Prolonged Hemodynamic Effectiveness of Sustained Release Isosorbide Dinitrate

To the Editor:

In their very interesting contribution "Antianginal Efficacy of Oral Therapy with Isosorbide Dinitrate Capsules" (Chest, 73:327-332, 1978) the authors contend that, so far, no controlled study has been performed to evaluate the effect of sustained-release organic nitrates six hours after administration ( ...).

I should like to inform you that studies of this kind have been done, at the initiative of our Cardiovascular Research Department, using a sustained-release tablet of 20 mg isosorbide dinitrate (ISDN).*

Thus, six hours after administration, Stegaru et al1 still found a stroke volume (SV) decrease from 80.9 ± 17.2 to 76.5 ± 17.3 ml and a fall in cardiac output (CO) from 5.8 ± 1.7 to 4.5 ± 1.2 l/min in 15 patients with chronic coronary heart disease (CHD), while in five patients with additional congestive heart failure (CHF) the SV rose from 65.2 ± 24.9 to 81.8 ± 27.5 ml and CO from 4.1 ± 1.2 to 5.6 ± 2.0 l/min.

Roknann2 found a highly significant increase in exercise tolerance (from 24.6 to 46 and 49 W respectively on the bicycle ergometer) 2, 4, 6, and 8 hours after oral administration of 2 tablets (40 mg) of sustained-release ISDN to nine CHD patients.

Likewise, Zerzawy and Bachmann3 studied 14 patients with angiographic evidence of CHD prior to, and after oral administration of 40 mg sustained-release ISDN and found significant hemodynamic improvement for as long as eight hours: systemic blood pressure fell to its lowest values between the 4th and 6th hour; pulmonary artery pressure during exercise fell from 47/26 to 35/17 mm Hg and 36 mm Hg after 6 and 8 hours respectively. In ten of the patients concomitant determinations of ISDN plasma concentrations showed values ranging from 2 to 107 ng/ml which made the authors believe that there were no statistically demonstrable correlations between their clinical findings and the rate of ISDN biotransformation.

On the other hand, all of the above observations, as well as those of the authors of your paper, are borne out by the findings of Assinder et al4 after oral administration of 20 mg ISDN in a sustained-release tablet: 6 hours after dosing, 1.9 ± 0.8 ng/ml were still detectable in the plasma of six volunteers (Fig 1).

References

2 Roknann H: Rehabilitation für Herz- und Kreislaufkrank. Benedikt Kreuz Rehabilitationszentrum (unpublished data)

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To the Editor:

We thank Dr. Pascal for his kind interest in our original clinical investigation in which we demonstrated objectively, for the first time, that high-dose long-acting nitrate therapy (using 40 mg sustained-release isosorbide dinitrate in the form of Isordil Tembids every 8 hours for one month; Ives Laboratories, New York) provides prolonged prophylactic antianginal action capable of increasing pain-free exercise tolerance (Bruce multistage treadmill procedure average exercise duration increase 20 percent, maximal O2 consumption increase 15 percent, with ST-segment depression reduced 40 percent) for at least 6 hours per capsule in patients with angiographically documented coronary artery disease employing controlled methodology (double-blind protocol comparing these beneficial results to a randomly selected concordant control group of similar ischemic heart disease patients receiving placebo without salutary effects undergoing identical exercise stress testing). Further, we are pleased that Pharma Schwartz Laboratories (Monheim, West Germany) will now be able to offer sustained-release isosorbide dinitrate capsules for oral administration to control anginal pain.
Neisseria sicca Pneumonia

To the Editor:

Acute pneumonia caused by species of Neisseriaceae are uncommon. Most of the reported cases are due to Neisseria meningitidis group Y and Branhamella catarrhalis (formerly known as Neisseria catarrhalis). This report describes the first case due to Neisseria sicca.

Case Report

An 80-year-old white man was admitted with a one-day history of cough, chills and fever. Three weeks previously he had been hospitalized and was diagnosed as having "pneumococcal" pneumonia, treated with 1.2 million units of procaine penicillin intramuscularly daily for five days, and responded well. One week later the patient started coughing and produced purulent sputum. His family physician prescribed ampicillin 250 mg four times a day for two weeks. Three days after ampicillin was discontinued, he developed cough, shaking chills and fever, and was subsequently admitted. Past medical history indicated the patient has chronic atrial fibrillation and atherosclerotic heart disease.

Physical examination revealed an elderly male in acute respiratory distress. His temperature was 102°F (38.9°C), pulse rate 110 per minute, blood pressure 110/70 mm Hg, respiratory rate 28 per minute. Fertile physical findings were limited to the chest; crepitant rales and bronchial breathing were heard over the left mid and lower lung fields.

Laboratory data: white blood cell count 12,000/cu mm with 71 percent polys, 12 percent bands, 11 percent lymphocytes, 6 percent monocytes; hemoglobin 12.3 gm percent; hematocrit 37 percent; BUN 34 mg percent; creatinine 2.8 mg percent; urine specific gravity 1.015; pH 6.0; WBC 100/high power field, RBC 10-15 per high power field. Arterial blood gas levels: Pao2 58 mm Hg; pH 7.42; O2 saturation 100 percent, Pco2 41 mm Hg, HCO3 25 mEq/liter. Chest x-ray film (Fig 1) revealed fluffy alveolar infiltrates involving the left lower lobe.

Because of recent antibiotic therapy and the patient's inability to cough effectively, a transtracheal aspiration was done. Purulent sputum was obtained and cultured aerobically and anaerobically. Gram stain showed numerous polymorphonuclear and gram-negative diplococci. The patient was started on gentamicin 80 mg every 12 hours and aqueous penicillin G 6 million units daily. The patient improved over the next two days. Gentamicin was stopped on the second day when sputum culture grew Neisseria sicca in pure culture. On the seventh hospital day, penicillin was stopped. The patient remained afebrile and was discharged. Six months after discharge he continued to be well.

Discussion

Neisseria sicca is a member of the family Neisseriaceae. It is a normal inhabitant of the nasopharynx and is rarely pathogenic. A search of the literature reveals only a single case of meningitis and septicaemia due to this agent.8 Pulmonary infections due to Neisseria species are uncommon. In the normal host, most Neisseria species infections are due to Neisseria meningitidis group Y. Branhamella catarrhalis has been described among coal miners with chronic lung disease2 and in the immunodeficient host.4 Clinically and radiologically, pulmonary infections due to Neisseria species cannot be distinguished from other causes of bacterial pneumonias. The diagnosis of pneumonia due to Neisseria species remains difficult. Since Neisseria species are part of the normal flora of the upper respiratory tract and considered as "nonpathogenic," routine culture of sputum is of little value. However, the use of transtracheal aspiration may aid in diagnosis.

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