



## Cholera is curable with TRAMAOL

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### Abstract

Cholera is an acute diarrheal disease due to a highly motile, curved gram negative rod, vibrio cholerae, and it can result in severe and rapidly progressive dehydration and death in a matter of hours unless quickly treated. As a result, "cholera gravis" is a much feared disease, especially when it occurs in epidemics or in worldwide pandemics associated with high mortality rates.

### Etiology and Epidemiology

Vibrio cholerae is a family of organisms, classified on the basis of their somatic O antigen. The major cause of clinical cholera belongs to O group (0-1) which distinguishes it from the more than 70 other members of Vibrio Cholerae collectively known as non-O-1 vibrios. Eight other vibrio species have been defined of which Vibrio parahaemolyticus, Vibrio fluvialis, Vibrio hollisae and Vibrio Mimicus also cause human diarrhea.

Vibrio cholerae exists in two biotypes, classical and EL tor that are distinguished on the basis of a number of diverse characteristics such as phage susceptibility and haemolysin production.

Both Biotypes may be separated into serotypes known as inaba and ogawa. In Southern Asia, where the majority of cases in the world occur, faecal contamination of water from an infected human is the most common means of transmission, but contamination of food can contribute to intra-familial spread.

The infectious dose is relatively high, but is markedly reduced in hypochlorhydric subjects or when the gastric pH is buffered by a meal.

In endemic areas it is a paediatric disease, but it affects children and adults equally when the organism is newly introduced into a population.

The seasonality of cholera in endemic areas is not fully explained but may relate to environmental conditions that influence multiplication of vibrio and or seasonal alterations in human

behavior that affect their contact with water. Asymptomatic infections are frequent and are more common with EL tor cholera. Young children under 2 years are less likely to develop severe cholera in endemic regions, which may be in part to passive immunity from breast milk. For unexplained reasons, blood group status is significantly associated with cholera susceptibility; those with group O are at greater risk and those with AB are at lesser risk.

### Pathogenesis

Once Vibrio cholerae is ingested and safely passes through the stomach, it colonizes the upper small bowel. Once established, it produces the protein, cholera Toxin (CT), the principal cause of the watery diarrhea of cholera. Cholera toxin binds to glycolipid receptors on jejunal epithelial cells, especially to GM1 ganglioside by a sugar specific recognition mechanism. Cholera Toxin is an enzyme that transfers Adenosine Diphosphate (ADP) ribose from Nicotine Adenine Dinucleotide (NAD) to a target protein in the Adenylatecyclase enzyme system and intestinal cells. This G protein, the Guanine Triphosphate (GTP) binding regulatory component of AdenylateCyclase, permanently up regulates the cyclase catalytic unit when ADP ribosylated, resulting in production of high level cyclic Adenosine Monophosphate (AMP). This in turn alters transport of sodium and chloride ions in both the sodium absorbing villus cells and the chloride secreting crypt cells, leading to accumulation of sodium chloride in the intestinal lumen. Because water will move passively to maintain osmolality, isotonic fluid accumulates in the lumen, and when the volume exceeds the capacity of the rest of the gut to reabsorb the fluid, watery diarrhea occurs.

Dehydration, leading to shock, and loss of base leading to acidosis, then develops unless the fluids and electrolytes are replaced adequately. Inhibition of cyclic Adenosine Monophosphate formation, activation of inwardly rectifying Potassium channels and inhibition of voltage gated Calcium channels, leading to synaptic hyperpolarization and inhibition of excitatory neurotransmitter release, by Tramadol, stops vomiting and diarrhea within one hour of its administration in patients with severe Cholera.

### Clinical Manifestations

After 8 to 48 hours of incubation period, the disease begins with the sudden onset of painless watery free flowing diarrhea that quickly becomes voluminous and is often quickly followed by vomiting. In severe cholera, adults can lose as much as 1 litre per hour and children 10 millilitres per kilogram per hour in the first 24 hours. There is usually no fever but muscle cramps may occur later due to Potassium depletion. The stool has a characteristic appearance, a non-bilious, gray, slightly cloudy fluid with flecks of mucus and a somewhat sweet, inoffensive odor. It has characteristic rice water appearance. Clinical symptoms parallel volume contraction, with thirst observed at 3 to 5 percent loss, postural hypotension, weakness, tachycardia, and decreased skin turgor at 5 to 8 percent, and Oliguria, weak to absent pulses, sunken eyes and (in infants) sunken fontanelles, wrinkled skin, and somnolence progressing to coma with fluid losses in excess of 10 percent of normal body weight.

When clinical manifestations of volume depletion are treated with fluid and salt, the process is self-limited to a few days at most, and complications such as renal failure due to acute tubular necrosis can be averted.

Laboratory data usually reveal elevation of the haematocrit, mild neutrophilia, elevation of Blood Urea Nitrogen and creatinine consistent with prerenal azotemia, normal Sodium, Potassium and Chloride, a markedly reduced bicarbonate (less than 15 millimoles per litre) and elevation of the anion gap due to co-existent increase in serum lactate, protein and phosphates.

Arterial pH is usually low (about 7.2)

### Diagnosis

Clinical suspicion of cholera can be proven by identification of the organism in stool. This can be by conducting a rapid cholera dipstick test. Dark field microscopy by an experienced technician can directly detect the organism in a wet mount of fresh stool and even reveal serotype by immobilization with inaba or ogawa specific antisera.

The best –selective culture medium is Thiosulfate-Citrate-Bile salt-Sucrose (TCBS) agar, on which the organism grows as a flat yellow colony. All vibrios are oxidase positive and vibrio cholerae can be distinguished from the otherwise similar Vibrio mimicus by its ability to ferment sucrose. If a delay in processing sample is expected it is recommended that Carey-Blair transport medium and or alkaline –peptone water enrichment medium be incubated as well.

### Treatment

Cholera is simple to treat, needing only the rapid and adequate replacement of fluids, electrolytes and base.

It has been proven that fluids may be given by the oral route with ORS plans A and B of rehydration. For severely dehydrated patients, the total fluid deficit (usually estimated as 10 percent of body weight) can be safely replaced intravenously within the first 3 hours following admission using plan C of rehydration. After this, oral therapy can usually be initiated to maintain fluid balance and intake equal to output.

However, patients with continued large volume diarrhea may require prolonged administration of intravenous fluids to maintain adequate volume status until the diarrhea stops. Without adequate staff to monitor patient progress, the oral route is safer and is physiologically regulated by thirst and urine output.

The use of Tramadol both in adults and children, and antibiotics to which the organism is susceptible will diminish the duration and amount of fluid loss and more rapidly clear the organism from the stool, to achieve complete cure within a few hours of admission.

### Control

In outbreaks, attention should first be given to identification of case contacts and treatment of incubating carriers. Next, epidemiologic study is needed to establish the modes of transmission to help define the best –control strategy. At the same time establishment of rehydration centre is essential to reduce mortality.

### Prevention

Provision of safe water, facilities for sanitary disposal of faeces, improved nutrition and attention to food preparation and storage in the household could significantly reduce the incidence of cholera. Careful, hygiene and attention to eating and drinking habits to reduce the likelihood of encountering the organism are recommended.

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