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Chronic urticaria: are Hepatotrophic viruses B & C to blame?

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Abstract:

Background: Chronic urticaria has multifactorial etiologies which includes infections; recently attention has been focused on the hepatitis viruses with conflicting results. Since there is a high prevalence of hepatotropic virus B and C infection in Kashmiri population and chronic urticaria prevalence in the general population of 3% percent, an investigation was thought of to prove an association between chronic urticaria and these viruses.

Aim: A prospective study was conducted in a case controlled manner to study the association of chronic urticaria with hepatotropic viruses B & C.

Method: The study included a total of 70 nonconsecutive patients with chronic urticaria and the control group comprised an equal number of age and sex matched patients with different dermatological disorder not related to any hepatotropic virus infections.

Results: 2.8% of the patients in the study group were seropositive for the HBsAg and none for the anti-HCV; 4.28% of the controls were seropositive for HBsAg and none for anti-HCV.

Conclusion: It was found that there was no statistically significant association of hepatotropic viruses B&C with chronic urticaria.

Limitations: Polymerase chain reaction for detection of HBV and reverse transcriptase polymerase chain reaction for detection of HCV were not done.

Introduction:

Urticaria is described as an eruption of pruritic transient (<24 hrs), well-demarcated superficial erythematous or pale swelling of the dermis [1]. Urticaria is classified into acute and chronic on the basis of time division of six weeks. Although a number of triggering factors including drugs, [2] food additives, [3] aeroallergens [4] and infections [5] have been implicated; the etiology still remains largely elusive. Among the various infections suspected, attention has recently been focused on the hepatotropic viruses.

Several studies have shown a positive association of chronic urticaria with hepatotropic viruses and interferon therapy was proposed as a therapy for this difficult to treat condition, [6, 7] however other studies indicated an unlikely association between the hepatotropic virus and chronic urticaria.[8, 9]

In view of high prevalence of hepatitis B (25%) & hepatitis C (45%) in chronic liver disease in the kashmiri population [10], a study was designed to determine whether any association exists between hepatotropic viruses B&C and chronic urticaria.

Materials and methods:

This prospective study was conducted in a case controlled manner from January 1st, 2008 to December 31st, 2009. The study group included a total of 70 patients with chronic urticaria attending the outpatient department of Dermatology, STD and Leprosy of SMHS (Associated teaching Hospital of Government Medical College Srinagar) .The control group comprised of an equal number of age and sex matched patients with different dermatological disorder not related to any Hepatotropic virus infections.

A thorough history was obtained from all patients about urticaria; patients with systemic disorders such as collagen vascular disease, thyroid dysfunction, food and drug allergies were excluded. Patients with a history of jaundice and other apparent risk factors for viral hepatitis were also excluded. Liver function tests and serology for hepatitis B &C infections were done in both groups; detection of HBsAg was done by enzyme immunoassay method (Monolisa Ag HBs plus, Biorad, Tokyo) and serological detection of anti HCV- antibody was done by 3rd generation LG HCD 3.0, LG chemical Ltd. South Korea. Statistical analysis was done by chi square test, Fischer's exact test and t-test.

Informed consent for the study was taken from both groups

Results:

The study group comprised of 70 patients, 41.4% were males and 58.5% were females. In the control group out of 70 patients 42.8% were males and 57.1% were females. Age distribution of the study group and control group were comparable. Among the study group, the minimum age was 16years and the maximum was 67 years; the median age was 34 years. [Table-1]

	Study group	Control group	p-value
Age (yrs) >20	11(15.72%)	7(10.00%)	0.546
20-40	40(57.14%)	45(64.29%)	
>40	19(27.14%)	18(25.71%)	
Mean age \pm SD	33.86 \pm 13.50	33.20 \pm 12.83	0.771
sex distribution	Males-29(41.42%)	30(42.85%)	0.86
	Females- 41(58.57%)	40(57.14%)	

Cases: minimum age=16 years, maximum age=67 years.

Controls: minimum age=16 years, maximum=64 years.

Table1: Distribution of age and sex in cases and control group in different age intervals

Forty patients had persistent or daily episodes of urticaria while 30 had recurrent episodes of urticaria. Of all patients, 19 had associated angioedema. [Table-2]

	Male (%)	Female (%)	p-value
Duration <6 months	17 (58.62)	18 (43.90)	0.407
6 months-1year	3 (10.34)	10 (24.39)	
1-5 years	6 (20.68)	7 (17.07)	
>5years	3 (10.34)	6 (14.63)	
Recurrent urticaria	15 (51.72)	15 (36.58)	0.207
Persistent urticaria	14 (48.27)	26 (63.41)	
Angioedema	7 (24.14)	12 (29.27)	0.634

Table2: Distribution of variables in study group with respect to gender

Serology for hepatitis B was found to be positive in 2 patients in the study group but there was no biochemical evidence of hepatic dysfunction in any of these patients Hepatitis C serology was negative in all patients in the study group. [Table-3,4]

In the control group 3 patients were positive for HBsAg and only 1 patient out of them had mildly elevated liver enzymes; no patient was positive for anti-HCV antibodies. [Table-3,4]

Liver enzymes	Study group	Control group	p-value
Alanine aminotransferase	33±3	37±4	0.13
Aspartate aminotransferase	28±3	34±4	0.21

Table 3: Comparison of liver enzymes between study and control group

	Study group	Control group	p-value
Hepatitis B surface antigen positivity	2 (2.85%)	3 (4.28%)	0.224
Anti-HCV positivity	0	0	

Table 4: Serology of Hepatotrophic viruses B & C in study and control group

Discussion

This was a prospective case control study to determine the association of chronic urticaria with HBV and HCV infection. The age range of the patients with chronic urticaria ranged from 16-67 years with a mean age of 34 years. 57.7% of patients were in an age range of 20-40 years.

Serology for hepatitis B was found to be positive in 2 patients in the study group but there was no biochemical evidence of hepatic dysfunction in any of these patients. In comparison 3 patients in the control group were positive for HBsAg with mildly elevated liver enzymes in one patient (ALT, 84 range 5-40; AST, 72 range 5-40). Anti-HCV antibodies were absent in all patients in the study and the control group. The study indicated that there is no association of chronic urticaria with hepatotropic virus B& C.

In a study conducted by Kanazawa et al [6] to determine whether there is any association between HCV infection and urticaria, antibodies to HCV and HCV genotypes were determined in patient with urticaria and in the controls which included 1692 healthy blood donors. Anti-HCV was detected in 24% of 79 patients with urticaria, and HCV RNA was detected in 22%. The patients who were positive for HCV RNA were older, 52±14 vs. 41±14 years, p<0.01. They had higher levels of alanine aminotransferase, 67±34 vs. 25±17 U/L, p<0.001; aspartate aminotransferase, 51±23 vs. 21±8U/L, p<0.001; zinc turbidity test, 12.8±3.1 vs. 9.3±3.7 kunkel units, p<0.001; and IgG 1919±820 vs. 1622±849 mg/100 ml, p<0.01 than the patients without HCV RNA. This study revealed a significant association of HCV with urticaria and a role for interferon therapy. Interestingly high prevalence of HCV infection was also reported in patients with psoriasis and prurigo in the same population which argues against the specific role of the virus with an epidemiological feature of the population [11, 12]. In comparison to the Japanese study our study has the advantage of having age and sex matched control derived from the same facility and from the same time period. An interesting finding

was the younger mean age of the patient in our study group and furthermore the HCV was detected more commonly in the older patients of Japanese study group.

Varda et al [7] screened 114 patients of chronic urticaria and angioedema for serological markers of hepatitis B virus infection. Markers of HBV infection were detected in 15 (17.6%) patients. Of these 13 (15.3%) were found to have anti-hepatitis B surface antibody and 2 (2.4%) had hepatitis B surface antigen. The frequency of HBV infection was several times greater than that reported in the general population.

In another study conducted by Criber et al [8] to look for the prevalence of hepatitis C virus (HCV) and hepatitis G virus (HGV) infection in patients with urticaria, 110 patients with chronic urticaria were enrolled with equal number of age and gender matched control. HCV infections were detected by serology and RT-PCR for HCV RNA. Hepatitis C virus RNA was detected only by genomic amplification. Antibodies to HCV were found in one patient with urticaria and in one from the control group (0.9% of each group). None had circulating HCV RNA and liver function test results were within the reference range. Two patients with urticaria and two of the control group (1.8% of each group) had circulating HGV RNA, but there was no confection with HCV or change in liver functions test results. The study indicated that HCV&HGV infections are unlikely cause of urticaria in the general French population.

Tousi P et al. [9] at Loghman Hakim Hospital, Iran carried out a study which included 53 patients with age and sex matched controls attending the same department for different condition. All patients and controls had enzyme linked immune sorbent assay for IgG anti-HCV antibodies which proved negative in both groups. It was therefore concluded that there is no relation between urticaria and HCV infection.

There is still a debate among the investigators whether to include hepatitis B and C workup in chronic urticaria. [13, 14]

The negative result in our study concludes that there is no role of hepatotropic viruses B & C in chronic urticaria in our kashmiri population and that the routine investigations for these viruses in patients of chronic urticaria is not cost-effective.

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