Effect of single-dose administration of recombinant interferon-alpha2b on gastric myoelectrical activity in patients with chronic hepatitis C

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Introduction

Chronic hepatitis C virus (HCV) infection is a major cause of cirrhosis and hepatocellular carcinoma worldwide. The use of interferons is currently one of the very few treatment modalities which can be offered to patients suffering from chronic liver disease caused by HCV.¹⁻¹⁰ Recent metaanalyses and consensuses reached by prominent hepatologists indicate that monotherapy with interferon alpha may be helpful as an initial management in patients assessed as good responders, in whom it may bring about viral clearance. However, the current standard of chronic hepatitis C management is the combination of interferon alpha with ribavirin, which is recommended for relapsers, nonresponders, or patients with a forecast poor response.⁴,⁵,⁷,⁹,¹⁰ During the course of interferon therapy, patients not infrequently report abdominal complaints, such as discomfort, loss of appetite, epigastric pain, nausea, and vomiting.²,⁷,¹⁰⁻¹² Investigations by two groups of Japanese researchers disclosed recently that these undesirable symptoms may be related to delayed gastric emptying occurring during interferon therapy.¹¹,¹² Based on objective results of the measurement of gastric evacuation kinetics, as well as on a subjective symptom score assessment, a low-dosage regimen of cisapride was demonstrated to relieve both the retardation of gastric emptying and the upper abdominal complaints in patients undergoing treatment with this drug.

Key words: electrogastrography, gastric myoelectrical activity, HCV, interferon
discharge of spike action potentials, which, in turn, initiates motility events, the net result of which is gastric emptying. In the light of the outlined reasoning, and taking into account the findings quoted in the preceding paragraph, we decided to test a hypothesis—whether acute administration of interferon alpha affects gastric slow-wave activity in humans. We therefore undertook a study with the use of surface electrogastrography—a convincingly validated technique enabling noninvasive registration of gastric myoelectrical activity (GMA).13,14

**Methods**

**Subjects**

The study population comprised 25 patients admitted to the Department of Internal Medicine, Medical University of Silesia, Sosnowiec, with a diagnosis of chronic hepatitis C. The diagnosis was established on the basis of elevated serum alanine aminotransferase levels, exceeding at least two times the upper limit of the normal range for at least 6 months; by seropositivity for antibodies to HCV, using a second-generation enzyme-linked immunoassay (ELISA); by the presence of bodies to HCV, using a second-generation enzyme-linked immunoassay (ELISA); and by histological evidence of chronic hepatitis C at liver biopsy.15 Exclusion criteria comprised: circulating autoantibodies (anuclear antibod- ies [ANA], smooth muscle antibody [SMA], liver-kidney microsomal antibody type 1 [LKM-1], antimitochondrial antibodies [AMA]); excessive consumption of ethanol; evidence of drug-related or metabolic liver diseases (hemochromatosis, alpha-1 antitrypsin deficiency, Wilson disease); history of surgery affecting the digestive tract anatomy, except for appendectomy or cholecystectomy; and current use of any drugs which might affect gastrointestinal motility. None of the patients was treated with immunosuppressive, immunomodulatory, or antiviral agents during 6 months prior to the study. All the patients were naïve to interferon.

The research project was approved by the Bioethics Committee of the Medical University of Silesia. The study was conducted in accordance with the Helsinki Declaration, and every patient gave written consent to participate after getting information as to the aim, protocol, and methodology of the study.

**Study protocol**

The research was performed on patients reporting to the laboratory in the morning, after a 12-h overnight fast and abstaining from cigarette smoking. Three Ag/AgCl electrodes suitable for the prolonged recording of bioelectrical signals (type EK-S 55P; Sorimex, Toruń, Poland) were placed on the abdomen. The first active (A1) electrode was fixed in the midline, half way between the xyphoid process and umbiculus, the second active (A2) electrode was fixed at a point lying 5 cm distant to A1 on a line leading up at a 45° angle towards the left costal margin, whereas the reference electrode (R) was positioned on the right side of the abdomen below the right costal margin at its intersection with the right anterior axillary line. The preparatory procedure involved shaving of the skin if necessary, and then careful abrasion until pink, with the use of Every paste (Sorimex). Finally, a drop of a high-conductive gel for electroencephalographic recordings (MediGel; Sorimex) was applied directly to the conductive surface of each electrode just before fixing it to the skin. The electrical resistance between each pair of electrodes was checked with the use of a digital ohmmeter (type M3850D; Metex, Korea), and if it exceeded 5 kohms, the respective electrodes were removed and the whole preparatory procedure was started from the beginning. The electrodes were connected to a MicroDigitrapper 4 Mbyte Flash series recording device (Synectics Medical, Stockholm, Sweden).

Every patient attended two examination sessions on separate days. The examination always commenced with a 25-min basal GMA registration performed with the subject in the recumbent position. Subsequently in group A (12 patients) placebo (normal saline) or 5 million i.u. recombinant interferon alpha-2b (IFNA; Intron A; Schering-Plough, Brinny, Ireland) was administered s.c. and the GMA was recorded in the fasted state for two periods (2 h and 4 h), separated by a 15-min break. In group B (13 patients), placebo or 5 million i.u. IFNA was injected s.c. after the ingestion of a semiliquid test meal of 364 kcal (1524 kJ), which consisted of 400 g fruit yoghurt and contained 10.8 g protein, 61.2 carbohydrates, and 10 g fat. The patients were allowed to consume the meal in a sitting position within up to 5 min. Subsequently, the postprandial GMA was recorded for two periods (2 h and 4 h), separated by a 15-min break. During the 15-min break, the registration was interrupted, leading wires were disconnected from the electrodes, and the patients were allowed to walk round and use the restroom if necessary, whereas for the entire time of the interdigestive or postprandial GMA recording they remained lying on a couch.

The study was performed in a double-blind manner, i.e., neither the patient nor the researcher in charge of performing the analyses of GMA tracings (A. K.-J.) was aware of what had been injected. The order of injections was, however, fixed, so that placebo was always administered in the first examination session, and IFNA always in the second. This was necessary because the patients were entering their cycle of everyday IFNA administration, and while planning the study scheme