CLINICAL STUDY

Hepatitis C virus infection is not associated with a marked increase in the prevalence of ophthalmic morbidity

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Abstract

Background **Chronic infection with the hepatitis C virus has been reported to cause a wide variety of ophthalmic lesions. The incidence and significance of these lesions in an unselected population has not been assessed.**

Methods **We studied a group of unselected patients with chronic hepatitis C and performed a full ophthalmic examination on each. As a control group we studied patients with chronic hepatitis B infection.**

Results **In 25 patients with chronic hepatitis C we found no increase in the prevalence of significant ocular disease when compared with a cohort of patients with chronic hepatitis B.**

Conclusion **Chronic heptatitis C does not cause any marked increase in the incidence of ocular disease.**

Key words Hepatitis C, Keratoconjunctivitis sicca

Chronic infection with the hepatitis C virus (HCV) is estimated to affect over 170 million people worldwide.[1] The virus usually gives rise to a chronic infection and leads to advanced liver disease in a large proportion of patients over a period of several decades.[2] Chronic HCV infection has been associated with a range of different conditions (reviewed by Hadziyannis[3]) which may, or may not, be causally linked to the hepatic infection. A wide range of ocular disorders have been reported to be associated with chronic HCV infection, most commonly keratoconjunctivitis sicca[4] but also Mooren's ulcer keratitis[5,6] and uveitis.[7] The association between keratoconjunctivitis sicca and HCV remains controversial, with some studies reporting an increased incidence of dry eyes in patients with chronic HCV[8–10] and others finding no association between the clinical symptoms of ocular disease and infection with hepatitis C.[11,12] The difference between these studies may be partly explained by the lack of a 'gold standard' for the diagnosis of keratoconjunctivitis sicca and the high prevalence of mild ocular surface disease in the general community.

To determine whether chronic HCV is associated with an increased incidence of ocular disease we performed a prospective, observer-masked evaluation of patients with chronic HCV infection for ophthalmic disease and compared the prevalence of ocular disease with that in a control group with chronic hepatitis B virus (HBV) infection.

Patients and methods

Consecutive patients with viral hepatitis attending the Liver Clinic at St Mary's Hospital were considered for inclusion in the study if they had clear serological and virological evidence of HCV or HBV infection in the absence of any other cause for liver disease (HCV antibody and PCR positive by third generation RIBA and Quanticor assay (Hoffman La Roche) or HBeAg positive by standard laboratory assays (Abbott)). Patients who were receiving therapy or who had undergone treatment with interferon during the previous 6 months were excluded from the study as were patients with any evidence of autoimmune liver disease (any autoantibody titre greater than 1:20). All patients were examined by an ophthalmologist (M.L.) who was not aware of their hepatic diagnosis. The study was approved by the local ethics committee and written informed consent was obtained from each patient.

The ophthalmic assessment included:

- History of ophthalmic disease.
- 'Dry Eye Questionnaire', a validated instrument for screening for dry eye disorders.[13,14]
- Visual acuity, pupil responses, confrontation fields.

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Table 1. *Characteristics of the study population*

	HBV	HCV
No. of patients	10	25
Mean age (range)	40 (26–71) years	54 (29–76) years
Sex	8M : 2F	13M : 12F
Histology	5 inactive	7 mild
	1 active	6 moderate/severe
	1 cirrhosis	11 cirrhosis
	3 no biopsy	1 no biopsy

- Ocular surface examination. The eyelids were inspected for signs of blepharitis. Tear film quality was assessed and tear meniscus height measured. Fluorescein break-up time was measured[15] and fluorescein and Rose Bengal staining patterns examined.[16] Schirmer tests are too variable for dry eye screening;[17] they were not used in this study.
- Slit-lamp examination: anterior chamber, Goldmann tonometry, dilated fundoscopy.

Results

The patient characteristics are shown in Table 1. Thirty-five patients were seen: 25 with HCV and 10 with HBV. None had clinical findings suggestive of systemic vasculitis. General ocular examination was unremarkable in all patients. Intraocular pressure was within the normal range in all cases and there were no signs of past or present uveitis. Three patients with HCV and one with HBV had myopic degenerative retinal changes but there were no signs of retinitis, vasculitis or optic nerve disease. Corneal abnormalities were seen in one eye of an HCV-infected patient, who had a previous history of herpes simplex keratitis in that eye. Neuro-ophthalmic examination was normal in all except for one HCV-infected patient who had a long-standing convergent strabismus.

The results of the ophthalmic assessment for dry eyes is shown in Table 2. The McMonnies Dry Eye Questionnaire score was normal in all patients with chronic HCV (mean score 6.2 ± 2.0; normal scores are less than 13), showing that patients with this infection do not have symptoms of dry eyes. One patient with HBV had an abnormal Dry Eye Questionnaire score, but this was in the presence of moderately severe chronic blepharitis which was thought to be sufficient to explain the symptoms. No patient had any evidence of significant conjunctival damage secondary to decreased tear formation (assessed by Rose Bengal staining) except for the one patient with HBV and blepharitis. Similarly all patients had normal fluorescein staining patterns, except for the subject with blepharitis. No patients had a tear meniscus height less than 0.5 mm.[9] The incidence of rapid fluorescein break-up times (mean of 5 measurements ≤10 s[16]) was high, but similar in HBV-infected (40%) and HCV-infected (44%) patients. Thus there was no evidence of any significant ocular disease secondary to abnormal tear formation in any patient with HCV.

Table 2. *Ophthalmic assessment for dry eyes in patients with chronic viral hepatitis*

	HBV (n = 10)	HCV (n = 25)
McMonnies score >13	1 (10)	0
Blepharitis	2 (20)	7 (28)
Tear debris	4 (40)	3 (12)
Tear film meniscus ≤ 0.5 mm	0	0
Fluoroscein break-up time ≤ 10 s	4 (40)	11 (44)
Rose Bengal stain (van B scores) ≥ 3.5	1 (10)	0

Numbers of patients are shown, with percentages in parenthesis.

Discussion

Our study was designed to determine whether there was a high prevalence of clinically significant ocular lesions in patients with uncomplicated chronic HCV infection. We excluded patients with coexisting cryoglobulinaemia in whom keratoconjunctivitis sicca has been reported, and we did not study patients with other autoimmune disorders. It is therefore possible that in patients with other autoimmune manifestations of chronic HCV infection, ocular lesions may be detected and clinicians should be aware of this possibility.

We studied patients attending the specialist hepatology clinic at a London teaching hospital. It is therefore likely that the patients will have more advanced liver disease than is typical for patients with chronic HCV, and this is borne out by the high prevalence of patients with cirrhotic liver disease in our study. If chronic HCV does cause significant ocular disease, it is more likely to be detected in patients with the more advanced forms of HCV, and our finding that there was no increased prevalence of ophthalmic disease in patients with chronic HCV is likely to be true for patients with less advanced disease. As controls for the HCV-infected patients we chose a group of patients with chronic HBV infection to control for the non-specific effects of liver damage and systemic ill-health, and to ensure that the ophthalmic observer was truly masked as to the patients' diagnosis. The HCV-infected patients tended to be older than the HBV group (although this difference was not significant), and there were more women. Both these differences would be likely to exaggerate any increased tendency towards dry eye in the HCV group as dry eye is more common in women and with increasing age.[15]

Early reports linking chronic HCV infection to Sjögren's syndrome appeared to be confirmed by studies reporting abnormal histological findings in salivary gland biopsies from patients with chronic HCV,[8,12] although significantly less than the changes seen in patients with classical Sjögren's syndrome. For this reason dry eye was specifically looked for in this study. We used a battery of tests that measured symptoms, tear composition (tear film meniscus height and fluorescein instillation test) and corneal and conjunctival injury (fluorescein and Rose Bengal staining). We found no evidence of any clinically relevant tear defects in patients with chronic HCV infection. The high incidence of rapid

fluorescein tear film break-up times may indicate a non-specific effect of chronic illness or liver disease on tear film quality (but not quantity, as in keratoconjunctivitis sicca), but we found no evidence for a specific increase in the prevalence of dry eyes in patients with chronic HCV. The absence of symptoms or other signs of dry eyes suggests that any abnormality is unlikely to be clinically significant.

Our study shows that in a population of patients with uncomplicated HCV infection who are likely to be at risk of developing dry eyes (advanced disease, old age, female sex) there is no increased prevalence of keratoconjunctivitis sicca, and screening for ocular disorders in patients with chronic HCV is unnecessary.

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