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Full Length Research Paper

Quantitative changes of serum immunoglobulins A, G and M among patients with Hepatitis A

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There is evidence of change in the level of serum immunoglobulins (Ig) in patients with hepatitis A and attempts for these changes to be associated with the clinical course of the disease. The aim of this study is to establish the quantitative changes of IgA, IgG and IgM in hepatitis A patients and to evaluate their significance for the clinical course of the disease. A total of 125 persons were examined: 35 patients with prolonged form of HAV; 51 patients with self limited form of HAV; 35 healthy persons – control group. In comparison with the control group, a substantial increase of IgA, IgG and IgM was found in patients with prolonged form of HAV. In patients with self limited form of HAV, the increase was significant for IgG and IgA, and insignificant for IgM. The research on serum Ig supplements the research panel performed for patients with HAV and may have prognostic importance in determining the severity of the disease and the prolonged forms of HAV.

Key words: Hepatitis A, serum immunoglobulins, quantitative changes.

INTRODUCTION

Several studies have established the occurrence of serum immunoglobulins (Ig) alterations (level changes) after acquiring hepatitis A. Gupta and Garg (1994) have reported significant increase in values of IgM in sick compared to those in healthy subjects while the levels of IgG and IgA have not undergone reliable changes.

Fukuda et al. (1985) have established an increase of IgA, which was parallel with total bilirubin. IgA peaked (reaches maximum values) later than the liver transaminases and it was assumed that the IgA increase was probably related to liver regeneration. In a study of 30 patients with hepatitis A, Akzu and Mietens (1984) have established minimum changes of IgA - in about 75% of the subjects its level was within normal range, while elevated values of IgG were found in 44.2%, and of IgM – in 96.1% of the cases. No significant difference was found between the various age groups – 0-1, 1-2, 3-5, 6-8 and 9-15 years. On the 14th day after hepatitis A diagnosis, increased IgM values started to decline, those of IgG continued to rise and IgA remained at the same level. Zhuang et al. (1982) have identified elevated levels of IgM and almost normal levels of IgG in patients with hepatitis A. Ilieva (2005) has detected different changes in serum Ig in patients with different forms of acute hepatitis A - mild, moderate, severe and prolonged. Cheema et al. (2004) have reported a patient with serologically confirmed hepatitis A infection and nephrotic syndrome (a rare complication associated with hepatitis A virus). Renal biopsy showed that IgA is dominant glomerulonephritis with subendothelial immune deposits.

Kano et al. (2000) have described an association with

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Abbreviations: Ig, Immunoglobulins.

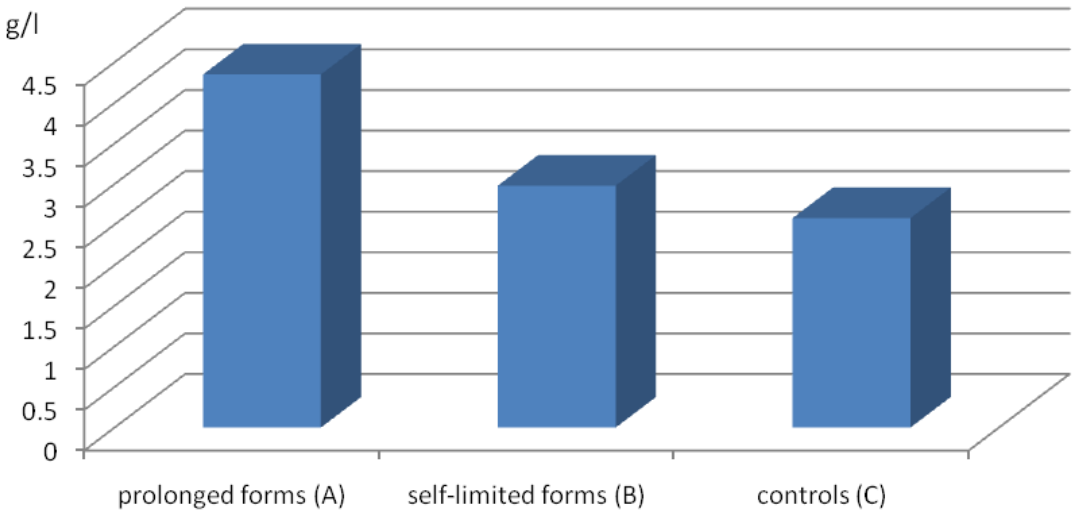

Figure 1. Levels of serum IgA. **A,** n=35, $\bar{x}$ =4.35±1.37; **B,** n=51, $\bar{x}$ =2.98±1.25; **C,** n=39, $\bar{x}$ =2.58±1.17; **A:B,** t=4.80, P<0.001; **A:C**, t=5.99, P<0.001; **B:C,** t=1.55, P>0.05.

the hepatitis A virus infection skin rash, which otherwise occurs rarely. The authors have reported a hepatitis A sufferer, who appeared in rubella-like rash, accentuated at exposed to the sun body areas. Direct immuno-fluorescence study of the lesions found deposition of IgA on endothelial cells in the upper skin layer. It was suggested that the described manifestation could be due to increased levels of IgA in patients with hepatitis A.

The aim of the study is to establish the changes in the levels of IgA, IgG and IgM in hepatitis A virus patients with different clinical manifestation of the disease.

MATERIALS AND METHODS

The study covered 3 groups of persons over 20 years: (A) 35 patients with prolonged form of hepatitis A; (B) 51 patients with self-limited form of hepatitis A; (C) control group of 39 healthy persons. Patients were treated in the Clinic of Infectious Diseases – University Hospital, Plovdiv. Diagnosis was confirmed by positive anti-HAV IgM in all of them. As a prolonged form of the disease we have considered the cases in which up to day 40 after onset, there were still subjective complaints and ALT values were above 100 IU/L. For patients with no complaints on the 40th day (at the first examination) and ALT values below 40 IU/L, we have assumed the infection as self-limiting. Those are criteria adopted by other authors - Glikson et al. (1992) and Arshan et al. (2002). Blood samples were taken between the 37th and 45th day since onset of jaundice in patients. Tests for IgA, IgG and IgM were carried out in the Central university clinical laboratory of Medical University-Plovdiv. The Turbo-dimetry method for quantitative examination of serum Ig was performed by the help of Konelab machine (Finland).

For timely detection of HAV patients and for holding measures for disease prevention and control the method for epidemiological research was used: epidemiological history and tests directed at identifying the source of infection, determining the type of isolation (home or infectious disease department), regular clinical examination of the patient after discharge, detecting the contacts of patients and conducting the necessary measures, clinical supervision, immunoprophylaxis, disinfection where the outbreak occurred, and analysis of survey data in regard to the effectiveness of measures taken for prevention and control.

Clinical analyses included: diagnosis based on clinically overt symptoms, assessment of the severity of the clinical course and biochemical tests (blood bilirubin, alanine transaminase, aspartate transaminase, fibrinogen and blood count).

RESULTS

The obtained results for the levels of serum IgA are presented on Figure 1. In Group (A), the levels varied from 2.4-6.85, average 4.35±1.37; in Group (B) – from 1.17-5.7, average 2.98±1.25 and in Group (C) – from 1.05-5.35, average 2.58±1.17. Reference value for serum IgA is 0.7-4.5. IgA was within the reference values for all three tested groups. In patients with prolonged disease course, the average value is slightly below the maximum reference value - 4,35 g/L at a maximum of 4.5 g/L.

The results for the levels of serum IgG are shown on Figure 2. For group (A), the levels ranged from 12.1-37.7, average 19.89±6.71; for Group (B) – from 9.9-31.1, average 17.84±5.66 and for Group (C) – from 4.5-20.7, average 13.1±5.21. Reference value for serum IgG is: 7.0-16.0. The level of serum IgG was higher than both the reference values and the controls' average values for patients with protracted disease course and for those with shorter convalescent period.

Figure 3 shows the obtained results for the serum IgM. In Group (A), values were from 1.4-5.6, average 3.02±1.29; in Group (B) – from 0.3-4.3, average 2.08±1.43 and in Group (C) – from 0.25- 4.4, average 1.86±1.07. Reference value for the serum IgM is from 0.4-2.3. Serum IgM was the highest in patients with

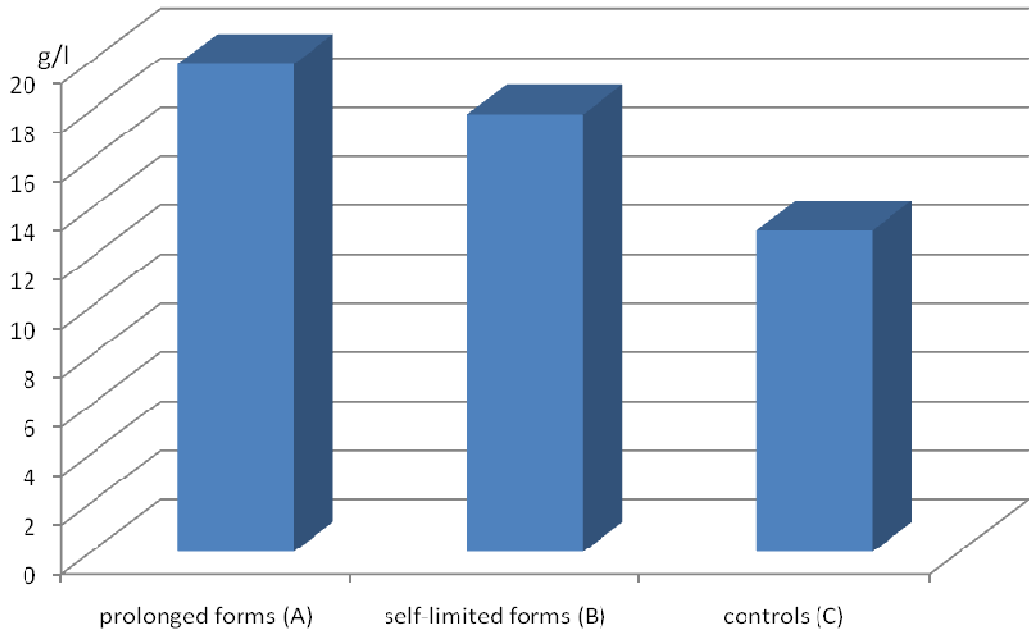

Figure 2. Levels of serum IgG. **A,** n=35, $\bar{x}$ =19.89±6.71; **B,** n=51, $\bar{x}$ =17.84±5.66; **C,** n=39, $\bar{x}$ =13.1±5.21; **A:B,** t=1.53, P>0.05; **A:C,** t=4.89, P<0.001; **B:C,** t=4.07, P<0.001.

prolonged disease course. It is above the reference value - 3.02 g/L at maximum reference 2,3 g/L. For patients with self-limiting form of the infection and for the control group, IgM was within the reference values (0.4-2.3 g/l).

DISCUSSION

The level of the serum IgA was in reference values for all three tested groups. Although the level for the patients with prolonged course of the disease was considerably higher than the levels of the patients with self limited form of hepatitis A and the control group (A:B – t=4.80, P<0.001; A:C – t=5.99; P<0.001). This is not in correspondence with the results received by Gupta and Garg (1994), who have established that IgA have not undergone reliable changes in patients with hepatitis A. Akzu and Mietens (1984) have obtained minimum changes of IgA - in 75% of the patients with hepatitis A its level was within normal range. The data of our study correlate with the investigation of Fukuda et al. (1985) who have established an increase of IgA later than the liver transaminases. We have not observed nephritic complications among the patients with elevated values of IgA, described from Cheema et al. (2004). We did not found and patients with skin rush as Kano et al. (2000) have been established.

The average level of the serum IgG in all patients (with prolonged and self limited form of infection) was higher than the reference value. They are statistically higher than those of the control Group (A: C – t=4.89, P<0.001; B: C – t= 4.07, P<0,001). These results are similar to those, received by Akzu and Mietens (1984) who have established elevated values of IgG in 44.2% of the patients. In the same time they do not correspond to the results of Zhuang et al. (1982) and Gupta and Garg (1994) who found almost normal levels of IgG among patients with hepatitis A.

The average level of the serum IgM in patients with prolonged form was considerably higher compared to the other two Groups (A: B – t=3.18, P<0.01; A: C – t=4.18, P<0.001). Among patients with self limited form IgM was slightly increased in comparison with the control group (B: C – t=0.83, P>0.05). Ilieva (2005) has established increased levels of IgM among patients with hepatitis A and different clinical form: mild, moderate and heavy. The levels of IgM have been increased for all clinical forms but they have been the highest among the patients with moderate form of the disease. Akzu and Mietens (1984) have established elevated values of IgM in 96.1% of the cases.

Conclusion

Research data indicate the occurrence of significant changes in the level of the three classes of serum Ig – A, G and M among the patients with prolonged form of HAV in comparison with the control group. These changes are less expressed among the patients with self limited form

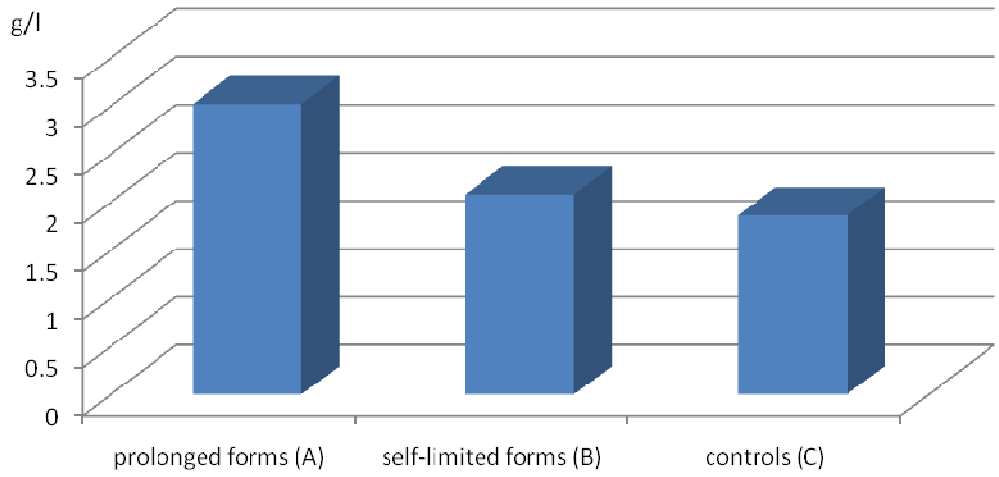

Figure 3. Levels of serum IgM. **A,** n=35, $\overline{x}$ =3.02±1.29; **B,** n=51, $\overline{x}$ =2.08±1.43; **C,** n=39, $\overline{x}$ =1.86±1.07; **A:B,** t=3.18, P<0.001; **A:C,** t=4.18, P<0.001; **B:C,** t=0.83, P>0.05.

of HAV and are insignificant for the levels of IgA and IgM. Research on serum Ig complements the panel of tests performed for HAV patients and may have occasional prognostic significance in determining the severity of disease or cases with protracted course.

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