consent of parents, switched to IV paracetamol due to thrombocytopenia and grade III IVH. The follow-up echocardiogram (9th day) showed a small and haemodynamically non-significant ductus arteriosus. The PDA reopened at 11 days. Surgical closure was performed the next day with poor outcome: abdominal distension, septic appearance. The infant died 2 days post surgery.

Approximately three years ago, Hammerman et al.1 published their initial experience with pharmacological closure of PDA with oral paracetamol in 5 patients. In the index patient, a newborn with 26 weeks of GA, paracetamol was administered for a different indication at $2^{1/2}$ weeks of life and it was observed that a hsPDA that had not responded to two courses of ibuprofen had suddenly closed two days later. Following this, another four neonates of 26–29 weeks of GA in whom treatment with ibuprofen was contraindicated or had failed were treated with paracetamol. All patients showed either closure or a significant reduction in the size of the ductus 48 h after administration of paracetamol, and full closure in one week. On the basis of this first experience, other authors have used oral or intravenous paracetamol to treat PDA in small series of patients. A review of these studies has been recently published by Allegaert et al.2

The main concern raised by these studies has to do with the lack of data on the pharmacokinetics and pharmacodynamics of paracetamol in extremely preterm newborns and the safety of its use in this population. There is also considerable controversy regarding the dosage used, which is double the dose used for analgesia in term newborns. The mechanism of action of paracetamol is not fully understood either, and in many of the published cases its use followed the administration and failure of ibuprofen, so it is not possible to know whether there was a synergistic effect between the two medications.

In the only randomised study conducted to date,⁴ 80 patients completed the course of treatment. The efficacy in the pharmacological closure of PDA was similar for ibuprofen (77.5%) and paracetamol (72.5%) administered by the oral route, and both drugs proved to be safe.⁴ These are relevant findings, since COX inhibitors, despite having a success rate of 70–85%, are not free from side effects, such as, oliguria, gastrointestinal perforations, impaired platelet aggregation, hyperbilirubinaemia, etc. Ibuprofen has also been associated with an increased risk of BPD.⁵

In summary, although further prospective, controlled and appropriately designed studies are needed to establish the safety, efficacy and optimal dosage of paracetamol for the treatment of PDA in extremely preterm infants, these last experiences appear promising, at least in cases where traditional drugs fail or are contraindicated, and when avoiding surgery is deemed reasonable.

References

M.E. Pérez Domínguez, S. Rivero Rodríguez, F. García-Muñoz Rodrigo

Complejo Hospitalario Universitario Insular Materno-Infantil, Las Palmas de Gran Canaria, Spain

Corresponding author.
E-mail address: fgarciam@gmail.com (F. García-Muñoz Rodrigo).

Obesity in Oviedo: Prevalence and time trends from 1992 to 2012

Obesidad en Oviedo: prevalencia y tendencias temporales de 1992 a 2012

Dear Editor,

Spain has one of the highest prevalences of childhood overweight and obesity in Europe. The frequency of excess weight has increased considerably between 1985 and 2000, although it seems to have stabilised in the past 10 years.⁴

In order to fight this emerging epidemic, we need to monitor the secular trends of obesity by means of population studies or surveys. This surveillance must be done in reference to standardised consensus definitions of terms such as obesity, overweight and normal weight specific for age and sex."²

We analysed the trends in overweight and obesity in children 5–14 years of age over three sequential time intervals corresponding to years 1992, 2004–2006 and 2012. We performed a cross-sectional observational study, requesting the participation of all the students enrolled in 3 elementary and 2 secondary schools in Oviedo.

Weight was measured to the nearest 100 g using a mechanical scale. Height was measured with a Leicester® stadiometer to the nearest 0.1 cm. We based our definitions of overweight and obesity on mean percentiles calculated

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Table 1  Descriptive statistics of the 3 cross-sectional studies done in 1992, 2004–2006 and 2012.

<table>
<thead>
<tr>
<th>Cohort (year)</th>
<th>Statistic</th>
<th>Age (years) ANOVA P &gt; .05</th>
<th>BMI ANOVA P &gt; .001</th>
<th>Height (cm) ANOVA P &gt; .493</th>
<th>Weight (kg) ANOVA P &gt; .011</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992 cohort</td>
<td>Mean</td>
<td>10.13</td>
<td>18.8</td>
<td>139.8</td>
<td>37.76</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>2.30</td>
<td>2.8</td>
<td>14.21</td>
<td>11.53</td>
</tr>
<tr>
<td>2004–2006 cohort</td>
<td>Mean</td>
<td>10.13</td>
<td>19.3</td>
<td>140.4</td>
<td>39.08</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>2.15</td>
<td>3.24</td>
<td>13.6</td>
<td>12.54</td>
</tr>
<tr>
<td>2012 cohort</td>
<td>Mean</td>
<td>10.15</td>
<td>18.2</td>
<td>140.73</td>
<td>37.18</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>2.61</td>
<td>2.9</td>
<td>15.8</td>
<td>12.6</td>
</tr>
</tbody>
</table>

BMI, body mass index; SD, standard deviation.

according to the sex- and age-specific BMI criteria of the International Obesity Task Force (IOTF).

We measured 734 children in 1992, 735 between 2004 and 2006, and 709 in 2012, out of a total of 1100. The final sample consisted of 2178 individuals. We did not find differences in the distribution by age or by sex (Table 1).

The overall prevalence of obesity was significantly higher in the 2004–2006 period compared to 1992 (8.4% vs 4.9%; \( P = .01 \)). However, there was a decrease in the overall prevalence of obesity between the 2004–2006 period and 2012 (8.4 vs 5.1%; \( P = .01 \)).

We found statistically significant differences between cohorts in the overall prevalence of overweight. We observed a decline of 8.2% between the 2004–2006 period and 2012 (25.9% vs 17.7%; \( P = .0001 \)), and a decline of 6.9% between 1992 and 2012 (24.6% vs 17.7%; \( P = .004 \)), respectively (Table 2).

We grouped participants in two categories according to the age of onset of puberty: children (<11 years) and adolescents (>11 years). In children, the prevalence of obesity was significantly lower in the 2012 cohort (8.8% in 2004–2006 vs 4.1% in 2012; \( P = .021 \)), while no significant differences were observed between adolescent cohorts.

When we stratified the data by sex, the prevalence of obesity decreased significantly from 9.6% in the 2004–2006 period to 5.4% in 2012 in boys, but not in girls (7.1% vs 4.6%, \( P = .17 \)), in whom the difference was not statistically significant. In the 2012 cohort, the prevalence of obesity was significantly higher in boys, especially in the preadolescent age group, than in girls.

The prevalence of childhood overweight has increased in nearly every country for which data are available. A systematic review published in 2006 on the secular trends of childhood obesity concluded that its prevalence had increased in the past 2 or 3 decades in nearly every developed country, especially in urban areas.3

We described an increase in children’s weight between 1992 and 2006,4 but to our knowledge the decreasing trends observed in our study have not been described before in Spain. The prevalence of childhood obesity in Oviedo has decreased considerably in the past 7 years, showing a clear trend towards a sharper decline in males in older age groups. In any case, generalising the findings of our study may not be possible, as our sample came from a middle-class population from a specific geographical area.

Similar trends have been observed in the United States, where the increase in the prevalence of childhood overweight and obesity has been documented extensively since the 1960s.5

We do not know what has caused this marked change in trend.

Since 2009, efforts had been made to educate children on healthier alternatives, introducing better-quality foods in the lunchroom menus and vending machines of Oviedo schools, and expanding school sports and physical activity programmes to weekends and summers.

In recent years, the recommendations of the WHO and UNICEF on the optimal duration of breastfeeding that call for delaying the introduction of solids until 6 months of age, maintaining exclusive breastfeeding until 6 months of age and continued breastfeeding until 2 years of age or more, may be contributing to the decline in the prevalence of childhood obesity.

Table 2  Prevalence of childhood overweight and obesity in Oviedo in years 1992, 2004–2006 and 2012.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>No. of participants</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal range</td>
<td>518</td>
<td>70.5%</td>
</tr>
<tr>
<td>Overweight/obese</td>
<td>217</td>
<td>29.5%</td>
</tr>
<tr>
<td>Overweight</td>
<td>181</td>
<td>24.6%</td>
</tr>
<tr>
<td>Obese</td>
<td>36</td>
<td>4.9%</td>
</tr>
<tr>
<td>2004–2006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal range</td>
<td>482</td>
<td>65.7%</td>
</tr>
<tr>
<td>Overweight/obese</td>
<td>252</td>
<td>34.3%</td>
</tr>
<tr>
<td>Overweight</td>
<td>192</td>
<td>25.9%</td>
</tr>
<tr>
<td>Obese</td>
<td>62</td>
<td>8.4%</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal range</td>
<td>547</td>
<td>77.1%</td>
</tr>
<tr>
<td>Overweight/obese</td>
<td>162</td>
<td>22.8%</td>
</tr>
<tr>
<td>Overweight</td>
<td>126</td>
<td>17.7%</td>
</tr>
<tr>
<td>Obese</td>
<td>36</td>
<td>5.1%</td>
</tr>
</tbody>
</table>
Although obesity has become a world epidemic, our understanding of this condition in childhood is limited by a lack of representative data from different countries for their comparison, as well as by the different criteria used to define it.

The IOTF has developed charts for an international growth standard that allows the comparison of prevalences across the world. There is evidence that the IOTF classification has a high specificity but a low sensitivity, although many countries continue using their own national charts, including Spain and the United States, where the standards in use were developed from data acquired in nationwide surveys.

At present we do not have a general consensus standard to classify overweight and obesity in children and adolescents. The use of universal criteria for classifying obesity could help make international comparisons.

Acknowledgments

We want to thank Dr Juan José Díaz Martín for giving us access to the data of years 1992 and 2004-2006, and for supervising our study.

References


R. Llada Suárez a, L. del Fresno Marqués b, J.J. Díaz Martín a, S. Málaga Guerrero a, C. Rey Galán a

a Facultad de Medicina, Universidad de Oviedo, Oviedo, Principado de Asturias, Spain

b Atención Primaria, Servicio de Salud del Principado de Asturias (SESPA), Oviedo, Principado de Asturias, Spain

c Sección de Gastroenterología y Nutrición, Hospital Universitario Central de Asturias (HUCA), Oviedo, Principado de Asturias, Spain

d Sección de Nefrología Pediátrica, Hospital Universitario Central de Asturias (HUCA), Oviedo, Principado de Asturias, Spain

e Sección de Cuidados Intensivos Pediátricos, Hospital Universitario Central de Asturias (HUCA), Oviedo, Principado de Asturias, Spain

*Corresponding author.
E-mail address: lladarubn@gmail.com (R. Llada Suárez).

Congenital lactase deficiency: Identification of a new mutation

Déficit congénito de lactasa: identificación de una nueva mutación

Dear Editor,

Congenital lactase deficiency (CLD, OMIM 223000) is a rare genetic disorder that belongs to the subgroup of enteropathies caused by carbohydrate malabsorption.1 We present a case recently diagnosed in our paediatrics department.

The patient was a newborn of 20 days of age with a history of 6–8 episodes of diarrhoea a day since birth and with stunted growth despite breastfeeding with formula supplementation. He is the first child born to second-degree consanguineous parents. He presented with a dystrophic appearance and signs of dehydration. Laboratory analyses revealed metabolic acidosis, mild hypernatraemic dehydration, and normal blood chemistry, liver function and urine tests. The main findings of the stool analysis included stool acidity (pH 6), normal ion levels, a high positive level of reducing bodies and an osmotic gap of 282 mOsm/kg (normal gap < 50 mOsm/kg). Intravenous fluids were initiated with the patient kept on an absolute fast, and the watery stools resolved after 12 h. The working diagnosis was chronic osmotic diarrhoea due to carbohydrate malabsorption. Since CLD was suspected, a diet based on lactose-free hydrolysed formula was initiated. The patient tolerated it well and his weight curve rose. Genetic testing was positive and revealed the presence in homozygosis of a new mutation in the LTC gene, c.2232,2253dup22 (p.L752KfsX18). Genetic testing of both parents was positive in heterozygosis. The patient remained asymptomatic and showed adequate growth in subsequent checkups.

Congenital lactase deficiency was first described in Finland in 1959 with an estimated prevalence of 1 in 60,000 inhabitants. It was included in the group of congenital diarrhoeas, a heterogeneous set of rare diseases associated to specific genetic defects. The onset of symptoms typically occurs in early infancy and the course and prognosis vary depending on the underlying cause.

Congenital lactose deficiency is caused by very low levels or the absence of lactase-phlorizin hydrolase (commonly known as lactase) in the gut resulting from a mutation in the LTC gene (OMIM 603202), and has an autosomic recessive inheritance pattern.2 The correct hydrolysis of lactose, the disaccharide found in milk, is essential to adequate nutri-