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Abstract no. 100

The antibacterial action of bismuth: early results of antibacterial regimens in the treatment of duodenal ulcer

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IN-VITRO STUDIES: Discs containing 0.05 mg of bismuth subcitrate (De-Nol), bismuth subsalicylate (Pepto-Bismol), bismuth subnitrate (Roter), cimetidine (Tagamet), ranitidine (Zantac), sucralfate (Ulsanic) and carbenoxolone (Biogastrone), were applied to brain-heart-infusion blood-agar plates inoculated with *Campylobacter pyloridis* (CP). After 72 h in a 10% CO₂ incubator at 37 °C, large zones of inhibition were visible around the bismuth-containing discs but were less than 3 mm radius around cimetidine and ranitidine; no zones were present around the other drugs. Antibacterial activity of the bismuth salts was related to their solubility: B/subcit., 25 mm radius; B/subsal., 18 mm; B/subnitr., 12 mm. Agar plate dilution indicated that the MIC of 12 CP isolates to bismuth subcitrate was less than 25 mg/l. Other organisms with potentially useful MICs to bismuth citrate were *C. jejuni*, *Bacteroides* spp., *Vibrio cholerae*, *Clostridium difficile* and *Pseudomonas* spp.

ELECTRON MICROSCOPY: Patients with CP colonisation and gastritis underwent biopsy 40-100 minutes after taking a standard dose of liquid De-Nol. After De-Nol, compared with baseline results, the bacteria had detached from the gastric epithelium and many of the organisms had lysed. Electron-dense granules of bismuth were deposited on the cell walls of the damaged bacteria. Similar but less obvious changes were noted when patients received DeNol or Pepto-Bismol in tablet form. In two patients who underwent biopsy 24 h after commencing a standard dose of De-Nol tablets, the bacteria could not be seen. These findings suggest that the traditional use of bismuth compounds in the treatment of dyspeptic and diarrhoeal diseases is justified by its antibacterial effect. An interesting finding was the presence of Bacteriophage in *C. pyloridis* organisms in the baseline biopsy specimens of two patients.

DUODENAL ULCER: During 1984, 24 consecutive patients with duodenal ulcer disease, biopsy proven gastritis and CP infection were treated with an antibacterial regimen consisting of 28 days of De-Nol tablets (bismuth subcitrate 120 mg q.i.d.) plus an antibiotic, usually tinidazole or amoxicillin, given concurrently from day 14 to day 28. Where possible, patients underwent biopsy 2 weeks after ceasing therapy and were treated again (with a different antibiotic) if CP was still present.

Eradication of CP, with resolution of active chronic gastritis, was confirmed by biopsy in 15 patients. The organism was not cleared in two patients, and seven

patients were not re-endoscoped. No patients were given maintenance therapy. They were followed up by questionnaire and interviewed by a research assistant in May 1985. Of 15 patients with confirmed bacteriological clearance of CP, one had a duodenal ulcer relapse without CP and one had a clinical relapse and had recommenced cimetidine. The remaining 13 patients (average follow-up 9.2 months) were on no therapy.

Overall, 16 of the 24 patients (average follow-up 8 months) were asymptomatic, and two others had symptoms which were proven not to be due to CP infection or duodenal ulcer. Of the remaining six patients, five had ulcer symptoms which had recommenced within a month of ceasing therapy. Two of these clinical relapses had persistent CP when re-biopsied, the other three were not followed up endoscopically. The remaining patient relapsed after 3 months and was found to have small aphthous ulcers of the duodenal cap without histological gastritis or recurrence of CP.