



Cardiotoxicity of high-dose continuous infusion fluorouracil: a prospective clinical study

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PURPOSE:

A prospective clinical study was performed to determine the incidence of high-dose continuous intravenous infusion fluorouracil (5FU-CIV) cardiotoxicity.

PATIENTS AND METHODS:

Three hundred sixty-seven patients who were given first-cycle high-dose 5FU-CIV were monitored for cardiac function by clinical examination, ECG, and laboratory tests. 5FU-CIV was administered during a 96- or 120-hour period at doses that ranged from 600 to 1,000 mg/m²/d. Associated drugs included cisplatin (56%), mitomycin (12.5%), folinic acid (leucovorin) (7%), and others (14%). Thirty-nine patients (10.5%) received 5FU as a single agent.

RESULTS:

5FU-induced cardiac events occurred in 28 patients (7.6%; 95% confidence interval, 4.9% to 10.3%). Nine of them had a history of cardiac disease. Primary tumors included head and neck (n = 13), gastrointestinal (n = 6), breast (n = 3), and others (n = 6). The mean onset time of cardiac symptoms was 3 days (range, 2 to 5). Inaugural symptoms included angina pectoris (n = 18), hypotension (n = 6), hypertension (n = 5), malaise (n = 4), dyspnea (n = 2), arrhythmia (n = 1), or sudden death (n = 1). At 5FU discontinuation, six patients' cardiac symptoms returned to baseline, but 21 patients experienced unstable angina (n = 8), hypotension/cardiovascular collapse (n = 11), pulmonary edema (n = 1), or sudden death (n = 4). The lethality rate was 2.2% (five sudden deaths plus three irreversible collapses). ECG showed repolarization changes (ST segment deviation; T-wave inversion) in 65% and/or diffuse microvoltage in 22% of the patients who presented with cardiac events. Echocardiography showed partial or global hypokinesia in nine of the 16 patients who were examined, and one case of prolonged akinesia. Cardiac enzymes rarely showed an increase (n = 2). In severe but reversible cases, clinical, ECG, and echographic parameters returned to baseline status within 48 hours after the drug discontinuation. A fluorine 19 nuclear magnetic resonance (19F NMR) analysis of urine was performed on 14 patients; six had cardiac symptoms and eight did not. Fluoroacetate (FAC), a known cardiotoxic compound, was detected in all cases.

CONCLUSION:

In our study, the incidence of high-dose 5FU-CVI cardiotoxicity was 7.6%. The hypothesis of a toxic cardiomyopathic process requires further confirmation.

Résumé en
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