eosinophilic gastritis, respectively. Recently, Choi et al.[4] published a study assessing the clinical, endoscopic and histologic features and the response to treatment of 13 children with a histological diagnosis of EGE. They found that the most prevalent symptom at onset in the infant group (8 patients) was haematemesis (7 patients, 87.5%), followed by melena (2 patients, 25%). In contrast, recurrent abdominal pain was the predominant symptom in the group of children aged more than 1 year (60%). Furthermore, CMP was the allergen most frequently suspected to be involved based on the clinical manifestations, suspected in 76.9% of patients, and all infants in this study responded favourably to switching from cow's milk to extensively hydrolysed/elemental formula. These findings are consistent with the outcomes of the two patients managed in our hospital, although it is important to keep in mind that absence of peripheral eosinophilia or negative results of specific IgE assays are not sufficient to exclude a diagnosis of EGE.[1,2]

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Paracetamol: Useful treatment of choice for persistent arterial duct in very low weight premature newborns☆

Paracetamol: tratamiento útil de elección para el ductus arterioso persistente en prematuros de muy bajo peso

Dear Editor:

The presence of a haemodynamically significant patent ductus arteriosus (hsPDA) in preterm newborns (PTNBs) is associated with prolonged need of mechanical ventilation, bronchopulmonary dysplasia (BPD), necrotising enterocolitis (NEC), metabolic acidosis, intraventricular haemorrhage (IVH), pulmonary haemorrhage and periventricular leukomalacia.[1] For this reason, pharmacological closure of the ductus is common practice, usually through administration of non-selective cyclooxygenase (COX) inhibitors, indomethacin or ibuprofen. Since these drugs may cause adverse events, other agents, such as paracetamol, are being investigated that may be safer while still effective. In this article, we describe our experience with paracetamol in these patients.

In our unit, active measures for closure of PAD are implemented in PTNBs that develop symptoms or with sonographic signs of moderate to severe haemodynamic compromise in whom spontaneous closure is unlikely. The first line of treatment is ibuprofen, which is delivered intravenously. In the last 4 years, we have used paracetamol by the oral or intravenous route in 15 PTNBs with satisfactory results. In all these newborns, paracetamol was administered because treatment with ibuprofen had failed or the patient had contraindications for it. Parents gave consent to the use of paracetamol after being informed that it was an off-label use of the drug. Table 1 summarises the basic characteristics of the patients. The mean gestational age at birth was 26^{+4} weeks (median, 26^{+6} weeks; range 24^{+6}–29^{+1} weeks) and the mean birth weight was 928 g (median, 980 g; range, 480–1480 g). The most frequent indication for treatment with paracetamol (7/15 patients) was a recent history of IVH, which had been severe in 6/15 patients. Three patients developed NEC and 2 died. Table 2 summarises the findings of the sonographic assessment of PDA and the main treatment-related variables. Half of the patients had been previously treated with ibuprofen. Paracetamol was given at a dose of 15 mg per kilogram of body weight every 6 h. We considered that closure of the PDA was successful if complete closure was achieved, or if the hsPDA improved to a minor PDA with no haemodynamic effects and requiring no further treatment. In our case series, successful closure was achieved in 10/15 patients, with the remaining 5 requiring surgical closure. None of the patients had side effects that could be attributed to paracetamol in the short term.

Since Hammerman et al.[2] discovered by chance that paracetamol can achieve closure of PDA in PTNBs, several studies have been published that propose its use as

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Table 1 Patient characteristics.

Patient	Birth weight (g)	Gestational age (weeks)	Sex	Prenatal steroids	CRIB II	IVH (grade)	NEC	Discharged alive
1	990	28^{+5}	Male	Full course	5	Yes (II)	No	Yes
2	480	27^{+4}	Female	Full course	8	Yes (IV)	Yes	Yes
3	1080	27	Male	No	3	Yes (III)	No	Yes
4	800	25^{+5}	Male	Full course	4	Yes (I)	No	Yes
5	1000	26^{+2}	Female	Full course	1	No	Yes	No
6	980	26^{+6}	Male	Partial course	2	Yes (III)	No	Yes
7	700	24^{+6}	Female	Full course	7	Yes (III)	No	Yes
8	1250	27^{+5}	Male	Partial course	2	No	No	Yes
9	1480	29^{+1}	Male	Full course	1	No	No	Yes
10	820	25	Male	Full course	6	Yes (III)	Yes	Yes
11	980	26^{+6}	Male	Partial course	3	Yes (III)	No	No
12	840	25^{+5}	Male	Full course	2	No	No	Yes
13	690	27^{+5}	Female	Full course	9	No	No	Yes
14	660	27^{+3}	Female	Full course	9	No	No	Yes
15	1170	26^{+6}	Male	Partial course	7	Yes (II)	No	Yes

Table 2 Sonographic features of patent ductus arteriosus and treatment characteristics.

Patient	PDA size (mm/kg)	LA:Ao ratio	Previous ibuprofen treatment	Initiation paracetamol (days of life + weight)	Paracetamol (days)	Indication	Success	Surgery
1	1.8	–	Yes (1 dose)	7, 900 g	3	IVH + thrombocytopaenia	Yes	No
2	5	–	No	8, 550 g	6	IVH	Yes	No
3	2.59	1.6	No	7, 1140 g	7	IVH	Yes	No
4	2.5	1.7	Yes (1 cycle)	27, 960 g	7	IVH + treatment failure	No	Yes
5	1.6	1.6	Yes (1 cycle)	14, 1100 g	7	Treatment failure	Yes	No
6	2.75	2.7	No	3, 880 g	6	IVH	Yes	No
7	3.57	2.5	No	10, 710 g	7	IVH	No	Yes
8	1.44	1.8	No	15, 1280 g	7	Risk of NEC	Yes	No
9	1.55	2.3	Yes (2 cycles)	21, 1760 g	5	Treatment failure	Yes	No
10	3.9	1.56	No	4, 820	6	Pulmonary haemorrhage + thrombocytopaenia	No	Yes
11	2.93	1.3	Yes (2 cycles)	13, 1680 g	3	Thrombocytopaenia + sepsis	Yes	No
12	2.3	2	Yes (1 cycle)	19, 1000 g	6	Sepsis	No	Yes
13	2.33	–	Yes (2 cycles)	15, 770 g	7	Sepsis	No	Yes
14	2.6	1.46	No	9, 760 g	3	Thrombocytopaenia	Yes	No
15	2.56	1.8	No	3, 1770 g	6	IVH	Yes	No

an alternative treatment in cases where first-line drugs have failed or are contraindicated. Recently, several clinical trials[3,4] have shown that paracetamol may be as efficacious as ibuprofen, reporting proportions of PDA closure nearing 75%, somewhat higher than the proportion achieved in our small sample (10/15 patients; 66.7%); however, this approach is used infrequently, almost incidentally, in Spain. Paracetamol is currently proposed as an efficacious and possibly safer alternative to traditional COX inhibitors, whose use is limited due to their contraindications and potential adverse effects (kidney failure, NEC, severe hyperbilirubinaemia, sepsis, coagulopathy, haemorrhage, etc.). The short-term side effects of paracetamol observed to date have been minimal, and paracetamol may have the additional advantage of being more effective in hypoxic states (which are frequent in PTNBs), as it is believed to act on the peroxidase function of COX.[5] However, further evidence from clinical trials is required to establish its non-inferiority in comparison to treatment indomethacin or ibuprofen as well as its safety, especially in the long term. On the other hand, PTNBs are at higher risk of liver toxicity due to their immaturity, and the dose of paracetamol used for PDA closure is higher than the dose used for analgesia or reduction of fever (45–60 mg/kg/day compared to 30–40 mg/kg/day). Furthermore, some case series have found a long-term association of paracetamol use with autism spectrum disorders and neurodevelopmental disorders, and it is recommended that patients treated with this approach are followed up closely with thorough neuropsychiatric evaluations.[6] In our small series, all survivors have had adequate psychomotor development, including the two patients that have already reached 2 years of corrected age.

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