and epigastric pain. After a month she stopped taking the drug and two weeks later was admitted as an emergency case because of several haematemeses and melaena stools. On admission her haemoglobin concentration was 5.0 g/dl. Endoscopy showed a large duodenal and a gastric ulcer. She improved after a blood transfusion but then deteriorated; abdominal films showed free gas in the peritoneum. Emergency surgery disclosed perforation by the duodenal ulcer and also stercoral perforation of the sigmoid colon. The perforated duodenal ulcer was oversewn and a left hemicolectomy performed; she made a slow but satisfactory recovery.

Case 3—A 78-year-old woman had a duodenal ulcer confirmed by barium meal in 1966 but had had no further dyspeptic symptoms until she started taking benoxaprofen 600 mg daily for osteoarthritic pain in her right knee. After one month she complained of gnawing epigastric pain associated with nausea but no vomiting. She stopped taking benoxaprofen two weeks later. Three days after stopping the drug she passed several melaena stools and became dizzy and faint. On admission her haemoglobin concentration was 9.7 g/dl. She was transfused with 4 units of packed cells and endoscopy showed two active duodenal ulcers. Cimetidine was prescribed, her stools became negative for occult blood, and she was discharged.

Comment

The incidence of peptic ulceration in patients taking benoxaprofen is about 0.4%,¹ with only one case of gastrointestinal haemorrhage occurring four months after the drug had been discontinued. The incidence of gastrointestinal disturbance may be low because benoxaprofen is a relatively weak inhibitor of prostaglandin synthetase.³ Gastrointestinal haemorrhage in the three patients described here may have been unrelated to benoxaprofen. Nevertheless, the timing strongly suggests that the development of peptic ulceration was associated with the administration of benoxaprofen at the recommended daily dosage. The assertion that benoxaprofen is less likely to cause serious gastrointestinal disturbance than other non-steroidal anti-inflammatory agents⁴ requires further evaluation, especially in the elderly.

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Immune response of infants in tropics to injectable polio vaccine

As a result of two decades of experience with oral polio vaccine (OPV, Sabin) in India, certain problems have come to light.¹ When it is used in the conventional manner, the protective efficacy of oral polio vaccine is only moderate and vaccine failure is common.² To improve efficacy, a five-dose schedule for primary immunisation has been recommended, but this is out of step with the diphtheria, pertussis, and tetanus vaccination, for which only three doses are sufficient.³ Injectable polio vaccine (IPV, Salk) is, however, available as an alternative vaccine, and it is important to evaluate its efficacy in developing countries. If found suitable its use may simplify routine immunisation of children as it can be combined with the diphtheria, pertussis, and tetanus vaccine into a quadruple vaccine and does not need to be frozen for long storage. We examined the immune response of infants given three doses of injectable polio vaccine incorporated

with diphtheria, pertussis, and tetanus vaccine into a quadruple vaccine, as a first step in its evaluation in India.

Patients, methods, and results

Infants aged 6 to 45 weeks attending our immunisation clinic were given three doses of the quadruple vaccine. Each dose (1 ml) contained 20, 2, and 3.5 D antigen units of killed poliovirus types 1, 2, and 3 respectively, and was administered at four or eight weekly intervals to infants beginning their immunisation on alternate weeks. Blood was collected before the first dose and four weeks after the third dose by heel prick. The paired sera were simultaneously tested for the presence and titre of poliovirus-neutralising antibodies in steps of serial twofold dilutions starting from 1/8 against 30 to 300 median tissue culture infective doses of each type of poliovirus, according to methods previously described.⁴

Out of 153 infants tested, 67 were seronegative to the three types of poliovirus before immunisation. The three doses were given at four-weekly intervals to 45 and at eight-weekly intervals to 21. The table shows seroconversion rates.

Seroconversion in tritypic seronegative infants

Interval between doses	No	Seroconverted to poliovirus			Sero-conversion index (%)
		Type 1	Type 2	Type 3	
4 weeks	45	45 (100%)	41 (91.1%)	41 (91.1%)	94.1
8 weeks	22	22 (100%)	22 (100%)	21 (95.5%)	98.5
Both groups	67	67 (100%)	63 (93.9%)	62 (92.5%)	95.5

Seroconversion to type 1 was complete in both groups. Response rates to types 2 and 3 were better in infants given the vaccine at eight-weekly intervals than in those given it at four-weekly intervals, but these differences were not statistically significant ($p > 0.05$). The overall response was 100% to type 1 and over 90% to types 2 and 3. The seroconversion index, which is the mean response to the three types, was over 98% when injectable polio vaccine was administered at eight-weekly intervals.

Comment

Injectable polio vaccine is routinely used for infants and children in the Netherlands. The poliovirus antigen is formulated according to local needs and standards and contains relatively low levels of types 2 and 3. This is reflected in the seroresponse in our study. The response will probably improve further if the antigenic content of types 2 and 3 is enhanced.

This study suggests that the quadruple vaccine may be used in the routine immunisation of infants in developing countries, starting as early as 6 weeks of age, with better antibody response than with oral polio vaccine.¹ The seroconversion index after three doses of injectable polio vaccine given at four-weekly intervals was 94.1% whereas it was only 78% after three doses of oral polio vaccine given under similar conditions.⁴ If injectable polio vaccine could be manufactured in sufficient quantities and at an economic price, it would be an effective alternative to oral polio vaccine in tropical countries.

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