INTRODUCTION

Diarrhea is a leading cause of death among children under 5 years of age in developing countries ***(WHO, 1985)***.

In Egypt, on average, children under 3 years of age suffer 3 bouts of acute diarrhea per year. The widespread use of oral rehydration therapy has successfully lessened the severity of diarrheal episodes, sharply reduced the number of subsequent deaths, but the incidence of diarrheal diseases has not declined ***(Cairo, United Nations Children Fund, 1990)***.

Oral rehydration treatment, including rehydration and maintenance fluids, is the most beneficial treatment. Treatment with ORS is simple and facilitates the management of uncomplicated cases of diarrhea of any etiologic agent at home ***(King et al., 2003)***.

Pure honey is bactericidal for many pathogenic organisms, including enteropathogens such as salmonella species, shigella species, enteropathogenic Escherichia coli, and other gram negative organisms ***(Jeddar, 1985)*** and is a readily available source of glucose and fructose ***(British Pharmaceutical Society of Great Britain, 1979)***. Honey given with oral rehydration fluid was shown to shorten the

duration of bacterial diarrhea ***(Haffejee and Moosa, 1985)***.

AIM OF THE STUDY

The aim of the present study is to evaluate the efficacy of honey (added to ORS) in treatment of acute gastroenteritis in infants and children.

DIARRHEAL DISEASE

DEFINITION:

Diarrhea is defined as the passage of three or more abnormal loose watery stools per 24 hours. The volume of fluid lost through stools can vary from 5ml/kg body weight/day to more than 200ml/kg body weight/day ***(WHO, 1995)***.

EPIDEMIOLOGY:

Acute diarrhea accounts for >1.5 million out patient visits, 200000 hospitalizations, and approximately 300 deaths/year. In developing countries, diarrhea is a common cause of mortality among children aged <5 years with an estimated 2 million deaths annually ***(WHO, 2003)***.

Pathophysiology (Acute watery diarrhea):

The human intestine (both large and small) is a tube within which a large amount of water and electrolytes is delivered (in the form of drinks and through secretion); however, most of this is absorbed by processes of transport and exchange. Normally, absorption and secretion of water and electrolytes occur through out the intestine. In the small intestine, water and electrolytes are simultaneously absorbed by the villous cells and secreted

by the crept cells of the intestinal epithelium, resulting in a bi-directional flow of water and electrolytes between the intestinal lumen and the blood. Since fluid absorption is normally greater than secretion, the net result is fluid absorption. Any change in the bi-directional flow of water and electrolytes in the small intestine (i.e., decreased absorption, increased secretion, or both) results in either reduced net absorption or actual net secretion causing an increased volume of fluid entering the colon ***(Fine et al., 1989)***.

Glucose and other actively absorbed non electrolytes stimulate small intestinal fluid absor-ption, but the absorptive capacity of the colon cannot be enhanced by glucose ***(Fine et al., 1989)***. Diarrhea ensues when the volume delivered to the large intestine exceeds the absorptive capacity of the colon.

ETIOLOGY:

The important pathogens responsible for causing watery diarrhea in children in developing countries include ***(Rodriguez et al., 1980):***

1. Rota virus.
2. Enterotoxigenic E.Coli.
3. V. cholera 01.

4. Cholera 0139.
5. Enteropathogenic E.Coli.
6. Enteroadhernt E.Coli.
7. Campylobacter jejune.
8. Creptosporidium spp.

Diarrheal diseases may be infectious or non infectious. Infections of gastrointestinal tract are caused by wide variety of organisms including bacterial, viruses and parasites ***(Bern et al., 1992):***

The non infectious causes of gastroenteritis

1. Feeding errors.
2. Malabsorption:
    - Disaccharidase deficiencies.
    - Glucose-galactose malabsorption.
    - Pancreatic insufficiency.
    - Cystic fibrosis.
    - Cholestasis.
    - Heriditarry fructose intolerance.
    - Abeta lipoproteinemia.
    - Celiac diseases.
3. Anatomic defect:

- Malrotation.
- Intestinal duplication.
- Hirschsprung disease.
- Fecal impaction.
- Short bowel syndrome.
- Strictures.
- Microvillus atrophy.

4. Food poisoning:
    - Heavy metals.
    - Scombroid.
    - Muschrooms.
5. Endocrinopathies:
    - Addison disease.
    - Adrenogenital syndrome.
    - Thyrotoxicosis.
6. Neoplasms:
    - Neuroblastomas.
    - Ganglioneuromas.
    - Carcinoid.
    - Zollinger-Ellison syndrome.
    - Vasoactive intestinal peptide syndrome.

- Pheochromocytoma.

7. Miscellaneous:

- Milk allergy.
- Crohn's diseases.
- Familial dysautonomia.
- Ulcerative colitis.
- Protein-losing entropathy.
- Hartnup disease.
- Laxative abuse.
- Motility disorder.

Infectious agents of gastroenteritis:

(A) Bacterial:

- Escherichia coli.
- Salmonella.
- Shigella.
- Vibro cholera.
- Yersinia enterocoritica.
- Compylobacter perfringens.
- Aeromonas spp.

(B) Viruses:

- Rota virus.

- Adeno virus.
- Astro virus.
- Norwalk virus.
- Corona virus.

(C) Parasites:

- Entamoeba-histolytica.
- Giardia lambia.
- Crypto sporidium.
- Cyclospora spp.

MECHANISM OF DIARRHEA:

Secretroy diarrhea:

The secretory diarrhea is typically caused by Vibrio Cholera 01, V.Cholera 0139, enterotoxigenic Escherichia Coli, and sometimes V.Cholera non-01. After passing through the gastric acid barrier, they colonize the lower part of the small intestine, where they produce enterotoxins. For example after becoming attached to small intestine, V.Cholera 01 liberates cholera toxin (CT). Cholera toxin (CT) is a protein molecule (molecular weight 8400 Daltons) that consists of five β-subunits arranged in a circular fashion and linked non-covalently to the A subunit containing 2 peptides, A1 and A2, which are linked by a

disulfide bond. First, an irreversible binding occurs between the β-subunit of the toxin molecule and GM1 monosilogangliosides, the cell surface receptor for CT. Following this, the A subunit penetrates into the cell membrane and the active part (A1) is split off, which in turn stimulates the activity of the enzyme adenylate cyclase through cleavage of nicotinamide adenine dinucleotide. This increases cellular concentration of cyclic-AMP, which inhibits or blocks the chloride-linked neutral sodium absorption from the intestinal lumen by the villous cells (but not the glucose or other carrier-mediated sodium absorption) and directly stimulates chloride secretion by the crypt cells into the intestinal lumen. The net effect is a massive outpouring of fluid and electrolytes, resulting in classical secretory diarrhea ***(Fishman, 1980)***.

Osmotic diarrhea:

The permeability of the small intestinal mucosa allows rapid movements of water and electrolytes to maintain the osmotic balance between the intra-luminal contents and extracellular fluid. Presence of poorly absorbed, osmotically active substance will cause an increase in the intraluminal osmolarity, resulting in movement of water from extracellular fluid into the gut

lumen, causing diarrhea. Osmotic diarrhea may occur due to ingestion of purgatives (e.g., magnesium sulphate), or the presence of lactose or glucose in conditions associated with poor absorption. Rotavirus causes patchy damage to the small intestinal epithelium, resulting in blunting of the villi. This is associated with some reduction in the activity of lactase and other disaccharidases, leading to reduced absorption of carbohydrates; however, this is of less clinical significance because a large area still remains intact for absorptive function. The intestinal morphology and absorptive capacity returns to normal within 2-3 weeks ***(Walker-smith, 1999)***.

Invasive diarrhea:

Invasive diarrhea is caused by infection due to pathogens having an ability to invade the mucosa of the distal small intestine and colon, producing local and systemic inflammatory response, with ulceration of mucosa and hemorrhage, which clinically manifests as dysentery. Some invasive pathogens, such as entamoeba histolytica, shigella spp. and salmonella spp have the ability to invade the blood stream or may be carried by the lymphatic system to systemic circulation to affect distant organs, e.g., liver, spleen, central nervous system, and joints. The important pathogens that cause invasive

diarrhea, mainly in developing countries, include shigella spp., campylo-bacter spp., salmonella spp, entamoeba histolytica, enteroinvasive E.Coli, and enterohemorrhagic E.Coli ***(MOH, 1994)***.

COMPLICATIONS OF DIARRHEA:

The severity of acute diarrhea is mainly related to water and electrolyte disturbances. The most important acute complication is dehydration, which occurs when the child's overall output of fluid exceeds input ***(Walkers-Smith, 1999)***.

Hypernatremia is one of the most critical complications of diarrhea as it may lead to significant damage to central nervous system ***(Walker-Smith, 1998)***.

Hyperglycemia may often accompany hypernatremia and may lead to an incorrect diagnosis of diabetes mellitus. Such condition is transient and tends to occur when there is co-existent severe acidosis, acidosis occurs secondary to the loss of bicarbonate in stool. The loss of potassium in stool leads to hypokalemia ***(Cleary and Pickering, 1992)***.

Acute renal failure occurs as complication of gastroenteritis. It may be due to oligaemia, producing

reversible failure of renal function ***(Walker-Smith, 1998)***. Acute tubular necrosis and hypocalcemic tetany are less common complications.

DEHYDRATION ASSESSMENT:

Certain clinical signs and symptoms can quantify the extent of a patient's dehydration (Table 1).

Table (1): Symptoms associated with dehydration ***(Duggan et al., 1996)***

Symptoms	Severe deh. >9% loss of body Wt.	Mild to moderate deh. 3-9% loss of body Wt.	Minimal or no deh. <3% loss of body Wt.
Mental status	Apathic, lethargic, unconscious	Normal, fatigued or restless, irritable	Well; alert
Thirst	Drinks poorly; unable to drink	Thirsty, eager to drink	Drinks normally, might refuse liquids
Heart rate	Tachycardia, with bradycardia in severe cases.	Normal to increased	Normal
Quality of pulses	Weak, thready, or impalpable.	Normal to decreased	Normal
Breathing	Deep	Normal; fast	Normal
Eyes	Deeply sunken	Slightly sunken	Normal
Tears	Absent	Decreased	Present
Mouth and tongue	Parked	Dry	Moist
Skin fold	Recoil in >2 seconds	Recoil in <2 seconds	Instant recoil
Capillary refill	Prolonged; minimal	Prolonged	Normal
Extremities	Cold; mottled; cyanotic	Cool	Warm
Urine output	Minimal	Decreased	Normal to decreased

Assessment of the anterior fontanel might be helpful in selected instances, but it can be unreliable or misleading ***(Mackenzie et al., 1989)***.

Among infants and children, a decrease in blood pressure is a late sign of dehydration that heralds shock and

can correspond to fluid deficits >10%. Increase in heart rate and reduced peripheral perfusion can be more sensitive indicators of moderate dehydration, although both can be difficult to interpret because they can vary with the degree of fever. Decreased urine output is a sensitive but nonspecific sign. Urine output might be difficult to measure for infants with diarrhea; however, if urine analysis is indicated, a finding of increased urine specific gravity can indicate dehydration ***(Duggan et al., 1996)***.

The American Academy of Pediatrics (AAP) guidelines divide patients into subgroups for mild (3%- 5% fluid deficit), moderate (6%- 9% fluid deficit) or severe (≥10% fluid deficit, shock, or near shock) dehydration ***(American Academy of Pediatrics "AAP", 1996)***.

Other classification schemes, including the WHO and European Society of Pediatric Gastroenterology, hepatology and nutrition (ESPGHAN) guidelines divide patients into those indicating no signs of dehydration (<3%- 5%), some signs of dehydration (5%-10%), and severe dehydration ***(Sandhu, 2001)***.

Acute gastroenteritis therapy based on degree of dehydration:

Table (2): Seven basic principles guide optimal treatment of acute gastroenteritis ***(Sandhu, 2001)***