

## Paracetamol could be useful in the treatment of patent ductus arteriosus in the very-low-birth-weight infant<sup>☆</sup>



### El paracetamol podría ser útil en el tratamiento del ductus arterioso persistente en el recién nacido de muy bajo peso

Dear Editor,

Patent ductus arteriosus (PDA) is frequently found in preterm newborns and its incidence increases with lower gestational age (GA), rising up to 60% in neonates of gestational ages 26 weeks and less.<sup>1</sup> Clinically, it is associated with an increase in morbidity and mortality, including pulmonary oedema and haemorrhage, intra-ventricular haemorrhage (IVH), necrotising enterocolitis (NEC), bronchopulmonary dysplasia (BPD) and retinopathy of prematurity. The treatment of PDA includes fluid restriction, diuretics, nonselective cyclooxygenase (COX) inhibitors (indomethacin or ibuprofen) and, if all these fail, surgical closure. Recently, several authors have proposed the use of paracetamol for pharmacological closure of PDA if traditional medications fail or are contraindicated. As far as we know, there is no evidence on the use of paracetamol for this purpose in extremely preterm newborns in Spain. We present the cases of two patients with haemodynamically significant ductus (hsPDA) with contraindications for the administration of ibuprofen in which we tried alternative treatment with paracetamol before surgical closure.

Cases (Table 1)

1. Twin, female, second-born at 26<sup>+0/7</sup> weeks of GA with a birth weight of 720 g. Prenatal corticosteroids administered. Delivery by urgent caesarean section due to placenta praevia. Apgar score: 6/8. Noninvasive ventilation until 14 h of life, when intubation and surfactant administration were required, with good response. Reintubation 12 h later due to clinical deterioration and NEC. Two days later a hsPDA, anaemia and thrombocytopenia were detected. Consent was obtained from parents and treatment with intravenous (IV) paracetamol initiated. A control echocardiogram showed a closed ductus and normal haemodynamic parameters. Normal liver function. The patient evolved favourably and she was discharged at a postnatal age of 72 days.
2. Neonate, female, born at 23<sup>+5/7</sup> weeks of GA with a birth weight of 690 g. Chorioamnionitis. Prenatal corticosteroids (partial course). Vaginal delivery with cephalic presentation. Apgar score: 3/5. Intubated and given a dose of surfactant at birth. Mechanical ventilation and vasoactive medication since admission. On day 6, a hsPDA was diagnosed. Intravenous ibuprofen was initiated (one dose) and, with the verbal

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**Table 1** Characteristics of patent ductus arteriosus at initiation of treatment, and outcomes.

	Age at initiation of paracetamol	Inner diameter of PDA (mm)	Left atrium/aorta ratio	Reverse diastolic flow	Previous ibuprofen	Contraindication for ibuprofen	Dose and duration of paracetamol	Outcome
Patient 1	3rd day	3.5	2	Yes	No	Severe thrombocytopenia NEC	15 mg/kg/6 h × 48 h	Closure in 48 h Survival
Patient 2	7th day	2.3	1.9	Yes	1 dose	Severe thrombocytopenia IVH grade III	15 mg/kg/6 h × 72 h + 7.5 mg/kg/6 h × 48 h	Initial improvement Reopening Surgical closure Death

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<sup>2</sup> 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<sup>1</sup>/<sub>2</sub> 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.<sup>3</sup>

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,<sup>4</sup> 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.<sup>4</sup> These are relevant findings, since COX inhibitors, despite having a suc-

cess 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.<sup>5</sup>

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.

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## Obesity in Oviedo: Prevalence and time trends from 1992 to 2012<sup>☆,☆☆</sup>



## 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

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weight has increased considerably between 1985 and 2000, although it seems to have stabilised in the past 10 years.<sup>1</sup>

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.<sup>2</sup>

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