunately, immediate complications are still observed: some examples are arrhythmias, asystoles, thromboses, embolisms, septicemias, hemorrhages due to plateletopenia or hyper-heparinization, perforation of vessels, hypothermia, electrolytic alterations, and hypoglycemia. Late complications, although not always acknowledged as related to the procedure, are necrotizing enterocolitis, regional hepatic necrosis, and the other complications usually found in transfusions.

Thus, although the exchange transfusion may present brilliant results in extremely severe cases, it must be seen as a high-risk measure, and should be used only when other less aggressive methods for the treatment of hyperbilirubinemias have failed.

Based on Mollison & Cutbush’s observations, McKay established some rules for the indication for early exchange transfusion, using bilirubin and hemoglobin dosed in the blood collected from the umbilical cord.

In 1978, Wennberg et al. acknowledged the incapacity of identifying cases of hemolytic disease of the newborn through dosages of cord blood; the severity of the cases would certainly lead to exchange transfusion due to hyperbilirubinemia. The rules established according to Mollison’s and Diamond’s works, which are based on bilirubin and cord hemoglobin levels, reflect a tendency to severity, but they are not absolute concerning the rise of bilirubin levels. Maybe even more important is the fact that these rules were created before the arousal of phototherapy, or at least when this technique was starting to arise, or when medications such as phenobarbital started to be used.

Phenobarbital acts as an enzymatic inductor, increasing the intracytoplasmic transport of bilirubin by Y (Ligandin) protein, and also increasing the excretion of conjugated bilirubin. Its therapeutic qualities overreach any possible secondary effect. It should be used to decrease bilirubinemia in newborns who are obvious candidates to severe forms of jaundice. It is important to remember that phenobarbital is only used in cases of hyperbilirubinemias due to hemolytic diseases (like in the present case) as a coadjuvant drug, since it takes from 48 to 72 hours to induce the maturity of the hepatic glucuronization system. So, because of its late effect, the administration must be initiated soon after birth.

Nowadays, new concepts were associated with phototherapy. In the application of this technique, we should observe: spectral band of the source used, the radiance used, and the area exposed to light. The blue spectral band is the biggest transformer of bilirubin into its photoisomers and other excretion products. The isomer mostly formed (4Z15E) is scarcely excreted by human beings, given its own capacity of reversion to the form 4Z15Z, native bilirubin, stabler, practically insoluble in plasma and potentially toxic for the central nervous system. If we use a source with an adequate spectrum (blue), with minimal radiance of 6 µW/cm²/nm, after 4 hours, about 20% of the bilirubinemia will be constituted by the isomer 4Z15E. As this isomer crosses the cellular membranes with great difficulty, it is potentially much less toxic for the central nervous system than the isomer 4Z15Z. The radiance intensity, on the other hand, is extremely important for the production of the stablist isomer, the lumirubin, which is directly responsible for the decrease in the bilirubin levels.
In the case described, we initially used double-phototherapy equipment, composed by two sets of seven lamps each (Figure 2). The lamps used were Philips 20WT52 (special blue lamps). The radiance at the superior tray of lamps, measured at a distance of 28 cm from the newborn's body surface, was 38.24 µW/cm²/nm, with an average of 18 points measured in a 20.0 x 53.0 cm area. In the inferior tray, radiance was 47.22 µW/cm²/nm, measured on the surface of the acrylic cradle where the newborn was put naked, only with ocular protection. The measure was equally performed in 18 points in the same area previously referred to. Total radiance made up 75.6 µW/cm²/nm. We calculated that the newborn’s irradiated surface was at least 50% of his body. Possibly, this area is larger, since his lateral parts receive reasonable quantity of radiance reflected by the lateral blue, plastic curtains, used in the double phototherapy machine. If we calculate the spectral force received by the newborn, we will obtain levels of 68.1 µW/mm. Thus, we really believe we are using a high-intensity phototherapy equipment, since until now, there is not any standardization to designate this type of equipment. In the Neonatology Service at the Centro de Atenção Integral à Saúde da Mulher, Universidade Estadual de Campinas, we decided to accept 40 µW/cm²/nm as the minimal radiance for high-intensity machines. If the radiance level was below this pattern, we replaced all the lamps of the machine.

We have been using the radiometer produced by Fanem, model 620, for radiance evaluation, and a Unistat bilirubinometer, model 10310/10311C, for bilirubin spectrophotometry.

In cases of hemolytic disease, we prefer to start with intensive phototherapy soon after birth, since, in general, jaundice is already present. We preferred not to wait for relatively elevated levels of bilirubinemia to start with phototherapy - although the action of light on the bilirubin deposited in skin is almost instantaneous, the elimination of the isomers and other transformation products is slow, and we know that the risk of kernicterus is related not only to elevated levels of bilirubinemia, but also to its duration.

We preferred to wait until the 3rd or 4th day of life, if possible, to perform an anemia correction through transfusion and to provide a good quantity of erythrocytes, avoiding the repetition of transfusions during the post-neonatal period.

According to what we showed, we consider that, if the characteristics of the equipment described in this study are respected, the intensive phototherapy becomes a significantly less difficult treatment, almost without risks, much cheaper, and of much simpler installation than the structure necessary to perform exchange transfusions.

References

Correspondence:
Fernando Perazzini Facchini
Rua Coronel Quirino, 910/ apt. 101
CEP 13025-900 – Campinas, SP, Brazil
Phone: +55-19-251-4735 – Fax: +55-19-289.2586
E-mail: fecefaca@supernet.com.br