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SHORT COMMUNICATION

An Assay: Hepatitis C Doesn´t Incite Increased C-Reactive Protein Level in Hemodialysis Patients Unless Another Inflammatory Condition is Associated

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ABSTRACT

C- reactive protein has been considered one of the most important tools to detect inflammatory reactions. This study intends to identify whether or not hepatitis C virus (HCV) infection, recognized through polymerase chain reaction- RNA (PCR-RNA), may incite an inflammatory response by itself, in the absence of other concomitant additional infection or inflammation in hemodialysis patients. All the hemodialysis 28 patients HCV positive in our Unit were included. Those 28 hemodialysis individuals were evaluated and divided in 2 groups: Group I (n = 14): positive HCV individuals with no other Infection- Inflammation detected and Group II (n = 14): positive HCV presenting another well-identified Infection- Inflammation.

RESULTS: HCV patients in Group I had adequate C - reactive protein, hematocrit, hemoglobin and transferrin serum levels while Group II- HCV reagent patients with another well-defined Infection-Inflammation associated- had increased C- Reactive Protein and decreased Hematocrit, Hemoglobin and transferrin.

CONCLUSION: Despite the small number of individuals, data suggest that HCV by itself does not incite inflammatory reaction in HD patients, except when another distinct kind of Infection-Inflammation associated was identified. This fact was not previously objectively reported.

Key words: C-reactive protein; Hemodialysis; Inflammation; Infection

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INTRODUCTION

C-reactive protein (CRP) serum levels have been considered one of the most important tools to detect inflammatory reactions. Almost all kinds of infectious organisms are able to increase this peptide[1,2]. However, only a few evidences exist to support its role as a reliable inflammatory marker in hepatitis C virus (HCV) infected individuals[3]. This study intends to verify whether or not HCV infection [identified by a PCR RNA test] is able - by itself - to promote an increment of CRP serum levels.

METHODS

This cross-sectional study was performed at the Hemodialysis Unit (HD) of the Hospital São Lucas – PUCRS, Porto Alegre - Brazil, which included 28 individuals with positive Hepatitis C (HCV) on chronic HD, who were evaluated and divided in 2 groups: Group I (n = 14): positive HCV individuals with no other detected infection; Group II (n = 14); positive HCV patients showing another very well identified infection associated.

Intravenous iron replacement was discontinued two weeks before laboratory determination. Hemogram was determined by SE 9500 equipment, Sysmex Co, Kobe, Japan, hematocrit (Htc) by cumulative pulse detection, the results being expressed as percentage. Sodium Lauril Sulphate method was used to detect hemoglobin (Hgb) levels, results being expressed in g/dL. Serum iron (mg/dL) and transferrin (µg/dL) were both determined by Merck® KgaA kits, from Darmstadt, Germany. CRP was evaluated by the N high sensitivity test, detected by potentialyzed nephelometry, from Dade Behring®, Marburg, GmbH, Germany, being the results expressed in mg/dL. Serum Ferritin through an Immulite 2000 kit, from DPC® Diagnostic Products Corporation, Los Angeles, CA, USA, results expressed in ng/dL. Albumin (g/L) was determined by the Green Bromocresol kit from ADVIA 1650/2400, Bayer, Co, Tarrytown, NY, USA. Erythropoietin (EPO) serum determinations (mlU/mL) were made with Immulite® DPC kit from Diagnostic Products Co, LA, Ca, USA. Anti-HCV tests were done by an ELISA kit specific from Ortho-Johnson,New Jersey, USA. HCV PCR-RNA was genotyped by the restriction fragment length polymorphism of PCR products. Informed consent was obtained from each participating patient and there was no conflict of interests involved.

Regarding statistics a Kolmogorov- Smirnov , Student´s t and chi-square tests were used to analyze the data. A $p < 0.05$ was considered as significant.

RESULTS

Age was not different among the groups: GI 55.7 ± 8.9 and GII 54.4 ± 11.6 years (p = 0.148).Time on HD (months) mean rank in GI was 52.4 and in GII = 52.3 months. The comparison of variables demonstrating significant differences among the groups (CRP, hematocrit, hemoglobin, transferrin and alanine transferase) are presented in Table 1.

Serum iron in GI was 76.3 ± 37.5 and in GII 65.1 ± 42.2 mg/dL (p = 0.156); Ferritin in GI: 574 ± 118 and in GII = 463 ± 718 ng/mL (p = 0.204); Albumin in GI was 3.90 ± 0.28 and GII= 3.90 ± 0.45 g/dL (p = 0.08). ALT in G I was 34.7± 7.8 and in G II 36.7 ± 21.1 U/L (p = 0.197). Erythropoietin serum determinations in GI was 23.1 ± 23.0 and GII 21.2 ± 18.2 mU/mL (p = 0.122).

Regarding HCV, In GI genotypes Type I appeared in 7, Type II in 2 and Type III in 5 individuals and in GII genotypes´ identification was disclosed as Type II = 9 patients, Type II = 2, Type III = 2 and Type IV= 1.

In GII the infectious diseases diagnosed were pneumonia in 4, urinary tract infections in 2, prostatitis in 2, infected Shilley catheter in 2 and sinusitis, sepsis, cellulites and acute cholecystitis in one patient each.

DISCUSSION

It is not unusual to exclude HCV patients from some studies due to the possibility they might incite inflammatory reactions. Evidences associating this condition as a primary cause of inflammatory reaction in HD patients are scarce. Iancu *et al* determined that 77.5% HD patients were anti-HCV reagents but only 12.19% had elevated CRP levels[4]. Zumrudtal *et al*, comparing anti-HCV (+) with anti-HCV (-) individuals, regarding some acute inflammatory markers, verified that these parameters were not different between the groups[5].

Table 1 Comparison of variables demonstrating significant differences among the groups.

Groups	C-reactive Prot (ng/dL + SD)	Hematocrit (% + SD)	Hemoglobin (g/dL + SD)	Transferrin (mg/dL + SD)
GI (N = 14)	2.47 + 2.34	29.5 + 4.4	9.5 + 1.5	237.2 + 52.6
GII (N=14)	0.62 + 0.51	35.2 + 5.1	11.5 + 1.8	273.7 + 51.9
P	0.0001*	0.001**	0.0001**	0.001**

* Mean rank and significance determined by Kruskall-Wallis non-parametric test, ** Student´s test.

On the other hand, it was shown that HCV (+) patients have more severe signs of malnutrition-inflammation complex syndrome than HCV non-reagent individuals[6]. So, a few studies compared acute phase reactants in HCV, and the results are conflicting and not explicitly reported[7]. Another study showed that HIV/ HCV co infection is associated with higher Interleukin- 6 but lower CRP levels[8].

In this paper the GI also presented the lowest CRP levels, the highest hematocrit and hemoglobin scores, as it normally occurs in HD patients HCV reagents with unassociated Inf- Inf. Higher serum transferrin levels, which has been considered a reliable negative acute phase reactant, such as leptin and albumin was also detected[9]. Albumin and ferritin determinations did not show any significant differences among the studied groups. These findings are in agreement with those previously mentioned, showing decreased oxidative stress in HCV (+) groups. On the other hand, in GII- group with Inf-Inf associated – CRP levels were higher, Htc- Hgb lower and transferrin diminished, as it should be expected in inflamed HD individuals.

Finally, despite the small number of patients studied, statistical analysis proved that in HCV-RNA reagent patients presenting increased CRP levels, this finding must be assigned with another associated infection or inflammation and it is not absolutely due only to the HCV infection by itself.

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