CHAPTER I

INTRODUCTION

Background and Rationale

Diarrhoea still ranks high as a major cause of illness in Thailand as in other developing countries (1-3). During the six-year period 1978-1983, 1,979,218 cases of diarrhoeal diseases in Thailand were reported to the Division of Epidemiology, Ministry of Public Health. In this period, the annual incidence has been steadily increasing from approximately 300/1,000,000 population in 1978 to over 1,000/1,000,000 population in 1983. The majority of cases were acute diarrhoea (77.4 %) (4).

Treatment of diarrhoea is complicated by a number of various potential causes (see page 15). As a result of recent advances in diagnostic methodology, the causative agents in most cases can now be identified. The majority of acute diarrhoeal diseases in developing countries are caused by bacteria (1,5). Although, most of the diseases are self limited and rehydration therapy alone is often sufficient especially in mild cases (6,7), sometimes it takes several days for the patients to recover especially in non-immuned person. It is not unusual for patients with acute bacterial diarrhoea to be treated with antibiotics.

Appropriate uses of antibiotics in selected cases of acute bacterial diarrhoea will decrease symptoms or reduce faecal shedding of the pathogens and prevent spread of the infection (5). However, wrong choice of antimicrobial agents will worsen the symptoms, change of intestinal microflora, promote the emergence of antimicrobial resistance strains and overgrowth of potential pathogenic bacteria and fungi (5).

Since the common causative pathogens of acute bacterial diarrhoea are gram-negative bacteria, one major problem in antimicrobial therapy is the acquisition and propagation of plasmids bearing these pathogens (8-13). These pathogens tend to increase percentage of resistance to trimethoprim, ampicillin and tetracycline which were commonly used (14-21). In the past there was no single available antimicrobial agent capable of adequately covering all bacterial pathogens implicated in acute bacterial diarrhoea. New quinolones have good activities against most of the bacterial enteropathogens. They might be used as a first line drug in case of severe bacterial diarrhoea before the pathogens are known.

Norfloxacin is a new 4-quinolone derivative. It is very active against most gram-negative and gram-positive organisms (see page 9). Norfloxacin has been raised for this research by the following concerns and properties :

1. From many reports, norfloxacin has excellent in vitro activity against most bacterial enteropathogens with very low minimal inhibitory concentration (MIC)(see page 9).

2. Norfloxacin has a selective decontamination of the digestive tract: aerobic gram-negative bacteria are suppressed to undetectable concentrations while anaerobic bacteria are left intact, thus preventing colonization of the digestive tract by potentially pathogenic aerobic species (22-28).

3. Norfloxacin produces high concentration in stool that surpass the MIC for most bacterial enteropathogens (28-30).

4. Norfloxacin resistance rarely happens. The resistance is neither dependent on destruction of antibiotic by enzymes nor plasmid mediated (31).

5. Preclinical and clinical data proclaim the efficacy of norfloxacin in the treatment and/or prevention of gastrointestinal tract infections (23,29, 32-35). Norfloxacin is also found to be well tolerated.

All these mentioned data had motivated the researcher to handle the study of "Microbiological and Clinical Efficacy of Norfloxacin in Acute Bacterial Diarrhoea".

Objective

The purposes of this research are as follows:

1. To study the in vitro efficacy of norfloxacin against bacterial enteropathogens.

2. To evaluate the clinical and bacteriological efficacy of norfloxacin 400 mg twice daily compared to co-trimoxazole 160/800 mg twice daily and placebo twice daily in patients with culture proven bacterial gastroenteritis caused by any of the following bacterial enteropathogens: Salmonella, Shigella, Escherichia, Aeromonas, Plesiomonas, Vibrio and Campylobacter.

3. To evaluate safety of norfloxacin 400 mg twice daily compared to co-trimoxazole 160/800 mg twice daily and placebo twice daily in patients with culture proven bacterial gastroenteritis.

Significance of the Study

1. If norfloxacin is found to be effective in treatment of acute bacterial diarrhoea, the advantages are:

1.1 Revelation the use of appropriate antibiotic in selected cases of acute bacterial diarrhoea.

1.2 If norfloxacin is bacteriological effective, norfloxacin will reduce faecal shedding of the pathogens and prevent spread of infection.

1.3 If norfloxacin is clinically effective, clinical symptoms will be improved in a very short time, thus the admission time will be reduced.

1.4 It will mean medical progress in finding another new antimicrobial agent for present or future use in treatments of acute bacterial diarrhoea, the disease with a tendency of higher drug resistance to the causative pathogens.

2. The in vitro study of drugs efficacy against bacterial enteropathogens will give the exact information of drugs susceptibility for the pathogenic strains isolated from Thai paients.

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