SCREENING FOR RETINOPATHY OF PREMATURITY.  
OUR EXPERIENCE ABOUT LIMITS OF BIRTH WEIGHT,  
POST-CONCEPTIONAL AGE AND OTHERS RISK FACTORS

DESPISTAJE DE LA RETINOPATÍA DEL PREMATURO. NUESTRA  
EXPERIENCIA SOBRE LOS LÍMITES DE PESO AL NACER, EDAD  
GESTACIONAL Y OTROS FACTORES DE RIESGO

ABSTRACT

Purpose: To assess the features of Retinopathy of Prematurity (ROP) in a Neonatal Intensive Care Unit during 8 years, analyzing the usefulness of the criteria in the screening protocol and the risk factors relating to the disease.

Methods: A retrospective study of the infants included in the screening program for ROP. The sensitivity of the criteria of birth weight (BW) < 1,500 g, post-conceptional age (PCA) < 32 weeks and subjective pediatric criteria (SPC) in the screening program were evaluated and compared with the incidence of ROP, and the need for treatment in these patient groups. Statistical analysis for ROP and no-ROP was then applied to the risk factors BW, PCA, oxygen therapy, and intercurrent diseases.

Results: Forty of 303 infants studied had ROP (13.2%). In ROP cases, 31 (77.5%) had spontaneous regression and 9 (22.5%) needed treatment. The screening program included 144 children with BW < 1,500 g and 159 children with BW > 1,500 g. The incidence of ROP was 26.4% in the first group and 1.3% in the second group (p<0.001). Two cases were detected with a BW > 1,500 g but with a PCA < 32 weeks, that did not require treatment. There were 84 cases (27.7%) included by SPC and in none of them ROP was detected.

RESUMEN

Objetivo: Registrar las características de la Retinopatía de la Prematuridad (RP) en una unidad neonatal a lo largo de 8 años, analizando los criterios del protocolo de despistaje y los factores de riesgo asociados.

Métodos: Estudio retrospectivo de los prematuros incluidos en el protocolo de despistaje. Evaluación de la sensibilidad de los criterios Peso al nacer (PN) < 1500 gr, edad gestacional (EG) < 32 semanas y criterio subjetivo pediátrico (CSP) del protocolo y comparación estadística de la incidencia de RP y la necesidad de tratamiento entre los distintos grupos. Análisis estadístico entre los grupos con y sin RP de PN, EG, oxigenoterapia y patologías asociadas.

Resultados: Cuarenta de los 303 niños revisados presentaron RP (13,2%). De ellos 31 (77,5%) regresaron espontáneamente y 9 (22,5%) requirieron tratamiento. Entre los 144 niños PN < 1,500 gr la incidencia de RP fue 26,4% y entre los 159 niños con PN > 1,500 gr fue 1,3% (p<0,001). Se detectaron dos casos de RP con PN > 1500 gr y EG < 32 semanas, que no requirieron tratamiento. Hubo 84 casos (27,7%) incluidos por CSP y en ninguno de ellos se...
< 32 weeks, and neither required treatment. There were 84 cases included because of SPC (27.7%); no cases of ROP were detected in these. The only independent risk factor found in a multivariant analysis was birth weight.

Conclusions: None of the children included with a BW > 1,500g required treatment for ROP, but several cases of ROP could be missed by using this criteria only. SPC must be restricted in the screening program (Arch Soc Esp Oftalmol 2006; 81: 275-280).

Key words: Retinopathy, prematurity, protocol, risk factors, birth weight, post-conceptional age.

INTRODUCTION

The number of premature babies has increased in Spain in recent years, reaching 7.1% of all births. One of the main problems of these low weight and small post-conceptional age babies is the Retinopathy of prematurity (ROP). Neonatologists are highly aware of the early detection of this condition and in all neo-natal care wards a screening protocol was established over a decade ago. This concern extends to countries in which the survival rate of premature babies is increasing (1). As early detection allows these babies to benefit from efficient therapy, a rigorous screening is essential, involving a bi-weekly binocular funduscopies for all babies with a Newborn Weight (NW) under 1,500 g and Post-conceptional Age (PCA) under 32 weeks. However, to avoid the risk of a serious ROP going unnoticed in premature babies with NW and PCA fulfilling said criteria, the American Pediatrics Academy recommends this screening for all premature babies considered to be at risk by intensive care pediatricians (2). These risk factors include intensive oxygen therapy (3) and diseases which could cause fluctuations in the oxygen tension in the retinal tissue since this would entail ischemia followed by a neovascular proliferative phase (4). The current trend is to limit the protocol to the two main objective criteria, even NW only (5,6). This article analyzes said criteria as well as the Pediatric Subjective Component (PSC) of the ROP screening protocol in the Neonatal Intensive Care unit of our hospital throughout an 8-year record. We also analyze the influence of some risk factors which some pediatricians invoke for subjective inclusion in the protocol.

SUBJECTS, MATERIAL AND METHODS

A retrospective study has been made of premature babies admitted to our Neonatal Unit who were included in the ROP screening protocol from August 1995 to December 2003. Said protocol was drawn up on the basis of international guidelines suggested by the CRYO-ROP multi-center study and recommended by renowned hospitals of our country (7,8). It consisted in an ophthalmological assessment twice a week for all premature babies with NW < 1,500 g and PCA under 32 weeks and for serious ROP cases the screening was done weekly. However, to avoid the risk of a serious ROP going unnoticed in premature babies with NW and PCA fulfilling said criteria, the American Pediatrics Academy recommends this screening for all premature babies considered to be at risk by intensive care pediatricians. Up to 2002 the screening was initiated the 6th week post-partum but since then it was initiated at the 4th week or 31 weeks of post-menstrual age, while for serious ROP cases the screening was done weekly.

The funduscopic assessment was always carried out by the same ophthalmologist (FRH) throughout the 8 years. The recorded additional risk factors were the amount of days with oxygen therapy, the appearance of sepsis, the need of blood transfusions, inter-current surgery and the appearance of intra-cranial hemorrhage. To assess the sensitivity of the screening criteria, we carried out a statistical comparison of the NW < 1,500 g, NW > 1,500 g and PCA < 32 weeks and NW > 1,500 g and PCA > 32 weeks (CSP) groups for ROP prevalence and for the need of treating ROP. The statistical studies were made with SPSS 11.0 for Windows, utilizing...
bi-variant comparisons and logistical regression analysis for risk factors between the group with and without ROP.

RESULTS

Forty of the 303 assessed babies evidenced ROP (13.2%). Of these, 31 did not reach 3 Plus grade and, allowing natural evolution, spontaneously remitted (77.5%) and 9 showed signs of progression to grade 3 Plus (22.5%), requiring treatment. In the protocol we included 144 babies with NW < 1,500 gr and 159 babies with NW > 1,500 gr. Utilizing only the NW < 1,500 gr criterion, we would have detected 38 ROP cases, which represents a sensitivity of 95%, while 100% sensitivity was obtained aggregating the NW < 1,500 gr and PCA < 32 weeks groups. The distribution of cases with ROP and normal cases according to the different groups of the screening criteria appears in Table 1. The prevalence of ROP in babies with NW <1,500 gr was of 26.4% and in babies with NW > 1,500 gr of 1.3% (p<0.001).

The two ROP cases of the NW > 1,500 g group exhibited a PCA < 32 weeks, and reached a maximum of grade 2 in zone 3, without plus signs and with spontaneous regression. Eighty-four cases (27.7%) were included due to PSC and ROP was not identified in any. In the bivariant analysis of risk factors with quantitative variables, significant differences were found between the group which exhibited ROP and the one without ROP for NW and days of oxygen therapy (p<0.05) but not for PCA (table II). The bivariant analysis for risk factors with qualitative variables, a significant association was found for the ROP with sepsis and inter-current surgery vis-à-vis the group without ROP (p<=0.05) (table III). When applying logistical regression, the only independent variable was low weight at birth (p<0.05).

DISCUSSION

The prevalence of ROP is abnormally low in our sample (13.2%) due to the inclusion of a large

Table I. ROP screening groups criteria

<table>
<thead>
<tr>
<th>Low weight and small post-conceptional age criteria</th>
<th>Number cases with ROP</th>
<th>Number cases without ROP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1,500 g y &lt;32 w</td>
<td>38</td>
<td>0</td>
</tr>
<tr>
<td>&lt;1,500 g y &gt;32 w</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>&gt;1,500 g y &lt;32 w</td>
<td>2</td>
<td>75</td>
</tr>
<tr>
<td>&gt;1,500 g y &gt;32 w</td>
<td>0</td>
<td>84</td>
</tr>
</tbody>
</table>

Table II. Analysis of quantitative variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measure</th>
<th>N</th>
<th>W/ROP Mean</th>
<th>TD</th>
<th>W/out ROP Mean</th>
<th>TD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>Grammes</td>
<td>261</td>
<td>998.8</td>
<td>294.3</td>
<td>1,688.1</td>
<td>535.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCA</td>
<td>Weeks</td>
<td>261</td>
<td>27.8</td>
<td>2.1</td>
<td>32.02</td>
<td>2.9</td>
<td>0.06</td>
</tr>
<tr>
<td>O₂</td>
<td>Days</td>
<td>225</td>
<td>5.6</td>
<td>9.7</td>
<td>34.3</td>
<td>41.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table III. Analysis of qualitative variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>ROP (n=40)</th>
<th>Without ROP (n=263)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH</td>
<td>4 (10.0%)</td>
<td>9 (3.4%)</td>
<td>0.077</td>
</tr>
<tr>
<td>Sepsis</td>
<td>30 (75.0%)</td>
<td>134 (51.0%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Transfusion</td>
<td>15 (37.5%)</td>
<td>84 (31.9%)</td>
<td>ns</td>
</tr>
<tr>
<td>Surgery</td>
<td>7 (17.5%)</td>
<td>15 (5.7%)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

ICH: Intra-cranial hemorrhage; Transfusion: Need for 1 or more transfusions; Surgery: surgery intervention due to inter-current pathology; Ns: not significant. Criteria for low weight and small post-conceptional age <1,500 g and <32 s <1,500 and >32 s >1,500 gr and <32 s.
group of babies (nearly one third) which exceeded the objective numbers recommended by the AAP. Taking into account only the babies with NW < 1,500 gr the prevalence of ROP increases to 26.6%, which is a very similar number to that of other studies carried out in Spanish hospitals [between 26.2% (9) and 29.2% (10)]. Sweden’s Karolinska Hospital published a prevalence 40.1% of the assessed population (11). The PSC frequently involves assessing an excessive number of babies which evidence-based medicine has proved to be without ROP risk (5).

Accordingly, the current tendency is to use NW < 1,500 gr as the sole criterion for screening. However, we must not forget that some babies with NW > 1,500 gr may exhibit ROP. We had two cases and, even though both regressed spontaneously, it is not advisable to let them go unnoticed, above all after the publication of long-term results of the CRYO-ROP study which detected some cases of belated retina detachment in untreated eyes (4). The legal dilemma is whether we can waive the PSC recommended by the American Academy of Pediatrics for children with NW and PCA parameters above the limits, not including in the screening the infants with «unstable clinical evolution». Common sense calls for at least a monthly assessment if selected by the obstetrician, but in turn that criterion cannot become the refuge of defensive pediatric medicine rife with prejudices against oxygen therapy (as was the case in our PSC, where the majority of these cases were included as soon as any grade of oxygen therapy was administered). A funduscopic assessment in midriasis for premature babies who do not need it is an unnecessary cost and, in addition, is not free of risk (12,13). The current trend is to reduce further the NW and PCA limits in the protocol, even with the possibility of leaving slight ROP cases unnoticed (14).

Low weight is a determining factor in the appearance of ROP, as confirmed once again by this article. The low post-conceptional age was statistically not significant, but only marginally so and should be reassessed with a larger sample. Of the other factors bearing on ROP, the most important one seems to be oxygen therapy: multiple recommendations call for adjusting it to the bare minimum in order to lower the prevalence of serious forms (15,16). As regards other risk factors, septicemia has been present in the majority of our serious cases, in accordance with observations by other authors (17,18). In addition, the need for surgery during the crucial weeks for ROP development has proved to be a highly influential factor in our study, although we did not find literature on the subject. Other risk factors described in literatures such as intra-cranial hemorrhage (19) or the need for blood transfusions (20) were not significant in our sample. We believe there isn’t sufficient evidence for neonatologists to add another objective factor to low weight at birth in the criteria for selection of screening groups.

REFERENCES