

Holistic Care

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Cholera treatment

Investigators from Bangladesh conducted a double-blind, randomized trial comparing single-dose azithromycin (1g) and ciprofloxacin (1g) for the treatment of severe cholera caused by *Vibrio cholerae* O1 or O139 in about 200 males.¹ Azithromycin was found to be an effective therapy clinically (shorter duration and reduced volume of diarrhea) and microbiologically. This study raises questions the antimicrobial susceptibility of *Vibrio cholerae* O1 to ciprofloxacin and raises concerns about resistance. It is important to rapidly put the lessons derived from this study into clinical practice in cholera endemic regions.

1. Saha D, Karim MM, Khan WA, Ahmed S, Salam MA, Bennis ML. Single-dose azithromycin for the treatment of cholera in adults. *N Engl J Med* 2006;354:2452-62.

Vitamins and obstetric complications

Supplementation with antioxidant vitamins has been proposed to reduce the risk of preeclampsia and perinatal complications, but the effects of this intervention are unclear. This multicenter trial, randomized about 1900

nulliparous women (14 to 22 weeks of gestation) in Australia and New Zealand to daily supplementation with 1000 mg of vitamin C and 400 IU of vitamin E or placebo (microcrystalline cellulose) until delivery.¹ It showed that there were no significant differences between the vitamin and placebo groups in the risk of preeclampsia, death or serious outcomes in the infant, or having an infant with a birth weight below the 10th percentile for gestational age. This trial concluded that supplementation with vitamins C and E during pregnancy does not reduce the risk of preeclampsia in nulliparous women, the risk of intrauterine growth retardation, or the risk of death or other serious outcomes in their infants.¹

1. Rumbold AR, Crowther CA, Haslam RR, Dekker GA, Robinson JS; ACTS Study Group. Vitamins C and E and the risks of preeclampsia and perinatal complications. *N Engl J Med* 2006;354:1796-806.

D-dimer and Pulmonary Embolism

Is it safe to withhold additional testing and anti-coagulation therapy in patients with suspected pulmonary embolism (PE) and negative D-dimer test results? This

study¹ tested over 1100 patients with suspected PE, of these, 456 patients with negative D-dimer test² results were randomly assigned to two intervention groups: those with a low clinical probability of PE (low-probability group) and those with a moderate or high clinical probability. In the control and experimental groups, anticoagulation was withheld or withdrawn if PE was not diagnosed.¹ The patients were monitored for symptomatic venous thromboembolism (VTE) during 6 months of follow-up. The study showed that in patients with a low probability of PE who had negative D-dimer results, additional diagnostic testing and anticoagulation could be withheld without increasing the frequency of VTE during follow-up. However, in patients with moderate to high clinical suspicion of PE based on a scoring table, it is advisable to monitor them further. Low clinical probability and negative D-dimer results occur in 50% of outpatients and in 20% of inpatients with suspected PE and therefore this test was of greater value in stratifying outpatients.

1. Kearon C, Ginsberg JS, Douketis J, Turpie AG, Bates SM, et al. Canadian Pulmonary Embolism Diagnosis Study (CANPEDS) Group. An evaluation of D-dimer in the diagnosis of pulmonary embolism: a randomized trial. *Ann Intern Med* 2006;144:812-21.
2. Ginsberg JS, Wells PS, Kearon C, Anderson D, Crowther M, Weitz JI, et al. Sensitivity and specificity of a rapid whole-blood assay for D-dimer in the diagnosis of pulmonary embolism. *Ann Intern Med* 1998;129:1006-11.

Pharmacodynamics and Holistic Care of the Patient

Thyroxine is one of those drugs requiring lifelong administration. Intestinal absorption can therefore play a major role in achieving therapeutic plasma levels. Thus conditions that alter intestinal absorption capabilities can impact thyroxine therapy. Malabsorption of thyroxine has been described in patients treated with drugs that modify an acidic environment. This study determined whether there was an increased need for thyroxine in patients with euthyroid multinodular goiter and impaired secretion of gastric acid.¹

The dose of thyroxine required to obtain a low level of thyrotropin (0.05 to 0.20 mU per liter) in 250 patients

with multinodular goiter was assessed.¹ About 50 patients had *Helicobacter pylori*-related gastritis and 60 had atrophic gastritis. The control group comprised 135 patients with multinodular goiter and no gastric disorders. In addition, variation in the level of serum thyrotropin was prospectively studied in 11 patients treated with thyroxine before and after *H. pylori* infection and both before and during treatment with omeprazole in 10 patients treated with thyroxine who had gastroesophageal reflux.

The daily requirement of thyroxine was higher (by 22 to 34 percent) in patients with *H. pylori* gastritis, atrophic gastritis, or both conditions than in the control group. In the 11 patients with *H. pylori* infection thyroxine treatment was therapeutic as measured by serum thyrotropin levels after eradication of the infection. Omeprazole reduced thyroxine absorption and therapeutic effect by decreasing the acidic environment of the stomach in a similar fashion to atrophic gastritis. A 37% increase in thyroxine dosage compensated for the effect of omeprazole. The study draws our attention to simple pharmacodynamic principles of drug therapy and behooves us to treat the patient holistically.

1. Centanni M, Gargano L, Canettieri G, Viceconti N, Franchi A, Delle Fave G, Annibale B. Thyroxine in goiter, *Helicobacter pylori* infection, and chronic gastritis. *N Engl J Med*. 2006 Apr 27;354:1787-95.

Videos and images in Clinical Medicine

The New England Journal of Medicine has started a "Videos in Clinical Medicine" section describing basic invasive procedures in clinical medicine such as arterial line placement, NG tube and urethral catheterization.¹ Heart sounds, murmurs and other audio recordings are available at the University of Washington, Department of Medicine website.² A detailed guide to the physical exam can be found on the University of California San Diego website³, which also lists other websites of clinical teaching interest.

1. <http://content.nejm.org>
2. <http://depts.washington.edu/~physdx/skillmodules.html>
3. <http://medicine.ucsd.edu/clinicalmed/links.html>