Drug reactions and interactions

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LOPERAMIDE TOXICITY IN A CHILD

Loperamide is an antimotility agent which inhibits peristalsis and has been used in the treatment of some diarrhoeas. Its use is controversial in acute infective diarrhoea since in slowing the motility of the gut it may delay the elimination of the causative organisms. Especially its use is not recommended in the treatment of acute diarrhoea in children particularly because of doubts about its safety[1-3]. Respiratory depression and coma may occur after overdosage[4]; however, a new aspect of its toxicity has been the report by Minton and Smith[5] from the National Poisons Unit, Guy's Hospital, London and the Department of Paediatrics, Addenbrooke's Hospital, Cambridge, U.K. of serious toxity in a child after a single dose of loperamide.

The patient, a 15-month-old girl weighing 8 kg, was admitted to hospital after accidental scalding, superficial burns covering 35 per cent of the body area. She was rehydrated with intravenous fluids, treated with flucoxacillin and penicillin, and on day 5 was transferred to a plastic surgery unit for assessment. At the time she was taking fluids and had copious green watery diarrhoea. Clinical examination showed no other abnormality and she was well-hydrated. Diagnosis was diarrhoea as a stress response to burns.

On day 9 she was still having diarrhoea and was prescribed an initial 1 mg oral dose of loperamide. Fifty minutes later she was collapsed, pale and unresponsive to pain. Her pulse was 120/min and her respiratory rate 14/min. She had not vomited or convulsed. She was resuscitated with oxygen by Ambu bag and given 0.3 mg naloxone intravenously. By 2 min conscious level was improved and her respiratory rate increased to 30/min. Next day she was still drowsy; blood values were: haemoglobin 8'7 g/l, urea and electrolytes normal, alanine aminotransferase activity 327 U/l, total protein 36 g/l and albumin 11 g/l. She was tranfused 200 ml whole blood and 100 ml plasma protein fraction. Conscious level became normal on day 11; serum alanine aminotransferase activity was then 76 U/l, total protein concentration 48 g/l, and albumin concentration 18 g/l. Her diagnosis was then changed to cows' milk protein intolerance, as the diarrhoea resolved on withdrawal of milk.

The authors of this report commented that the 1 mg dose of loperamide used for this child (0.125 mg/kg) may have been greater than necessary, as the manufacturer's data sheet recommended the dose for children aged 4-8 years as 1 mg every 6 h until diarrhoea settles. However, the reason for toxicity in this case was not clear. The low serum protein concentration may, they suggest, have been a contributory factor (loperamide is 97 per cent protein-bound) and absorption may have been increased by damage to the gut wall. The raised serum alanine aminotransferase suggests that a temporary hepatic disturbance might have impaired handling of the drug.

It should be emphasised that in the United Kingdom this drug (*Imodium*) is available without prescription; Mintom and Smith[5] have therefore warned that doctors should be alert to the possible hazards of accidental ingestion of this drug by small children and the specific treatment that may be required. Naloxone appears to be an effective antidote. Reports to the National Poisons Unit have suggested that although this drug causes symptoms in most cases of accidental overdosage, serious toxicity is rare[5].

However, there does seem to be a body of influential opinion that loperamide should not be used to treat acute diarrhoea in young children. World Health guidelines are against such use[1-3]. Martindale (The Extra Pharmacopoeia) states that 'It should not be used to treat young children', and it reviews some of the literature which indicates albeit anecdotally in some cases, that loperamide should not be used in acute infective diarrhoea in childhood[6]. The manufacturer states on the data sheet that 'there are no specific contra-indications to *Imodium*[7], there is good reason to suggest that this latter statement should be modified as a matter of urgency in view of this present case and of the other opinions. It would be prudent to suggest that loperamide should not be used in young children until more evidence was available as to its safety. It should also be recalled that with acute diarrhoea in children the major concern is dehydration and that the primary treatment for

such cases is the use of oral rehydration salts, preferably the W.H.O./UNICEF O.R.S. formulation[1].

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CONTAMINATION OF MULTIPLE APPLICATION EYE DROP BOTTLES

The isolation of the AIDS virus (HIV) from the tears of a patient[1] has aroused concern about the risks of transmission of the virus during various ophthalmic procedures[2]. Current procedures at the Western Ophthalmic Hospital, London, U.K. permit the use of multiple application dropper bottles in ophthalmic outpatient departments, though opened bottles are discarded at the end of the day. Two members of the department, Waylward and Wilson, carride out a simple study to discover whether such dropper bottles can become contaminated with tear fluid during normal use[3].

The study took place during a single ophthalmic outpatient clinic. Oxybuprocaine (*Benoxinate*) was supplied in glass multiple application dropper bottles incorporating a dropper in the screw cap. One bottle was provided for each of eight slit lamps. For tonometry, these investigators asked that a drop of oxybuprocaine should be installed into the tear sac after 1 per cent fluorescein; this was the reverse of the usual order of application of these solutions. At the end of the clinic the eight bottles were collected and examined for contamination with fluorescein by use of a Perkin Elmer 3000 fluorescence spectrometer set for an excitation frequency of 440nm and an emission frequency of 510nm. The volume of drops remaining in each bottle was also measured to give a rough guide to the number of times it was used.

Six of the eight bottles were contaminated with fluorescein and contamination was heaviest in those bottles which were used more frequently. The investigators considered the various ways in which this contamination could occur. If the drop is touched rather than dropped on to the conjunctiva there may be reflux into the dropper. This is especially likely when the patient's chin is resting on the slit lamp. Also, if the dropper is held too low and the patient's head is not sufficiently far back then the tip of the dropper may brush against the lashes of the upper eye lid.

Waylward and Wilson emphasise that the practical importance of their study relates to patients without obvious external eye disease who none-the-less have microorganisms in their tears. Commensal bacteria are present in the conjunctival sac, and bacterial contamination of dropper bottles is known to occur[4]. It has also been shown that contaminated ophthalmic solutions were responsible for the spread of infection with adenovirus type 8[5]. The obvious concern at present time is the possibility of an asymptomatic carrier of the AIDS virus infecting others via the virus in tears.

Although there is no present evidence to suggest that HIV has been transmitted through contact with tears, the possibility exists although there is, as yet, no way in which this possibility can be assessed. It would seem therefore that the sensible precaution would be to use single application packs of the eye drop solutions. They would be more expensive in use but they would eliminate the small but finite risk that such contamination represents.

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