The effect of immunosuppressive therapy on hepatitis B surface antigen (HBsAg)-positive chronic active hepatitis (CAH) is controversial. Discrepancies may be due to different criteria in selecting patients, different environmental factors or the ethnic background of patients.

The present paper describes the results of a prospective study conducted on 204 consecutive patients with HBsAg-positive CAH observed for at least one year and untreated, or treated with either prednisolone or azathioprine, or with a combination of these two drugs. All patients were born in Naples or the surrounding area and were Caucasian of Latin ethnic background.

MATERIALS AND METHODS

Patients

244 consecutive patients with biopsy-proven HBsAg-positive CAH were included in the study. CAH was diagnosed according to accepted criteria. All the patients had HBs antigenemia and abnormal values of serum aminotransferases (ALT and AST) and immunoglobulin G for at least six months before entering the study. The liver biopsy obtained by Menghini’s technique at the beginning of the study always showed periportal hepatitis with or without cirrhosis.

Key-words: Chronic active hepatitis, therapy; Chronic hepatitis; Hepatitis B surface antigen (HBsAg).

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Pregnant women, patients below 12-year-old, and patients with malignant diseases, tuberculosis, osteoporosis, diabetes mellitus, peptic ulcer, ascites or encephalopathy were not included in the study. Patients with a daily ethanol intake higher than 100 g and those taking drugs potentially inducing CAH were also not included in the study. Thus, 23 CAH patients (13 pregnant women, five patients with diabetes mellitus, two with peptic ulcer and three with a history of alcohol intake) were not included. An attempt to follow up these patients was made but it was not always successful. Only 16 patients were monitored for one year by physical examination and liver function tests, but a second liver biopsy was never performed.

Patients selected for the study were left untreated or assigned consecutively to one of the following treatments: 100 mg azathioprine daily; prednisolone (Dutimelan 8 15° given according to chronobiological criteria; prednisolone (Dutimelan 8 15° and azathioprine 50 mg daily, referred to as combination therapy. Each treatment group was composed of 61 patients. No patient had been receiving steroids or azathioprine at the time of the first observation. Since 40 patients dropped out (32 for lack of cooperation and 8 because of serious side-effects of the therapy) only 204 patients were observed for at least one year.

Of these 204 patients, 48 were treated with azathioprine, 52 with steroids, 54 with the combination therapy and 50 were not treated. Patients were seen every two months for physical examination and liver function tests. HBsAg, HBeAg, their corresponding antibodies and anti-HBc in serum were determined at the beginning of the study and thereafter at 6-month intervals. HBsAg, HBeAg, anti-HBc, anti-HBc and anti-HBs were determined by radioimmunoassay (RIA).

All patients were biopsied every 12 months. Morphological alterations (steatosis, mononuclear cell infiltration, piecemeal necrosis and fibrosis) were graded independently by two observers according to an arbitrary scale ranging from 0 to 4. The results of the two pathologists were almost always in good agreement. The small discrepancies that occurred occasionally concerned only the degree of the histological lesions. Discrepancies never exceeded one degree of the arbitrary scale and in these cases the two pathologists always achieved agreement after reviewing the slides together. All patients were observed for at least one year (mean 24 months, range 12-40 months).

Criteria for assessing improvement and deterioration

Patients were considered 'improved' when they showed for at least six months remission of clinical symptoms, normalization or 50% reduction of aminotransferases below initial values, and normal bilirubin levels associated with reduction of morphological alterations characteristic of CAH. Patients were considered 'deteriorated' when they developed clinical and/or histological evidence of cirrhosis, or when they showed two or more of the following: increase in piecemeal necrosis on liver biopsy; physical deterioration with inability to perform their usual occupation; 100% increase in aminotransferases above the initial values; 100% increase in bilirubin above the initial values.

Three patients showing severe biochemical and histological abnormalities throughout the period of observation and five patients who died from liver