

DOMPERIDONE (Comment)

Might use trigger a dangerous arrhythmia ?

Domperidone has never been licensed for use in North America, but it is now widely available and widely prescribed in Europe, particularly to treat the vomiting that often accompanies gastroenteritis in children (Pfeil *et al.*, 2008), even though its main effect is to enhance gut motility. It has also been used for some years in the management of gastro-oesophageal reflux, even though there is, as yet, no good quality evidence that it does much measurable good (Pritchard *et al.*, 2005), and such use became significantly more common after cisapride was eventually withdrawn from the market a few years after it was first shown to affect cardiac conduction, increase the QT conduction time and occasionally cause a potentially devastating arrhythmia (Wyowski, *et al.* 2001).

The four controlled trials of use for reflux in young children reviewed by Pritchard *et al.* were all conducted at least 15 years ago. Only the first trial by Clara, published in 1979, claimed to uncover evidence of significant symptomatic relief. This was a relatively small two week study of 32 children two and a half months to ten years old (mean age 5 years). In half the 14 patients receiving active treatment in this study benefit was only achieved after the initial dose (300 micrograms/kg three times a day) was doubled. Two further trials involving 47 children (De Loore and Ravensteyn, 1979) and 17 children (Bines *et al.*, 1992) found very little convincing evidence of benefit, and a further larger and more complex trial involving 80 children less than 18 months old (Carroccio *et al.*, 1994) also failed to come up with any evidence of worthwhile symptomatic relief. One study of the short-term effects of treatment in a small group of term babies some 2–6 weeks old actually found that treatment actually increased in the frequency with which reflux occurred, although the episodes did not last quite so long (Cresi *et al.*, 2008). The study failed to identify any evidence of clinical benefit.

Yet another small trial comparing the efficacy of domperidone and cisapride from Jakarta published in 2009 (Hegar *et al.* 2009) also failed to find much evidence of benefit with either drug. Indeed it concluded that cisapride (withdrawn from sale by the manufacturers in Europe and North America in 2002 when it was shown that the associated increase in the QT interval could some times cause a dangerous arrhythmia) probably performed better than domperidone.

It has been known for more than twenty years that domperidone can occasionally cause a sudden dangerous arrhythmia in adults when given as an IV injection (Quinn *et al.*, 1985). Now comes evidence that it can also prolong the QT conduction time not only in the laboratory (Drolet *et al.*, 2000) but also, rather unpredictably, when given to an infant by mouth (Rocha and Barbosa, 2005; Djeddi *et al.*, 2008) and a recommendation that, even though use in infancy has not yet been known to cause a fatal arrhythmia, continued use in the management of gastro-oesophageal reflux is becoming increasingly hard to justify (Collins and Sondheimer, 2008).

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