PostScript

LETTERS

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Intravenous atropine treatment in infantile hypertrophic pyloric stenosis

Hypertrophic pyloric stenosis of infancy is a disorder of early infancy with typical clinical features and well-established radiological appearance of the pyloric canal. Many studies with surgical and medical treatment have been reported over the past fifty years. Pylorotomy has tended to become the favoured method of treatment as with expert paediatric, surgical, anaesthetic, and nursing services and specialised accommodation for infants, the outcome is good with low mortality, short stay in hospital and few complications. However, a variety of studies of medical treatment with anticholinergic drugs and successful outcomes in some large series of cases have also been reported from Sweden, United States of America and the United Kingdom.

Since 1996 this group of workers from Osaka, Japan, has revived an interest in medical treatment with reports of a new regime using methyl atropine nitrate intravenously. To achieve satisfactory short term outcomes considerable variation in drug dosage and modified feeding regimes were necessary which involved much medical supervision and careful monitoring for toxic effects of the drug, which were minimal. The treatment was successful in the relatively small number of infants in the trial (19) with two infants being referred for pylorotomy, no mortality and no serious complications. An interesting part of this paper is the long term clinical follow up of the successfully treated infants over two years and ultrasonography of the pyloric canal which demonstrated the changes in muscle thickness and length of the canal. The disadvantages of the treatment mentioned by the authors are length of stay in hospital and the necessity to continue atropine medication orally after discharge home.

Comparing the use of this anticholinergic drug intravenously with oral treatment using methyl scopolamine nitrate and similar restricted feeding regime, oral methyl scopolamine nitrate suppressed vomiting more quickly and reliably, was also available for subcutaneous injection if vomiting recurred as size of feeds was increased, and no toxic effects were seen in any dosage used. It would be interesting if these workers would be prepared to try the use of methyl scopolamine nitrate intravenously as pharmalogically this compound was reported to have a spasmolytic effect on gut two to three times greater than methyl atropine nitrate[1] with lesser central nervous effects.

This paper serves to emphasise once more that these infants should always be treated in paediatric centres where there is a high level of experienced paediatric care and nurses trained for neonatal special care.

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Reference

1 **Corner BD**. *Arch Dis Child* 1955;**30**:377–86.

Author's reply

We appreciate the interest shown by Dr Beryl Corner with regard to our article.[1] Unfortunately, intravenous atropine therapy is not widely accepted in European countries or the United States; it is however now becoming popular in Japan.

We are truly honoured to receive the comments of Dr Corner, who is a pioneering neonatologist and reported medical treatment with methyl scopolamine nitrate for infantile hypertrophic pyloric stenosis (IHPS) in 1955.[2] She pointed out that methyl scopolamine might be better than atropine sulfate in terms of effectiveness and side effects. One of the reasons why atropine was used in our study is that methyl scopolamine is not available in ou country. Scopolamine butylbromide is an available quaternary ammonium derivative of scopolamine and lacks toxic side effects. However, this agent tastes bitter and is difficult to give orally to infants. Therefore, this agent is only given intravenously in infants with IHPS.

We do not know if it is worthwhile to attempt combination therapy with intravenous scopolamine butylbromide and oral atropine rather than the intravenous and oral atropine therapy. Secondly, we already knew that an intravenous atropine injection of 0.01 mg/kg was effective enough to abolish transiently the phasic and tonic pyloric contractions characteristics of IHPS.[3] We used an intravenous atropine injection of 0.01 mg/kg in our study to confirm that those pyloric contractions were the cause of disturbed transpyloric flow in this condition by seeing that their inhibition with the dose of atropine ameliorated symptoms.

We agree with Dr Corner's last comment, but believe that intravenous atropine therapy is possible not only in high level paediatric centres, but also in general hospitals where infusion therapy with intravenous atropine injections can be done safely in small infants. Clinical trials are now ongoing to establish more efficient treatment strategy for IHPS with medical and surgical therapy in our country.

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Hypothermia in a child secondary to ibuprofen

A 7 year old girl was admitted with right lower lobe pneumonia. On admission her temperature was 39.7°C. After five hours she received ibuprofen (6 mg/kg). Susequent to this single dose her temperature decreased to 33.5°C (core temperature 34.9°C) over four hours.

On examination her pulse was 90/min, blood pressure 90/50 mm Hg, SaO_2 96% in air, and respiratory rate 20/min. Respiratory examination was consistent with signs of right lower lobe consolidation. The rest of the examination, including the central nervous system, was unremarkable.

Results of investigations included: Hb 125 g/l; white blood cell count 10.7×10^9/l platelet count 81×10^9/l; C reactive protein 180 mg/l; blood glucose 4.6 mmol/l. Electrolytes and all other biochemical investigations were normal. Thyroid and cortisol assays were normal. Results of all tests to determine possible bacterial or viral aetiology were all negative (blood and urine culture, viral serology, and tests for mycoplasma). Magnetic resonance imaging (MRI) of the brain was normal.

The hypothermia was so marked that we had to use a hot air spacer blanket to raise her temperature. Despite all the efforts she remained persistently hypothermic for four days (see fig 1).

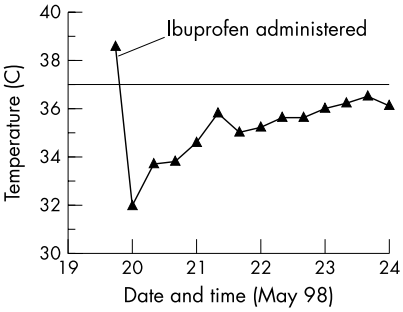

Figure 1 Temperature chart. After administration of ibuorifen, the temperature dropped considerably and remained low for five days.

A single dose of hydrocortisone and an albumin infusion were given initially. She was subsequently treated with warmed intravenous fluids for three days and antibiotics for 10 days. She recovered completely and continues to enjoy good health.

Profound hypothermia is extremely rare in children over 5 years of age. Results of investigations excluded infective and endocrine causes. A normal MRI brain scan showed there was no lesion of the hypothalamus or corpus callosum.

Ibruprofen is commonly prescribed for a raised temperature and is well tolerated in children. Side effects are not common, even in overdose.[1] Nevertheless we postulate that ibuprofen was responsible for hypothermia in this case. We are not aware of any published evidence documenting hypothermia after a single therapeutic dose of ibuprofen, but it has been recorded in a few cases of accidental and deliberate overdosage. Although patients may sometimes receive ibuprofen in toxic quantities, hypothermia is not a consistent feature.[2 3] Hypothermia in overdosage is attributed to central nervous system depression.[4]

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Vagal overactivity: a risk factor of sudden infant death syndrome?

Since early 1990, the incidence of sudden infant death syndrome (SIDS) has dropped sharply because of public health campaigns decrying the dangers of the prone sleep position. The other known risk factors, such as preterm birth and young maternal age, are less susceptible to prevention campaigns.[1]

Disordered autonomic function, including cardiorespiratory control, has been suggested to be involved in SIDS.[2 3] Vagal overactivity (VO), characterised by breath holding spells and repeated syncopes in specific circumstances, has been described as a manifestation of autonomic dysfunction.[4] To investigate a possible relation between VO and SIDS, we investigated 65 children presenting documented VO; for example, clinical characteristics and a positive test for eyeball compression and/or electrocardiographic monitoring. Parents of these children were interviewed about their family history, especially with respect to the occurrence of SIDS among their other children.

Among their siblings, five of 126 had died of SIDS. All five children were full term infants. The average maternal age, birth weight, and age at death were respectively 27.4 (3.5) years, 3.3 (0.3) kg, and 3.5 (1.1) months. The rates of SIDS in siblings of children with VO were compared to those in the general population using the standardised incidence ratio (SIR), which is the ratio of the observed number to the expected number of cases of SIDS calculated by French incidence rates. The expected number of SIDS was 0.17 and hence the SIR was 29.4 (95% CI 9.5 to 68.6; $p < 0.000011$). Our result showed an overall significant excess of SIDS among siblings of children with VO. We verified that recruited children had not come to the centre because of a family history of SIDS. Since children with a positive family history of SIDS could be followed up more regularly than others, we estimated the SIR separately among siblings of children recruited during their follow up and those of children recruited during their first visit, and verified that there was no significant difference in SIR between these cases.

Despite the marked decline in SIDS, it is still the leading cause of postneonatal mortality. Better knowledge of other risk factors may allow identification of populations at high risk and a possible decline in infant mortality from SIDS through the implementation of appropriate prevention measures. Our findings suggest that VO may be involved in SIDS and that children with VO or a family history of VO may be a population at potential high risk of SIDS.

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Perforated duodenal ulcer disclosing medium chain acyl-CoA dehydrogenase deficiency

Medium chain acyl-CoA dehydrogenase deficiency (MCADD; McKusick 201450) typically presents in the first two years of life with recurrent episodes of hypoketotic hypoglycaemia, lethargy, coma, or sudden infant death. The trigger may be fasting, intercurrent infections, anaesthesia, or surgery. Incidence in the UK is estimated at 0.45–1/10 000 live births.[1] We describe the case of a child who presented with marked encephalopathy unexplained by perforated duodenal ulcer, which led to the diagnosis of MCADD.

A 2 year old girl presented with a three week history of coryzal symptoms and three day history of frequent coffee ground vomiting. She was shocked, and had hepatomegaly and decreased conscious level. Blood glucose was 3.9 mmol/l (reference interval 3.3–5.5), plasma sodium 129 mmol/l (135–147), potassium 5.2 mmol/l (3.5–5.0), urea 17.8 mmol/l (3.3–6.6), creatinine 36 mmol/l (30–74), bicarbonate 15 mmol/l (21–28), base excess −5.4 mmol/l (−4 to +2) and C reactive protein 4 mg/l (0–5). Liver function tests and clotting were normal. She was resuscitated with a total of 50 ml/kg of colloid and crystalloid. The following day she relapsed with abdominal distension, shock, and deteriorating conscious level. Investigations showed glucose 14.2 mmol/l, amylase 20 IU/l (8–85), AST 186 IU/l (10–45), and ALT 129 IU/l (10–40). An *x* ray examination of the abdomen showed free air under the right hemidiaphragm. Emergency laparotomy revealed a single, 1 cm × 1 cm acute perforation in the second part of the duodenum. Histology and rapid urease test (CLO) of the duodenal biopsy for *Helicobacter pylori* were negative. Fasting blood gastrin was 20 mU/l (10–100). She was discharged home taking omeprazole. Upper gastrointestinal endoscopic biopsy (eight weeks later) for histopathology and CLO test from oesophagus, stomach, antrum, and duodenum were normal.

Analysis of urinary organic acids by gas chromatography and mass spectrometry, obtained a day after clinical presentation, revealed a marked increase in 5-hydroxyhexanoic acid (21% of total organic acids); a modest dicarboxylicaciduria (suberic accounted for 8% and adipic 6% of total organic acids); and a small but significant quantity of hexanoyl glycine (2% total organic acids) in the absence of ketonuria.

Blood obtained a week after clinical presentation, when analysed by tandem mass spectrometry, showed octanoylcarnitine 2.91 µmol/l (≤0.19), hexanoylcarnitine 0.67 µmol/l (≤0.29), and decenoylcarnitine 0.63 µmol/l (≤0.10), with a subnormal concentration of acetylcarnitine 4.0 µmol/l (6.2–27.5). This profile was consistent with MCADD. Polymerase chain reaction/restriction digests based method revealed two mutations in the MCAD gene.

The clinical details coupled with the absence of ketones and the increased 5-hydroxyhexanoic acid led us to look for an abnormality in the oxidation of fatty acids, and resulted in identification of the minor constituent, hexanoylglycine that is recognised as an indicative marker of MCADD. Increases in urinary hexanoylglycine and 5-hydroxyhexanoic acids in the absence of ketonuria have been reported previously in MCAD patients during clinical attack,[2] and also in a boy who died.[3] Our case was unusual in that the amount of 5-hydroxyhexanoic acid was greater than even the sum of the individual dicarboxylic acids present, although high levels of 5-hydroxyhexanoic acids are reported in acute episodes.[4] The increased concentration of octonoyl carnitine in blood was also consistent with a diagnosis of MCADD.

We believe that this is the first report of MCADD presenting with duodenal ulcer. It could be argued that the ulcer was the primary problem and that the decompensation was caused by the subsequent illness.