PHARMACEUTICAL RESEARCH

RESEARCH TOPIC

Treatment of Diarrhoeal disease with different types of Antibiotic in patients admitted to Institute of Child Health & Shishu Sasthya Foundation Hospital

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2005-1-70-003

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DEDICATED

TO

MY BELOVED PARENTS

FOR THEIR

UNPARELLEL INSPIRATION

AND GUIDENCE TO MY LIFE

CERTIFICATE

This is to certify that, the thesis 'Treatment of Diarrhoeal disease with different types of Antibiotic in patients admitted to Institute of Child Health & Shishu Sasthya Foundation Hospital' submitted to the Department of Pharmacy, East West University Mohakhali Dhaka in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (B.Pharm) was carried out by Md. Sohel Rana (ID: 2005-1-70-003) under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the sources of information and laboratory facilities availed of this connection is duly acknowledged.

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ABSTRACT

Diarrheal disease remains an important cause of childhood morbidity and mortality in developing countries, although diarrheal deaths have significantly declined in recent years, mostly due to successes in the implementation of oral rehydration therapy (ORT), which is the principle treatment for the diarrheal diseases.

Diarrhea may occur for various reasons; however, most episodes of diarrhea in developing countries are infectious in origin. Three clinical forms of diarrhea (acute watery diarrhea, invasive diarrhea, and persistent diarrhea) have been identified to formulate a management plan. Acute diarrhea is usually caused by infection.

Diarrhea is an illness caused by the bacteria, virus and parasites. It is a common disease in the developing countries like Bangladesh, where it affects about 21.5 million people every year.

The information about the treatment of children with diarrhea (below 10 years) admitted to Institute of Child Health and Shishu Sasthya Foundation Hospital, Mirpur, Dhaka was collected for this study. In addition to Oral Rehydration Solution some common antibiotics were used for the treatment of diarrhea. The antibiotics included Ciprofloxacin, Azithromycin and Ceftriaxone. The patients received antibiotics such as Imipenem, Gentamycin, Ampicillin for their associated illness like severe pneumonia, sepsis etc.

About 73% hospitalized patients (n=41) received antibiotic whereas 27% (n=15) did not receive any antibiotics. Out of 41 male and female children 20 received ciprofloxacin, 9 received gentamicin, 5 received ampicillin and rest of the patients received other antibiotics. The average duration of hospital stay of antibiotic group was 1.02 days and that of non-antibiotic group was 1.33 days. The results show that the duration of hospital stay of antibiotic group is less compared to non antibiotic group.

Chapter 1

1. Introduction

1.1 Diarrhea:

In medicine, diarrhea (from the Greek, "diarrhoia" meaning "a flowing through"), also spelled diarrhoea, is characterized by frequent loose or liquid bowel movements. Globally 4.5 million small children died because of infections in 1982. Diarrheal diseases, respiratory infections, and malnutrition are predisposing factors to infections. Diarrhea can be watery and dysenteric causing loss of body water. Oral rehydration therapy (ORT) prevented 700,000 deaths in 1986 period. Improved case management can prevent deaths: nutrition both during and after an episode of diarrhea, appropriate use of medications, antimicrobial agents in cholera, and factors that protect against enteric infections (gastric acid). (Taylor CE, 1989)

Current estimates of the global burden of disease for diarrhoea are reported and compared with previous estimates made using data collected in 1954-79 and 1980-89. A structured literature review was used to identify studies that characterized morbidity rates by prospective surveillance of stable populations and studies that characterized mortality attributable to diarrhoea through active surveillance. For children under 5 years of age in developing areas and countries, there was a median of 3.2 episodes of diarrhoea per child-year. This indicated little change from previously described incidences. Estimates of mortality revealed that 4.9 children per 1000 per year in these areas and countries died as a result of diarrhoeal illness in the first 5 years of life, a decline from the previous estimates of 13.6 and 5.6 per 1000 per year. The decrease was most pronounced in children aged under 1 year. Despite improving trends in mortality rates, diarrhoea accounted for a median of 21% of all deaths of children aged under 5

years in these areas and countries, being responsible for 2.5 million deaths per year. There has not been a concurrent decrease in morbidity rates attributable to diarrhoea. As population growth is focused in the poorest areas, the total morbidity component of the disease burden is greater than previously. (Bull World Health Organ. 2003).

1.2 Types of Diarrhea

1.2.1 Secretory diarrhea

Secretory diarrhea means that there is an increase in the active secretion, or there is an inhibition of absorption. There is little to no structural damage. The most common cause of this type of diarrhea is a cholera toxin that stimulates the secretion of anions, especially chloride ions. Therefore, to maintain a charge balance in the lumen, sodium is carried with it, along with water. (Viswanathan VK, 2009)

1.2.2 Osmotic diarrhea

Osmotic diarrhea occurs when too much water is drawn into the bowels. This can be the result of maldigestion (e.g., pancreatic disease), in which the nutrients are left in the lumen to pull in water. Osmotic diarrhea can also be caused by osmotic laxatives (which work to alleviate constipation by drawing water into the bowels). In healthy individuals, too much magnesium or vitamin C or undigested lactose can produce osmotic diarrhea and distention of the bowel. A person who does not have lactose intolerance can have difficulty absorbing lactose after an extraordinarily high intake of dairy products. In persons who do not have fructose malabsorption, excess fructose intake can still cause diarrhea. High-fructose foods that also have a high glucose content are more absorbable and less likely to cause diarrhea. Sugar alcohols such as sorbitol (often found in sugar-

free foods) are difficult for the body to absorb and, in large amounts, may lead to osmotic diarrhea. (Viswanathan VK, 2009)

1.2.3 Motility-related diarrhea

Motility-related diarrhea is caused by the rapid movement of food through the intestines (hypermotility). If the food moves too quickly through the GI tract, there is not enough time for sufficient nutrients and water to be absorbed. This can be due to a vagotomy or diabetic neuropathy, or a complication of menstruation. Hyperthyroidism can produce hypermotility and lead to pseudodiarrhea and occasionally real diarrhea. (Bull World Health Organ, 2005)

1.2.4 Inflammatory diarrhea

Inflammatory diarrhea occurs when there is damage to the mucosal lining or brush border, which leads to a passive loss of protein-rich fluids, and a decreased ability to absorb these lost fluids. Features of all three of the other types of diarrhea can be found in this type of diarrhea. It can be caused by bacterial infections, viral infections, parasitic infections, or autoimmune problems such as inflammatory bowel diseases. It can also be caused by tuberculosis, colon cancer, and enteritis. (Viswanathan VK, 2009)

1.2.5 Dysentery

Acute bloody diarrhea, which is also called dysentery.Generally, if there is blood visible in the stools, it is not diarrhea, but dysentery. The blood is trace of an invasion of bowel tissue. Dysentery is caused by an excess of water by a release of antidiuretic hormone from the posterior pituitary gland. Dysentery is a symptom of, among others, Shigella, Entamoeba histolytica, and Salmonella. (Bull World Health Organ, 2005).

1.2.6 Infectious diarrhea

Infectious diarrhea is diarrhea caused by a microbe such as a bacterium, parasite, or virus. (Viswanathan VK, 2009).

1.3 Signs and Symptoms of Diarrhea

1.3.1 Chronic diarrhea

Chronic diarrhea can be a symptom of many disorders:

- Irritable bowel syndrome
- Acute, recurrent or chronic intestinal infections
- Chronic intestinal inflammation (ulcerative colitis and Crohn's disease)
- Chronic pancreatitis, which produces fatty stools
- Laxatives
- Lactose intolerance
- Improper diet (consumption of too much alcohol, coffee or sweets)
- Metabolic disorders such as diabetes and thyrotoxicosis
- Intolerance to gluten (wheat protein). (Rutherford DD, 2005)

1.3.2 Warning signs

- Blood in the motions.
- Pus in the motions (yellow mucus).
- Inability to drink liquids because of vomiting.
- Dehydration - symptoms include excreting small amounts of dark urine, drowsiness, dry mucous membranes and thirst. Dehydration as a result of diarrhea is a particular risk for young children and the elderly.
- Pronounced drowsiness due to dehydration or intoxication.

- Acute diarrhea in infants. Acute diarrhea in very old people.

1.3.3 Signs

- Blood in the motions.
- Pus in the motions (yellow mucus).
- Inability to drink liquids because of vomiting.
- Pronounced drowsiness due to dehydration or intoxication.
- Acute diarrhoea in infants.
- Acute diarrhoea in very old people. (Rutherford DD,2005)

1.3.4 Post-mortem lesions

- Grey nodules in lungs, liver, gizzard wall and heart.
- Intestinal or caecal inflammation.
- Splenomegaly.
- Caecal cores.
- Urate crystals in ureters. (Viswanathan VK, 2009)

1.3.5 E. coli - Diarrhea

E. coli diarrhea is the most important diarrhea. At birth the intestinal tract is micro-biologically sterile and it has little immunity to disease producing organisms. Organisms begin to colonize the tract quickly after birth, among them potentially pathogenic strains of E. coli. After the cloistral antibodies have been absorbed into the blood stream, the immunity is maintained by the antibody (IgA) which is present in milk. IgA is absorbed into the mucous lining of the intestines. It is essential that the newborn piglet drinks sufficient colostrums soon after birth to prevent potentially pathogenic organisms multiplying against the intestinal wall and causing diarrhea. At weaning the loss of sow's

milk and secretory IgA allows the E. coli to attach to the villi of the small intestines, the toxins produced then cause acute diarrhea, usually within five days of weaning.

1.3.6 Symptoms of *E.coli* Diarrhea

1.3.6.1 In acute disease:

- The only sign may be a previously good pig found dead.
- Huddle together shivering or lie in a corner.
- The skin around the rectum and tail is wet.
- Watery to salad cream consistency scour - distinctive smell.
- Vomiting. (Kulkarni H, 2002)

As the diarrhoea progresses

- Dehydrated.
- Sunken eyes.
- Leathery skin.
- The scour often sticks to the skin of other piglets giving them an orange to white colour. (The Pigsite, 2009)

1.4.2 Food poisoning

Certain bacteria (usually staphylococci) irritate the digestive tract by producing toxins. These toxins affect the mucous membrane much sooner, a few hours after consumption, compared with bacterial infection. For this reason, people with inflammation or sores on their hands should not prepare food for others.

1.4.3 Other causes

When taking antibiotics, many people suffer diarrhea, which may continue after the antibiotic course has finished. The diarrhea occurs because the antibiotic alters the intestinal bacterial environment. It is not an allergic reaction. In rare cases it requires medical treatment. Diarrhea can also be caused by dairy intake in those who are lactose intolerant.

1.4.4 Other important causes:

- Ischemic bowel disease. This usually affects older people and can be due to blocked arteries.
- Bowel cancer: Some (but not all) bowel cancers may have associated diarrhea. Cancer of the large intestine is most common.
- Hormone-secreting tumors: some hormones (e.g. serotonin) can cause diarrhea if excreted in excess (usually from a tumor).
- Bile salt diarrhea: excess bile salt entering the colon rather than being absorbed at the end of the small intestine can cause diarrhea, typically shortly after eating. Bile salt diarrhea is a bad side-effect of gallbladder removal. It is usually treated with cholestyramine, a bile acid sequestrant.
- Celiac Disease

1.4.5 Epidemiology of Diarrhoeal Disease:

Diarrhea is the passage of loose or liquid stools more frequently than is normal for the individual. It is primarily a symptom of gastrointestinal infection. Depending on the type of infection, the diarrhea may be watery or passed with blood.

Diarrhea due to infection may last a few days, or several weeks, as in persistent diarrhea. Severe diarrhea may be life threatening due to fluid loss in watery diarrhea, particularly in infants and young children, the malnourished and people with impaired immunity.

The impact of repeated or persistent diarrhea on nutrition and the effect of malnutrition on susceptibility to infectious diarrhea can be linked in a vicious cycle amongst children, especially in developing countries.

Diarrhea is also associated with other infections such as malaria and measles. Chemical irritation of the gut or non-infectious bowel disease can also result in diarrhea. (Kulkarni H, 2002)

1.4.6 Prevalence of Diarrhea

Current estimates of the global burden of disease for diarrhoea are reported and compared with previous estimates made using data collected in 1954-79 and 1980-89. For children under 5 years of age in developing areas and countries, there was a median of 3.2 episodes of diarrhoea per child-year. This indicated little change from previously described incidences. Estimates of mortality revealed that 4.9 children per 1000 per year in these areas and countries died as a result of diarrhoeal illness in the first 5 years of life, a decline from the previous estimates of 13.6 and 5.6 per 1000 per year. The decrease was most pronounced in children aged under 1 year. A study done by Henry FJ showed that watery diarrhea was most prevalent in children aged 6-11 months, the prevalence of dysentery peaked between 18 and 23 months of age. Severely stunted children were found to have significantly prolonged episodes of dysentery. Shigella and persistent diarrhea were more frequent in children with dysentery than in those with nonbloody

diarrhea. A striking feature was that watery diarrhea, dysentery, persistent diarrhea, and malnutrition each account for less than 5% of all deaths among children aged less than 5 years.

Prevalence of diarrhea in Bangladesh: In Bangladesh, one third of the total child burden is due to diarrhea. Every year, a rural child suffers on average from 4.6 episodes of diarrhea, from which about 230,000 children die. In this study, information was collected from 8,287 children under five years of age and 7,082 caretakers in 120 clusters chosen by a two-stage random cluster sampling method. As compare to the baseline survey, carried out in 1996, children now are about 30% less likely to suffer from diarrhea, and the risk of dying has been reduced by 60%.(Piechulek H, 2003)

1.5 Treatment of Diarrhea:

Symptomatic treatment for diarrhea involves the patient consuming adequate amounts of water to replace that loss, preferably mixed with electrolytes to provide essential salts and some amount of nutrients. For many people, further treatment is unnecessary. The following types of diarrhea indicate medical supervision is required.

- Diarrhea in infants.
- Moderate or severe diarrhea in young children.
- Diarrhea associated with blood.
- Diarrhea that continues for more than two days.
- Diarrhea that is associated with more general illness such as non-cramping abdominal pain, fever, weight loss, etc.

- Diarrhea in travelers, since they are more likely to have exotic infections such as parasites.
- Diarrhea in food handlers, because of the potential to infect others.
- Diarrhea in institutions such as hospitals, child care centers, or geriatric and convalescent homes.

In many cases of diarrhea, replacing lost fluid and salts is the only treatment needed. This is usually by mouth – oral rehydration therapy – or, in very severe cases, intravenously.

Diet restriction such as limiting milk has no effect on the duration of diarrhea. Medicines such loperamide (Imodium), bismuth subsalicylate (as found in Pepto Bismol and Kaopectate) may be beneficial, however they may be contraindicated in certain situations. Prescribed medications sometimes contain pain-killers, such as morphine or codeine, to counter the cramps that can accompany diarrhea. (Viswanathan VK, 2009).

1.6 Interventions

1.6.1 Key measures to reduce the number of cases of diarrhoea include:

- Access to safe drinking water.
- Improved sanitation.
- Good personal and food hygiene.
- Health education about how infections spread. (Bull World Health Organ, 2005)

1.6.2 Key measures to treat diarrhoea include:

- Giving more fluids than usual, including oral rehydration salts solution, to prevent dehydration.
- Continue feeding.

Consulting a health worker if there are signs of dehydration or other problems. (Bull World Health Organ, 2005)

1.6.3 Role at Home:

- In cases of acute diarrhoea it would be wise to drink more fluids (3-4 litres a day), preferably containing sugar and salts. Ready-mixed rehydration sachets (eg Dioralyte, Rehidrat) can be bought from the pharmacist and added to drinking water.
- A sufficient intake has been obtained when the urine becomes light yellow in colour.
- Eat something containing salt, such as crisps or soup.
- Maintain good standards of hygiene.
- Eat normally as soon as your appetite returns but if you have suffered an acute attack of diarrhoea, avoid foods containing milk for a couple of days. (Rutherford DD,2005)

1.6.4 Role of Doctor:

- When one of the warning signs outlined above is present.

- When the diarrhoea has occurred during or following a trip abroad - travellers' diarrhoea.
- When the diarrhoea has lasted more than one to two weeks. (Rutherford DD,2005)

1.6.5 Treatment

Diarrhoea can usually be treated safely 'at home' and normally goes away by itself within a week. Treatment with antibiotics is therefore rarely needed, and may cause side effects, such as chronic diarrhoea. Antidiarrhoeal agents, such as loperamide (eg Imodium), may be used, except in cases where there is blood or pus in the motions or if the diarrhoea is accompanied by high fever. It has not been proven that freeze-dried lactic acid bacteria can prevent travellers' diarrhoea. During visits abroad, boil all drinking water, or drink water from sealed bottles only. In addition, you should only eat vegetables that have been boiled or peeled and avoid ice-cream and salads (which may have been washed with unclean water). (Rutherford DD,2005)

1.7 Prevention of Diarrhea:

Dehydration occurs when the body has lost too much fluid and electrolytes (the salts potassium and sodium). The fluid and electrolytes lost during diarrhea need to be replaced promptly--the body cannot function properly without them. Dehydration is particularly dangerous for children, who can die from it within a matter of days.

Although water is extremely important in preventing dehydration, it does not contain electrolytes. To maintain electrolyte levels, you could have broth or soups, which contain

sodium, and fruit juices, soft fruits, or vegetables, which contain potassium. For children, doctors often recommend a special rehydration solution that contains the nutrients they need. (Bull World Health Organ, 2005)

1.7.1 Food:

Until diarrhea subsides, try to avoid milk products and foods that are greasy, high-fiber, or very sweet. These foods tend to aggravate diarrhea. If we improve our diet, including bananas, plain rice, boiled potatoes, toast, crackers, cooked carrots, and baked chicken without the skin or fat. For children, the pediatrician may recommend what is called the BRAT diet: bananas, rice, applesauce, and toast.

1.7.2 Diagnosis

Isolation and identification. In clinical cases direct plating on Brilliant Green, Mc Conkey and non-selective agar is advisable. Enrichment procedures usually rely on selenite broth followed by plating on selective media. Differentiate from Typhoid, Paratyphoid, paracolon, other enterobacteria, chilling and omphalitis. This is based on the clinical examination, the response to treatment (viral diseases do not respond to treatment) and laboratory examination of the scour. A simple test to differentiate between virus causes and *E. coli* diarrhoea involves the use of litmus paper to determine whether the scour has an alkaline or an acid consistency. Soak the paper in the scour, *E. coli* diarrhoea is alkaline (blue colour change) whereas viral infections are acid (red colour change). It is not possible to eliminate organisms such as *E. coli* and *coccidiosis* from the herd and

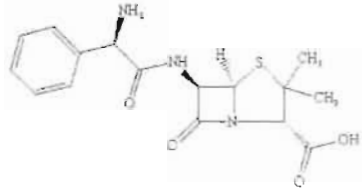
most if not all pigs will be infected with them. All herds carry clostridia but other factors are required to cause disease.But diarrhea also occurs due to lack of safe drinking water for the unusual rise in water borne disease. The scorching weather gives rise to a shortage of safe drinking water, which is the primary cause of high number of patients with water borne ailments. (Alam M, June 2009).

Diarrhoea is one of the primary causes of child death in Bangladesh. In Bangladesh, one third of the total child death burden is due to diarrhea. Every year, a rural child suffers on average from 4.6 episodes of diarrhea, from which about 230,000 children die. (Piechulek H, 2003)

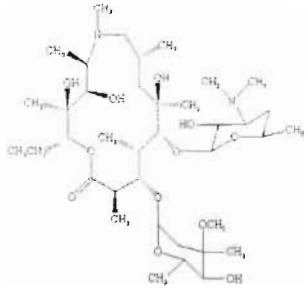
1.1. Table: Different antibiotic used for the treatment of diarrhea

Name of Drugs used for diarrheal Patient	Brand Name	Non Antibiotic
Ampicillin	Ampicillin	Normal Saline,
Azithromycin	Zita, Zisap	Rice Saline, Khecury
Ceftriaxone	Diceptin, Trizon, Ceftrazone	Oral Rehydration Saline
Ciprofloxacin	Ciprozid, Ciprocin, Cipro, Ciprod	Breast Feeding, Coloride
Gentamycin	Gentin	Lactose Free Diet
Imipenem	Imipenem	Normal Diet

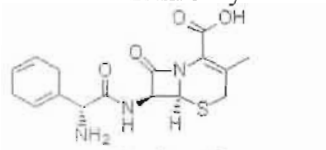
1.7.3 Structure of drugs different antibiotic



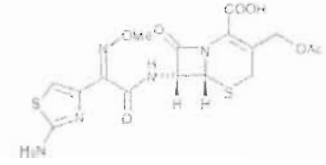
Ampicillin



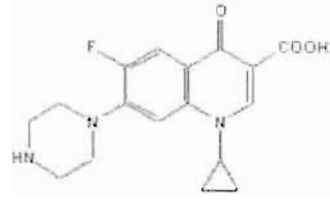
Azithromycin



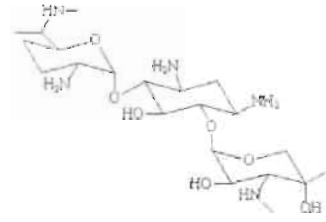
Cephradine



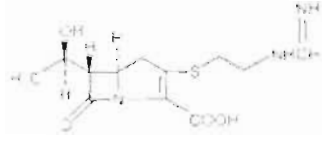
Ceftriaxone



Ciprofloxacin



Gentamycin



Imipenem

1.7.4 Mechanism of Individual Classes of Drugs

1.7.4.1 Beta lactum antibiotic: Under this class the drugs are Ampicillin, Ceftriaxone and Imipenem. The mechanism of antibacterial action in general is to inhibit the bacterial cell wall synthesis. Here the bacteria cell wall consists of strands of a linear peptidoglycan made up of alternating building blocks of N-acetylglucosamine and N-acetylmuramic acid. The synthesis of bacterial cell wall occurs in three steps,

i. In the first step formation of UDP-N- acetylmuramic acid-pentapeptide.

ii. In the second step formation of the linear peptidoglycan.

iii. In the third step there is transpeptidation of these linear strands occur by an enzyme 'transpeptidase'.

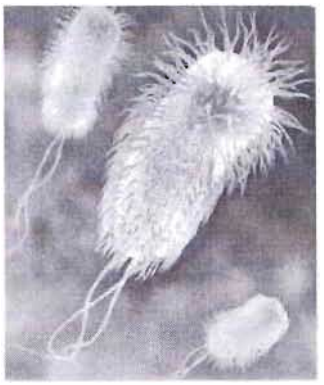
The beta lactum antibiotic interfere with this final step of bacterial cell wall synthesis, that they bind to this enzyme 'transpeptidase' and act as competitive inhibitors, leading to synthesis a defective cell membrane, which is osmotically less stable. In addition changes in the cellular shape of bacteria occur after binding of beta lactum antibiotic in cell wall. Finally cell lysis occurs. (Graham LP,2009)

1.7.4.2 Amino glycoside: After transport of amino glycoside (Gentamycin) through the bacterial cell wall and cytoplasmic membrane, this group of antibiotic will bind with 30S ribosomal subunit and interfere it, then result freeze initiation of protein synthesis. Binding of amino glycoside to 30S juncture causes distortion of mRNA codon recognition resulting in misreading of the code. So ultimately inhibition of protein synthesis occurs. (Graham LP, 2009).

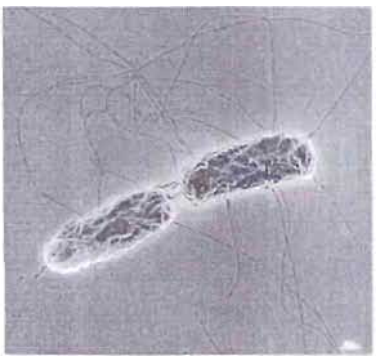
1.7.4.3 Macrolide: This group of antibiotic (Azithromycin) acts by inhibiting bacterial protein synthesis. They combined with 50S ribosome subunit and interfere with 'translocation'. After peptide bond formation between the newly attached amino acid and the nacent peptide chain at the acceptor site the elongated peptide is translocated back to the peptidyl site, making the first site available for next aminoacyl tRNA attachment. This is prevented by Macrolide and the ribosome fails to move along the mRNA to expose the next codon. As an indirect consequence peptide chain may be prematurely terminated so synthesis of larger proteins is specifically suppressed. (Tripathi KD, 2003)

1.7.4.4 Quinolone: The fluoroquinolone (FQ) is the principle compound under this class. Here the FQs (Ciprofloxacin) inhibit the enzyme bacterial DNA gyrase, which nicks double stranded DNA, introduces negative supercoils and then reseals the nicks end. This is necessary to prevent excessive positive supercoiling of transcription. So no DNA replication and no protein synthesis occur for microorganism. (Tripathi KD,2003)

1.7.5 Causative organism for Diarrhoeal disease:



Escherichia coli



Salmonella typhi

Staphylococcus aureus

Chapter 2

2.1 Objective of the Study

Diarrhoea is the major cause of mortality and morbidity in young children especially in many developing countries like Bangladesh. The main objective of this study is to provide an information about how the diarrheal diseases in children (less than 10 years) are treated with different antibiotics in a tertiary level hospital.

2.2 Significance of the Study

Diarrhoea is a major problem for developing countries like Bangladesh. In 1998, diarrhoea was estimated to kill 2.2 million people, most of whom were under 5 years of age. Each year there are approximately 4 billion cases of diarrhoea worldwide. The study was conducted to provide some information about the mode of treatment of diarrheal disease in patients under 10 years of age.

Chapter 3

3. Materials and Methods

3.1 Study Design

Diarrhea is a major public-health problem, with children most affected. However, effective single-dose antimicrobial regimens have been identified only for adults.

The study design was a descriptive study; where 56 patients with Diarrhoea were taken with 0-9 years old.

3.1.1 Subject: Children 0-9 years

3.1.2 Study site: The sample was collected for study, from the Institute of Child Health & Shishu Sasthya Foundation Hospital, Mirpur; Dhaka from 1st January to 31st Januaty, 2008. Fifty six subjects meeting the following inclusion criteria for the sampled.

3.2 Inclusion criteria:

- Patient : With Diarrhea and other associated illness.
- Age : Under 10 years
- Sex : Both

3.3 Demographic Data

The demographic data generally contains the patient's personal information, his or her family history and use of antibiotic and history of present illness at admission. Data about demographic characteristics of children was collected for the study.

3.4 Patient's Personal Information

Patient's personal information contains the

- Name
- Age
- Sex
- Date of admission
- Discharge date
- Symptoms

3.5 Patient's Family History

The family history of the patient contains:

- Mother's occupation
- Father's occupation
- Socioeconomic status
- Consumption water condition
- Any other family member who have same type of illness during past 14 days.

3.6 History of Present Illness (at admission)

The case report form also contains the history of present illness during the period of patient admission and which contain the following data:

- Type of diarrhoea
- Duration of diarrhoea prior to admission (hours)
- Dehydration status
- Number of stools/day
- Vomiting
- Duration of vomiting prior to admission (hours)
- Number of vomits/day

3.7 Hospital Course

Selection of antibiotics depends on patient's age, renal and hepatic function and also spectrum and sensitivity of drugs. Single and combination of antibiotics both are used for the treatment of patients.

3.8 Information about the use of antibiotics:

All patients did not receive the same antibiotics and also the dosage forms. Antibiotic therapy was given according to the illness of the patient. If the public health problem like diarrhea where children is affected. So, antimicrobial regimens should be identified.[8] Most of the cases use antibiotics were ciprofloxacin I.V & suspension, ceftriaxone injection.

3.9 Statistical Analysis:

Data were analyzed using SPSS. All the data of the study sample was entered from each patient's case report form. Descriptive statistics were done for major variables of interest including the age distribution, gender distribution, different antibiotics used in the hospital course and duration of hospitalization in days of patients.

Chapter 4

4. Results

4.1 Demographic profile of Patients

	name	age	sex	doa	dod
1	ORIN	8.00	Femal	11/1/09	13/1/09
2	MUIN	7.00	Male	7/1/09	12/1/09
3	MUHAMINU	1.00	Male	11/1/09	13/1/09
4	AFIA ANJ	8.00	Femal	8/1/09	13/1/09
5	MIM	6.00	Femal	12/1/09	13/1/09
6	JUTHE	15.00	Femal	10/1/09	12/1/09
7	ALIF	3.00	Male	12/1/09	18/1/09
8	JUBAYER	1.00	Male	15/1/09	18/1/09
9	DIPTY	108.00	Femal	12/1/09	17/1/09
10	NAIM	18.00	Male	15/1/09	17/1/09
11	TAZRIA	25.00	Male	16/1/09	18/1/09
12	ADRETA	2.00	Femal	13/1/09	15/1/09
13	MAHIN	53.00	Male	5/1/09	15/1/09
14	ALIF	5.00	Male	3/1/09	14/1/09
15	ALLRAFI	18.00	Male	13/1/09	14/1/09
16	OMOUR	14.00	Male	15/1/09	15/1/09
17	ALYAM	10.00	Male	12/1/09	15/1/09
18	AFSANA	.20	Femal	15/1/09	15/1/15
19	SRABON	12.00	Male	16/1/09	18/1/09
20	KAINATH	1.15	Male	15/1/09	18/1/09
21	SINTHIA	5.00	Femal	14/1/09	19/1/09
22	SINHA	.20	Male	17/1/09	19/1/09
23	SIYAM	18.00	Male	16/1/09	18/1/09
24	AMMAR	27.00	Male	18/1/09	20/1/09
25	CHRISTIN	16.00	Femal	18/1/09	19/1/09
26	MAHIN	6.00	Male	15/1/09	20/1/09
27	TEYABA	15.00	Femal	18/1/09	20/1/09
28	SADIUR	7.00	Male	18/1/09	20/1/09
29	RIA	13.00	Femal	10/1/09	13/1/09
30	CHOTON	6.00	Male	11/1/09	12/1/09
31	MIM	4.14	Femal	8/1/09	12/1/09
32	OMY	7.00	Male	9/1/11	11/1/09
33	MANIF	2.00	Male	8/1/09	11/1/09
34	RAZ	6.00	Male	15/1/09	20/1/09
35	MAHIN	6.00	Male	18/1/09	21/1/09
36	SABBIR	24.00	Male	16/1/09	19/1/09
37	ENAN	11.00	Male	15/1/09	19/1/09
38	SASHI	5.00	Femal	17/1/09	18/1/09
39	RIAD	15.00	Male	10/1/09	12/1/09

	symptoms
1	cough and cold and fevers for 2 days.Respiratory dist for 1
2	cough and for 7 days,Respiratory distress for 3 days.
3	Fever, loose stool and less activity e- poor feeding for 1 d
4	Loose watery for 3d,fever 2 d and vomiting for 1d.
5	Vomiting and loose watery stool for 4 days
6	Vomiting for several times for 1 day.
7	Loose stool for (5-6) days, cough and cold for few days
8	Loose stool aftar each feeder- 4 d.Jerky movement for 1 c
9	vomiting and fever for 1 day.
10	vomiting for several times for 2 days.
11	Loose motion 2 d, vomiting (3-4) times.
12	Yellow color body.excessivee crying,vomiting 3d.
13	Swelling body for 7 d,No H/O sore, throat and skin infection
14	Repeated convulsion for 3 times (within 3-6 hrs),fever 3 d.
15	Passage of loose watery stool and vomiting for 2 days.
16	Loose watery stool 2 d.and vomiting for 2 times.
17	Frequent watery stool for 2 d.and fever initially.
18	yellow color body 25 d.cough-cold 10 d.fever for 1day.
19	Passage of l. watery stool (2-3)d.Occasional vomiting 1/2 d
20	Excessive crying 2 week, known case of complex CHD.
21	Loose watery stool for 1 d.Occasional vomiting 1 time
22	Respiratory distress 1d.cough-cold for 3 days.
23	Loose stool 2days, fever 2days, loss of appetite 10days
24	Fever 2d,loose w.st.mixed e- mucous 2d, vomjting 2d(6-7)ti
25	Loose stool 2days, vomiting for several(10-12) times.
26	Frequent loose motion(5-10) times since yesterday.
27	Loose watery stool - vomiting occasional 8d,low gr. fever3
28	Passage loose stool ,vomiting, cough and cold, fever for 2d
29	Vomiting several times 1d, loose stool 3 times.
30	Loose watery stool for several times for 4 days.
31	Loose stool 2 d, vomiting 2 times since morning.
32	Loose mucoid stool e- blood 1 day.
33	Respiratory distr, cough-cold,fever,greenish stool 1day
34	H/O vomiting, passage of loose stool, fever 2days.
35	Loose watery stool 1day, vomiting 2times last day, fever 2d
36	Loose wt.stool 3d, vomiting fcr several times for 1d.
37	Loose stool,fever,cough,cold for 3d,convulsion single upset
38	Loose wt.stool,vomiting 3d,low grede fever 1d.
39	Vomiting for several times, loose blood mixed stool

		treatmen
	1	Gentin,inj.Lasix 6mg, NPO till FO.
	2	Inj Dicepin,Gentin D-6,Diet normal,add NPO 4h,ing,coloride.
	3	Inj Ciprozid D-3,breast feeding on demand.
	4	Syp:Ciprozid D-5,Tab-folism,diet normal.
	5	Diet normal,rice saline(15-20) tsf aftar l. motion, Retinol.
	6	Diet khecury,ORS 15-20 TSF after l.motion.
	7	Inj:Cipro d-5,lactose free diet.
	8	Inj Taxim,Geltin D-4,diet breast feeding on demand.
	9	Diet normal, inj-10% koloride,pls monitor P/T/R.
	10	Inj:Ciprozid 50ml,5% Koloride 500ml,diet normal,ORS,PTR
	11	Diet normal,ph N/F,ORS.
	12	Inj Sarbit D-7,breast feeding on demand,ph W/R routinely.
	13	Inj:Cipro D-10.
	14	inj.Imepenum D-7,Sedil,diet breast feeding on demand.
	15	Diet Khecury,ph W/R ORS routinely,ORS(12-15) TSK.
	16	NPO for 4hrs,Inj:Koloride 500ml,W/R vital sign.
	17	Ciprocin D-3,Syp:Metryl.KT,diet normal,ORS(10-10) TSK a.l.
	18	Inj:Lasix 4mg w.mid transfusion of blood.
	19	Inj.Koloride 500ml,record PTR,diet normal-khecury.
	20	Drop.Vanprox D-5,NG tube feeding 33ml 2wk,breast f.on d.P
	21	Inj:Madexon,diet normal-khecury.
	22	Inj.Maxaf,Gentin D-3,O2 inhalation sos,breast feeding on de
	23	Inj:Ciprozid 50ml,diet khecury,ORS(10-20) TSF.
	24	Diet khecury,ORS rice,ORS(10-12) TSF after l.motion.Re v.s
	25	Diet normal khecury,rice ORS,ORS by mouth,record HR,PT
	26	Inj:Cipro D-6,khecury D-5,diet normal,pg W/R vital sign.
	27	Inj:Cipro D-2,diet normal,khecury,record V/S regulars.
	28	Inj Ciprozid D-2,diet khecury,ORS normal 20 TSF a.each mo
	29	Syp.Zisap,diet normal and record PTR.
	30	Inj:Ciprozid,diet breast feeding,rice ORS 10 TSF a.each l.m.
	31	Inj:Ciprozid D-2,diet normal, ORS(4-5)TSF after loose motion
	32	Cipro D-2,diet lactose free milk,khecury,record V/S.
	33	Inj Ampicillin,Gentin D-4,breast feeding on demand,rec.PTR.
	34	Inj:Ciprod D-6,Tab:Folison,diet lactose free milk;ORS,PTR.
	35	Diet normal khecury,ORS(8-10)TSFa.e.loose m.record vital s
	36	Cipro D-3,diet normal.
	37	Inj:Trizon D-5,diet normal,record W/R vital sign.
	38	Diet lactose free milk,khecury,ORS,record PTR.
	39	H/S D-3,Syp:Zita,diet normal,ORS by mouth(8-10)TSF a.e.l.

	name	age	sex	doa	dod
40	MEGHLA	1.60	Femal	9/1/09	12/1/09
41	PRANTO	5.20	Male	29/1/09	31/1/09
42	ALLAMIN	10.00	Male	8/1/09	11/1/09
43	MARUF	5.00	Male	17/1/09	31/1/09
44	DOHA	7.12	Femal	29/1/09	31/1/09
45	SABBIR	13.00	Male	28/1/09	30/1/09
46	NABIL	12.00	Male	28/1/09	30/1/09
47	JIDNE	11.00	Femal	25/1/09	29/1/09
48	HADISUR	7.19	Male	21/1/09	31/1/09
49	NIROB	36.00	Male	28/1/09	29/1/09
50	AJAD	9.00	Male	25/1/09	28/1/09
51	RIFAT	10.00	Male	26//1/09	29/1/09
52	RABIL	4.00	Male	10/1/09	12/1/09
53	SANI	12.00	Male	8/1/09	11/1/09
54	MERAZ	15.00	Male	26/1/09	28/1/09
55	MUKTA	1.10	Femal	24//1/09	28/1/09
56	SATHI	1.10	Femal	24/1/09	29/1/09

	symptoms
40	Vomiting,loose stool for 2 days.
41	loose wt.stool 3days.
42	Loose stool , vomiting for 4 days.
43	Respiratory dist 3d,cough 2 days.
44	Loose motion,vomiting for 1 day.
45	H/O loose motion,fever, convulsion single episode(10-15) ti
46	Loose stool for 3d, fever for 2days.
47	Passage of loose wt. stool,fever & vorfolin for 2days
48	Abdominal distension 1d,passage of l stool for 10days.
49	Loose stool,fever,cough,cold for 3d.convulsion for 1 time.
50	Loose motion 2days, low grade fever for 2 days.
51	Loose watery stool 4d,repeated vomiting for 3 days.
52	Repeated vomiting ,loose motion and fever for 1 day.
53	Loose wt.stool 7d,abdomen discomford,fever for 5 days.
54	Loose wt stool and repeated vomiting for 3 days.
55	Loose watery stool (5-6) times per day for (4-5) days.
56	Passage of loose stool for 5 days.

	treatment
40	Inj.Ampicillin,Gentin D-4,lactose free milk on demand,r PTR.
41	Inj.Ciprofloxacin D-5.
42	Diet normal,ORS,record PTR routinely,add inj. Lasin.
43	Diet normal,record PTR routinely.
44	Syp:Zisap D-3,Diet normal,record V/S.
45	Diet khecury,ORS(10-12)TSF after each l.motion,pls W/R. P
46	Diet normal khecury,rice ORS,ORS by mouth.
47	Ciprozid D-5,diet normal,pls maintain vital sign.
48	Inj Ampicillin,Gentin D-5,diet normal.
49	Inj:Ceftrazone,Syp:Oradaxone D-5,diet normal.
50	Inj:Ciprozid D-5,Syp:KT D-3,khecury,Neosalin a.e.stool,PTR.
51	Inj:Ciprozid D-3,Syp:Metryl D-2,rice ORS.
52	Breast feeding on demand,ORS by motion (6-8)TSF,record
53	Diet normal,Glycerin suppository,pls record PTR routinely.
54	Diet normal,pls W/R vital sign regularly.
55	Inj.Ampicillin,Geltin D-5,breast feeding on demand,ORS(2-3).
56	Inj.Ampicillin and Geltin D-5,breast feeding on demand,ORS.

4.1. Table: Duration of Hospital stay of patient receiving Antibiotic

Number of Patients	Duration(days)
4	1
15	2
8	3
4	4
6	5
1	6
2	10
1	11
41(total)	**42(days)**

4.2. Table: Duration of Hospital stay of patient receiving Non antibiotic

Number of Patients	Duration(days)
4	1
7	2
3	3
1	14
15(total)	209(days)

4.3. Table: Mean duration of Hospital stay

Patients	Mean duration(days)
Antibiotics group	1.02
Non antibiotics group	1.33

4.4. Table: Number of patients (male & female) receiving different antibiotics

Name of the antibiotics	Number of Total Patients receiving antibiotics	Number of Male Patients receiving antibiotics	Number of Female Patients receiving antibiotics
Ampicillin	5	2	3
Azithromycin	3	1	2
Ceftriaxone	3	2	1
Ciprofloxacin	20	16	4

Gentamycin	9	5	4
Imipenem	1	1	0

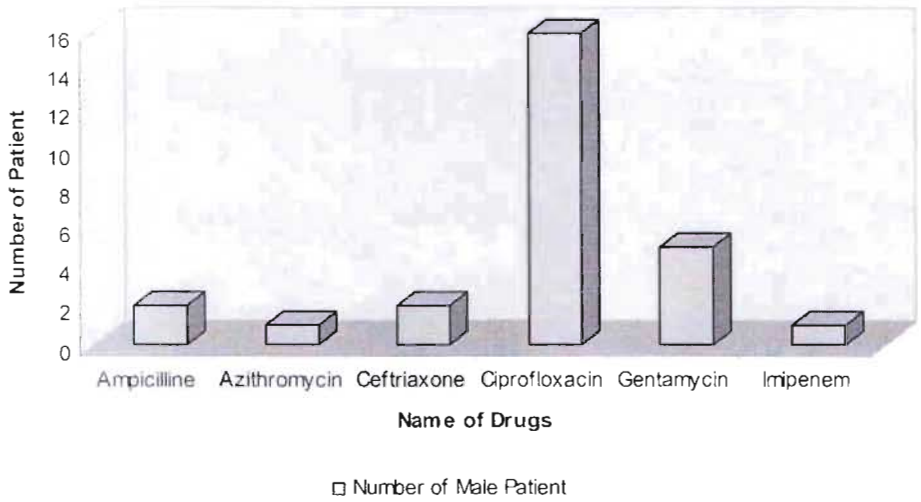
From the above table the number of total patient was 56, where only 41 received antibiotic therapy and others got treatment without antibiotic including intravenous saline, normal diet, rice saline, khicury, oral rehydration saline, breast feeding, lactose free diet etc.

4.5. Table: Diarrheal Patients receiving with Antibiotic and Non Antibiotic therapy

Total Patient	Receiving antibiotic therapy	Receiving non antibiotic therapy	Percent Receiving antibiotic therapy	Percent Receiving non antibiotic therapy
56	41	15	73.2 %	26.8 %

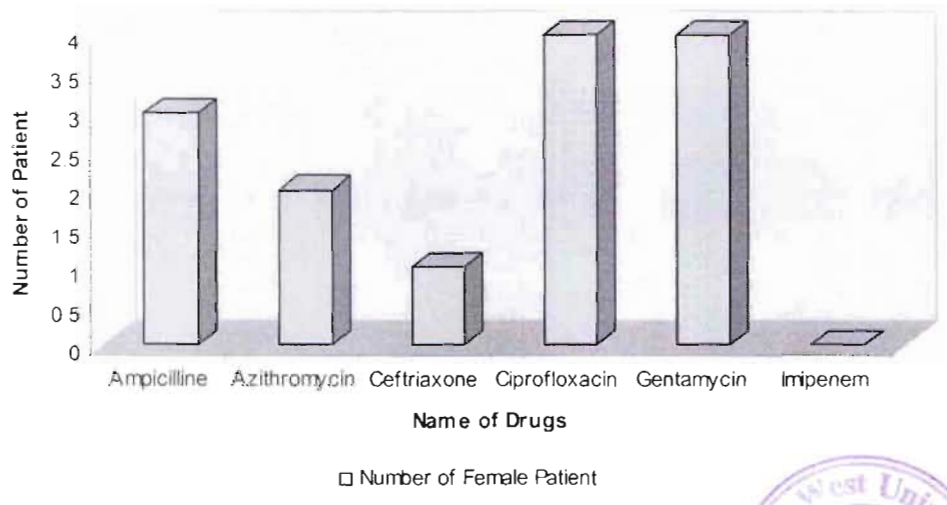
From the above table it has been seen that a total 41 patients (73.2%) among 56 patient received antibiotic therapy like Ampicillin, Azithromycin, Ceftriaxone, Ciprofloxacin, Gentamycin and Imipenem. Only 15 patients (26.8%).among 56 patient received Non antibiotic therapy like normal saline, normal diet, rice saline, khicury, oral rehydration saline, breast feeding, lactose free diet etc.

4.1. Figure: Number of Male Patients receiving different antibiotic



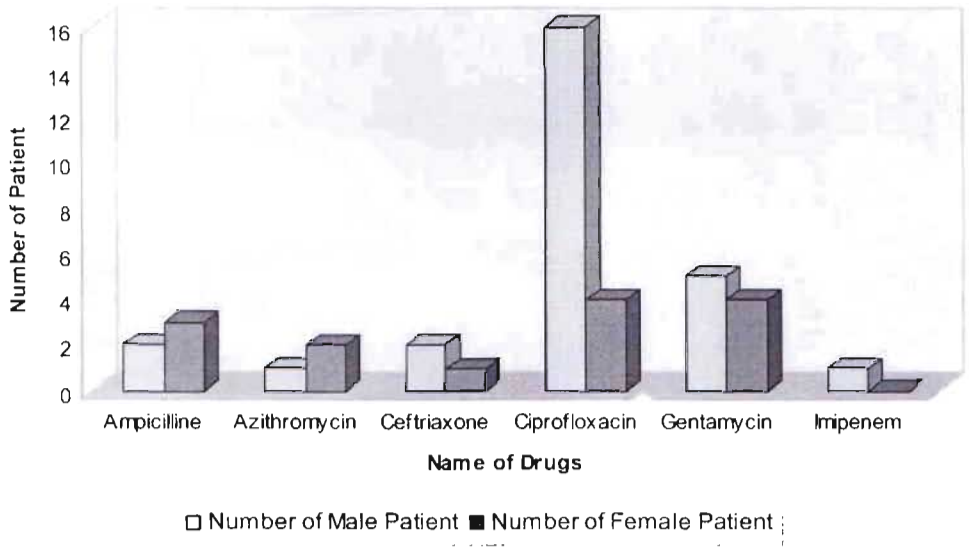
The figure shows that the majority of male patient (n=16) were treated with Ciprofloxacin. The second major drug to treat the diarrheal patients (n=5) was Gentamycin. Ceftriaxone, Ampicillin, Azithromycin and Imipenem were given to the rest of the patients for treating diarrhea.

4.2. Figure: Number of Female Patient receiving different antibiotics



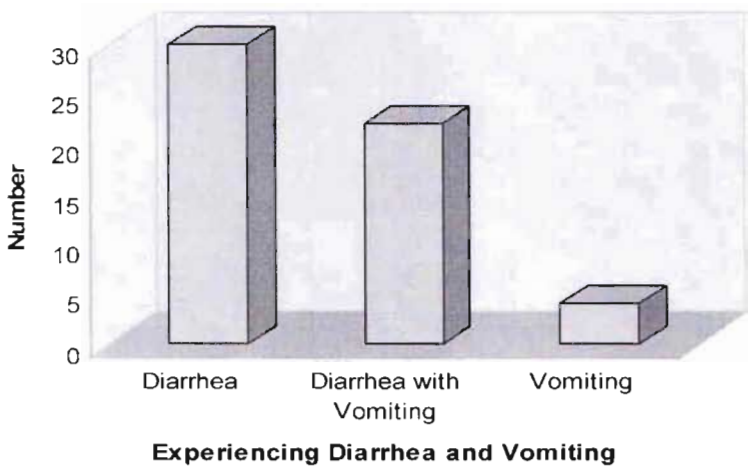
From this graph it has been seen that the majority of female patients were treated with Ciprofloxacin (n=4) and Gentamycin (n=4). The second major drug was Ampicilline (n=3) and Azithromycin (n=2).

4.3. Figure: Comparison of the gender differential receiving different antibiotic



This graph represents the comparison between number of Male and Female patients receiving different antibiotic therapy. The figure shows that Male patients received more antibiotics than the Female patient.

4.4. Figure: Symptoms Profile of diarrhoeal Patient



From the above graph it has been seen that only 30 patients experienced only diarrhea, whereas 22 patients experienced diarrhea along with vomiting and only 4 patients experienced only vomiting.

4.2 Treatment strategies

Actually different antibiotics have been used for treating Diarrhoeal disease. They are present in the following box.

Name of Drugs used for diarrhoeal Patient
Ampicillin
Azithromycin
Ceftriaxone
Ciprofloxacin
Gentamycin
Imipenem

It has been seen that Ciprofloxacin is more used than the other antibiotics. Here Ciprofloxacin was given more to male patient than the female patient.

Annexure:

For the treatment of diarrheal disease Normal Saline, Rice Saline, Khicury, Breast Feeding, Coloride, Lactose Free Diet, Normal Diet can be given. Other than these, the Oral rehydration Solution (ORS) can also be given to treat the diarrhea. The main composition of ORS is given below.

4.6. Table: Composition of Reduced Osmolarity ORS (Bull World Health Organ, 2004).

Reduced osmolarity ORS	**Grams / litre**
Sodium chloride	2.6
Glucose, Anhydrous	13.5
Potassium chloride	1.5
Trisodium citrate, Dihydrate	2.9
Total weight	**20.5**
Reduced osmolarity ORS	**Mmol / litre**
Sodium	75
Chloride	65
Glucose, Anhydrous	75
Potassium	20
Citrate	10
Total Osmolarity	**245**

Rice ORS:

The salt composition is the same as that in WHO ORS; only glucose or sucrose is replaced by 50 gram of rice powder. Rice powder and salts are dissolved in 1050 ml water (extra 50 ml water to allow for evaporation). The solution is heated while stiring frequently with a spoon, and allowed to boil for one minute.

It is allowed to cool down and then served. After cooking, the solution should be used within 6 hours in summer and within 8 hours in winter. (Bull World Health Organ, 2001)

Chapter 5

Discussion

Diarrhea is a global health problem, and it is more often seen in developing countries. This endemic disease is more seen in cities where the meal is prepared in unhygienic condition, also safe water supplies and sanitation facilities are inadequate. Diarrhea is a major cause of illness especially in children.

A community-based study was carried out in Chittagong metropolitan area of Bangladesh, aimed to determine the extent of misuse of drugs in acute diarrhea among under-five children. Data were collected from 360 mothers of under-five children suffering from acute diarrhea two weeks prior to interview. Information collected pertained to the type and duration of diarrhea and the treatment received. There were 339 cases of acute watery diarrhea and 21 cases of dysentery (i.e.bloody stools). The mean duration of the diarrheal episode lasted 3.17 ± 1.69 days. From the total cases, only 328 received treatment. Moreover, only 82 cases of acute watery diarrhea received WHO recommended treatment and only 5 from the total number of cases received appropriate antibiotic treatment, while the 241 cases received inappropriate medication. The commonly prescribed drugs were metronidazole and antibiotics. Results suggest that there is a significant misuse of antidiarrheal drugs among under-five children according to WHO treatment guideline

The information about the treatment of 56 children with diarrhea (below 10 years) admitted to Institute of Child Health and Shishu Sasthya Foundation Hospital, Mirpur, Dhaka was also collected for this study. In addition to Oral Rehydration Solution some common antibiotics were used for the treatment of diarrhea. The antibiotics included Ciprofloxacin, Azithromycin and Ceftriaxone. Some patients received antibiotics such as

Imipenem, Gentamycin, Ampicillin for their associated illness like severe pneumonia, sepsis etc.

From this study it has been seen that Ciprofloxacin under the class Fluoroquinolone, which is the principle compound of Quinolone class antibiotic is used for the treatment of diarrhea. It has been seen from the above study that treatment of diarrheal disease with huge antibiotic is used in the tertiary level hospital because complicated diarrhoeal illness. In primary level hospital WHO guidelines are followed to treat the patients where antibiotics uses are limited.

Lots of antibiotics are available in the market for the treatment of Diarrhoea. There are oral and intravenous saline and also some food supplements are also available in the market. Zinc supplementation is recommended as an adjunct therapy in addition to rehydration fluid intravenous or oral because it has been shown in many studies that Zinc supplemention significantly reduced the duration of diarrhoea and stool output in children with Diarrhea. Although many antibiotics such as Ampicillin, Azithromycin, Ceftriaxone, Ciprofloxacin, Gentamycin and Imipenem are used for the management of children with diarrhea and associated illnesses are used in the tertiary level hospital, however, whether the practices are rationale can not be determined from this study.

Every treatment center can formulate their own treatment protocol according to their needs determined on the basis of epidemiologic knowledge of the Diarrheal disease and sociocultural background, although most centers in developing countries follow WHO recommended treatment guidelines.

Chapter 6

Conclusion

Lots of antibiotics are available in the market for the treatment of Diarrhoea. Without this there is also some food supplement available in the market such as Oral saline, Normal diet, rice saline, Khicury etc. But in the primary level hospital Zinc supplementation significantly reduced the duration of diarrhoea and stool output in children with Diarrhea. Children with Diarrhea should be supplemented with zinc to reduce its duration and severity. For better management of Diarrhea in children treated with different types of antibiotic such as Ampicilline, Azithromycin, Ceftriaxone, Ciprofloxacin, Gentamycin and Imipenem in the tertiary level hospital. Every treatment center can formulate their own treatment protocol according to their needs determined on the basis of epidemiologic knowledge of the Diarrhea disease and sociocultural background, although most centers in developing countries follow WHO recommended treatment guidelines.

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