Efficacy of Tetracycline in the Treatment of Cholera Due to Vibrio Cholerae O139

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Objective: Evaluate the effectiveness of tetracycline in the treatment of acute watery diarrhoea due to *V. cholerae* O139.

Methods: A randomized placebo-controlled double-blind clinical trial was carried out during September through November 1993. Fory-three males with severe cholera (22 placebo and 21 tetracycline group) attending the ICDDR,B's hospital in Dhaka, Bangladesh were studied. Patients were randomized to receive either capsule tetracycline 500 mg six hourly for three days or an identical placebo.

Results: Results showed that stool weights were similar in two groups during the first 24 hours (drug 8,437 ± 5,601 g and placebo 8,767 ± 5,164 g, p=0.67). During the second 24 hours, there was a significant reduction of stool weight in the tetracycline group compared to placebo group (1,394 ± 1,512 g vs. 4,519 ± 3,574 g, p=0.0012). During the 3rd 24 hours, the difference of stool weight was more striking (drug 560 ± 1,010 g, placebo 3,587 ± 2,791 g, p=0.0001). Significant difference was also observed in the total weights of stool between start of treatment and end of diarrhoea (drug 9,527 ± 6,863 g and placebo 18,185 ± 11,695 g, p=0.015) The mean duration (h) of diarrhoea was reduced by 58% (32 ± 17 h vs. 77 ± 38 h, p=0.010). Tetracycline significantly reduced the faecal positivity rate of *V. cholerae* O139 at 48 hours (76% vs. 01%, p=<0.001). Tetracycline also reduced total amount of intravenous fluid required compared to placebo (drug 8,219 ± 4,165 ml and placebo 12,019 ± 8,401 ml, p=0.014).

Conclusions: These results suggest that tetracycline is an effective drug for the treatment of acute watery diarrhoea due to *V. cholerae* O139.

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Comparison of the Efficacy of a Single-Dose Ciprofloxacin and of a Single-Dose Doxycycline in the Treatment of Cholera Due to Vibrio Cholerae O139

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Objective: Compare the efficacy of a single 1 g dose of ciprofloxacin with that of a single 300 mg dose of doxycycline in the treatment of cholera due to *V. cholerae* 0139.

Methods: More than 100,000 diarrhoea patients are seen annually at the ICDDR,B's Dhaka-based hospital, and the Clinical Research and Service Centre. Cases were selected from these patients. Of 129 evaluable adult males with severe diarrhoea due to *V. cholerae* O139, fifty-nine were randomly assigned to receive ciprofloxacin and 70 to receive doxycycline.

Results: Treatment was considered to be clinically successful in 54 (91.5%) and 64 (91.4%) of the patients in the ciprofloxacin and doxycycline group respectively. However, the difference was not statistically significant. Similarly, the total volumes of watery stool during the entire period of the study were comparable in the treatment groups. However, only 1 (1.7%) patient in the ciprofloxacin group had bacteriologic failure compared to 15 (21.4%) patients in the doxycycline group (p=0.002).

Conclusions: Efficient management of dehydration remains the cornerstone in the management of patients with cholera. However, treatment with effective antimicrobial agents is useful in significantly shortening the duration of diarrhoea and the volume of watery stools, and in shortening the duration of faecal excretion of the pathogen. From

this study, it is concluded that a single 1 g dose of ciprofloxacin is as effective as a single 300 mg dose of doxycycline in terms of clinical response, and that ciprofloxacin is more efficient in eradicating *V. cholerae* from faeces.

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Inhibition of Cholera Toxin-Induced Salt and Water Secretion By Short-Chain Fatty Acids in Vivo

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Objective: Determine the effect of SCFAs on cholera toxin-induced colonic secretion. Short-chain fatty acids (acetate, propionate, butyrate) produced by the fermentation of unabsorbed carbohydrates by the colonic bacteria have been shown to stimulate Sodium chloride absorption in the isolated colonic epithelium *in vitro*.

Methods: The effects of SCFAs on cholera toxin (CT)-induced colonic ion and water secretion in adult rabbit have been determined in this study using a perfusion technique with polyethylene glycol as a non-absorbable marker. Facilities of the ICDDR,B's Dhaka-based hospital, the Clinical Research and Service Centre, and its Animal Resources Branch, were used for this study.

Results: The study indicates that an 18-hour exposure to purified cholera toxin (5-100 μg) resulted in colonic water and electrolyte secretion in a dose-dependent manner. Perfusion with different SCFAs significantly ($p<0.001$) inhibited net colonic water secretion; the rates ($\mu l/min^{-1}.cm^{-1}$) of inhibition being 99%, 94%, and 86% for butyrate (30 mM), propionate (60 mM), and acetate (90 mM) respectively. The rates of net sodium secretion were also significantly less ($p<0.01$) in the SCFA-treated colon than those treated with SCFA-free solution (Na^+, mean ± SD, $\mu M/min^{-1}.cm^{-1}$: 5.17 ± 0.95, 7.31 ± 0.65, 12.7 ± 0.8 for butyrate, propionate, and acetate respectively; and 80.2 ± 20.6 for controls). Butyrate (30 mM) induced the highest inhibition of Na^+ and water secretion followed by propionate and acetate. All 3 SCFAs significantly ($p<0.01$) inhibited Cl- secretion, whereas only butyrate and propionate inhibited K^+ secretion. There was no significant alteration of the colonic HCO3- secretion by the SCFAs, and none was able to reverse colonic secretion into net absorption.

Conclusions: SCFAs stimulate salt and water absorption from CT-stimulated colon and may be useful as absorption-promoting agents in oral rehydration solutions.

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Oxidative Stress in Patients With Severe Cholera

MA Khaled and GH Rabbani

Objective: Determine the adverse metabolic effects of oxidative stress in cholera. Oxidative stress is an adverse metabolic condition induced by the Reactive Oxygen Species (ROS). These ROS are produced and catabolized by specific enzymes during the normal course of metabolism. Lipid peroxidation due to ROS occurs during infection and malnutrition leading to oxidative stress and chemical injuries to the tissues. However, nothing is known about the adverse metabolic effects of oxidative stress in cholera.

Methods: To assess the degree of oxidative stress and lipid peroxidation in patients with severe cholera, the present investigators determined the faecal contents of thiobarbituric acid-reacting substances (TBARS), an index of lipid peroxidation, in 6 adults with severe dehydrating diarrhoea due to *Vibrio cholerae* infections and in 5 healthy adult volunteers. These volunteers were drawn each year from the 100,000 diarrhoea patients attending the ICDDR,B's Dhaka-based hospital, the Clinical Research and Service Centre.