ORIGINAL ARTICLE

Chlorpromazine-HCL in Acute Infantile Diarrhoea (A Brief Clinical Observation)

by

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Abstract

A total of 78 patients aged between 2 months and 3 years suffering from acute watery diarrhoea underwent investigation. Fifty-seven patients received chlorpromazinne-HCl 1 mg/kg B.W./day in addition to oral glucose electrolyte solution. Twenty-one patients were given a combination of chlorpromazine-HCl (1 mg/kg BW/day) and antibiotics in addition to oral glucose electrolyte solution.

In the first group diarrhoea stopped within 3 days in 70.4% and within 7 days in 85.2% of the treated patients. In the second group almost similar results were observed : resp. 70% and 85%. Three patients in the first group (5.3%) and one patient in the second group (4.8%) received i.v.f.d. because of the worsening of the diarrhoea.

Side-effects observed during the study, were irritability in one patient, heavy sedation in 2 patients and uncoordinated movements in one patient.

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Introduction

Chlorpromazine is a synthethic phenothiazine derivative which was investigated because of its antihistamine properties and came into use because of its antiemetic potentiality. However, both chlorpromazine and parent substance, promazine are potent tranquilizing agents (Lewis, 1957). It has the chemical name of 2 chloro 10 3 - (dimethylamine) propyl — phenothiazine. C. hydrochloride (USP), the hydrochloride of chlorpromazine, occurring as a white crystalline powder, used orally, muscularly or intravenously as a major tranquilized Dorland, 1974).

Little is known, however, of its effect on infantile diarrhoea, although Rabbani et al., (1979) proved that chlorpromazine has also the ability to reduce stool output in cholera patients.

The purpose of the present study is to know the effect of chlorpromazine HCl when given as a single drug or when combined with antibiotics in infants suffering from acute watery diarrhoea.

Materials and methods

A total of 78 patients aged between 2 months and 3 years suffering from acute watery diarrhoea of less than 3 days duration were arbitrarily divided into 2 groups :

Group I : consisting of 57 patients received chlorpromazine HCl 1 mg/kg body weight/day orally devided into 3 doses for 5 days.

Group II : consisting of 21 patients were given a combination of chlorpromazine HCL (1 mg/kg body weight/day) and antibiotics for 5 days.

In addition all the patients in both groups received oral electrolyte solution. Clinical assessments included the duration of illness, state of diarrhoea and possible development of dehydration and occurrence of side-effects. Patients who showed clinical deterioration were immediately admitted to the hospital to have i.v.f.d. administration.

Results

TABLE 1 : *Age distribution.*

	0 — 6 mo	7 — 12 mo	> 12 mo	Total
Chlorpromazine HCl	13	22	22	57
Chlorpromazine HCl + Antibiotics	9	8	4	21

The age groups were comparable($0.30 < p < 0.50$).

TABLE 2 : *Course of the disease.*

	< 3 days	⩾ 3 days	Total
1. Chlorpromazine HCl	38 (70.4%)	16	54*
2. Chlorpromazine HCl + Antibiotics	14 (70%)	6	20*

* 3 patients in group I and 1 patient in group II underwent i.v.f.d. administration because of the worsening of the diarrhoea.

Stool became solid within 3 days in 70.4% of the patients in group I and 70% in group II. The difference between both groups was not significant.

TABLE 3 : *Course of the disease.*

	< 7 days	> 7 days	Total
1. Chlorpromazine HCl	46 (85.2%)	8	54
2. Chlorpromazine HCl + Antibiotics	17 (85%)	3	20

Table 3 shows that the stool became normal in 85.2% of the patients in group 1 and 80% in group 2. Again no significant difference existed between the two groups.

Side-effects observed during the chlorpromazine therapy were irritability in one infant, deep sedation in 2 cases and uncoordinated movements in one case.

Discussion

Two mechanisms have been recognized whereby bacterial pathogens may produce the syndrome of acute gastroenteritis. There are toxin production and mucosal invasion.

Invasive organisms (e.g. Salmonellae, Shigellae and some strains of E. Coli) penetrate the mucosa of the distal small intestine and colon to produce morphological abnormalities and dysentery. The dysentery results from the mucosall disruption and diarrhoea from jejunal secretion overwhelming the reabsorptive capacity of the injured colon. Shigella can also produce an exotoxin which induces electrolytes, intestinall secretion of fluid and electrolytes, and it is possible that other invasive pathogens may, also have this capacity (Harries, 1977).

The non-invasive enteropathogens (e. g. Cholera and E. Coli) elaborate enterotoxins in the small intestine and induce secretion without affecting the mucosal structure. The absorptive defect is confined to the small bowel and colonic function is normal. Diarrhoea results from the small intestinal secretion overwhelming the normal reabsorptive capacity of the colon (Harries, 1977). Enterotoxins are synthesized within the bacterial cell body and are elaborated into broth cultures containing intact bacteria, whereas endotoxins are associated with the bacterial cell wall and so are not found in broths unless there is damage or destruction of the bacteria. Enterotoxins have classically been shown to be produced by vibrio cholerae but also by some strains of E. Coli and food poisoning, strains of Staph. aureus and Clostridium perfringens as well as Shigella shigae (Walker-Smith, 1979).

Since the successful purification of cholera toxin major advances have been made in our understanding of the precise mechanisms which mediate the secretory effects of bacterial toxins.

The toxins bind to the brush border of the surface epithelial cells and activate the enzyme adenyl-cyclase which is located in the basolateral membranes of the cell. Adenyl-cyclase catalyses the conversion of adenosine triphosphate to cyclic adenosine 3', 5' monophosphate (cyclic AMP). Cyclic AMP binds phosphoproteinkinase which consists of 2 components : R (regulator) and C (catalytic), the first of which remains fixed to cyclic AMP (AMP CR), while the C fragment goes to phosphorylize the endogenous protein (Protein ATPC) resulting in epithelial permeability and thus induces, secretion of fluid and electrolytes across the brush border into the small intestinal lumen to produce profuse diarrhoea (Harries. 1977; Meeroff, 1978).

Invasive enteropathogens such as Salmonellae as well as enterotoxin producing bacteriae like vibrio cholerae can produce elevated levels of adenylcyclase activity, resulting from stimulation by prostaglandin synthesized locally (Walker-Smith, 1979).

Little is known in man of the mechanism of diarrhoea in viral gastroenteritis. In animal model Corona virus causes decreased sodium and water flux, decreased mucosal activities of disaccharidases and sodium potassium ATP ase but normal adenylcyclase activity. It is also found in Rotavirus gastroenteritis, a state of accelerated epithelial cell turnover with functionally immature enterocytes clothing the villi. Gould in 1977 found normal levels of prostaglandin in stools of children with Rotavirus gastroenteritis.

Chlorpromazine in animal models has been shown to inhibit cholera toxin stimulated intestinal cyclase and fluid secretion and has been found to be able to reduce stool output in heavily purging cholera patients (Rabbani et al., 1979). In Rabbani's series eleven heavily purging cholera patients (360-1340 ml/hr) eight were given chlorpromazine intramuscularly (1 mg/kg or 4 mg/kg), and three were given a dose of 1 mg/kg by mouth. In these patients there was an overall reduction in stool output of 65 ± 5% during the period of 0 - 32 hours after treatment. This decrease was significantly larger than the 26 ± 9% reduction seen in patients not receiving the drug, who were observed at the same time in the course of their illness ($p < 0.005$).

In the present series, in the group of patients receiving chlorpromazine HCl as a single drug, the diarrhoea stopped within 3 days in 70.4% and within 7 days in 85.2% of the patients treated. While in the group of patients on chlorpromazine HCl combined with antibiotics, almost similar results were observed in 70% and 85% respectively of the patients studied. The difference between both groups was found statistically not significant

The patients in group 1 (5.3%) and 1 patient in group 2 (4.8%) receive i.v.f.d. because of worsening of the diarrhoea. All patients recovered uneventfully.

The side-effects observed during chlorpromazine HCl treatment were irritabillity in one patient, heavy sedation in 2 patients, and uncoordinated movements in one patient. Chlorpromazine like reserpine has been observed to produce a new type of syndrome resembling Parkinsonism. Further evidence of action on the mid-brain is to be found in the lowered blood pressure and increased appetite.

Other toxic effects, in addition to the symptoms of paralysis agitans are drowsiness, increased susceptibility to epilepsy and the occasional occurrence of jaundice. A few cases of agranulocytosis have been reported, but the drug has been used on a very large scale (Lewis, 1977).

In Rabbani's series (1979), the side-effects of decreased nausea and mild sedation due to chlorpromazine added to the patients comfort. No hypotension was seen in his well-hydrated patients.

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