

Improving Outcome in Hepatitis C Management: A Need for Dedicated Multi-disciplinary Service to Improve Compliance with Treatment

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results in improved patient compliance with medications as well as with follow-up appointments, leading to successful treatment outcome.

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Key words: Hepatitis C; Compliance; Multidisciplinary care

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ABSTRACT

AIM: Hepatitis C infection has affected more than 170 millions people worldwide. In recent years, the combination of Pegylated Interferon and Ribavirin has improved treatment outcomes and more than 50% of patients can achieve sustained virological response after 24-48 weeks of therapy. Poor compliance with medication and follow up are two main reasons leading to treatment failure. Dedicated and organized health care services have demonstrated to significantly improve compliance with medication across a broad range of conditions and disease severities.

METHODS: To assess the improvement in treatment compliance, we retrospectively studied 82 patients referred to our hepatology clinic at local district general hospital UK. Twenty-six of these patients received dedicated multidisciplinary care (MDC) from a team comprised of a hepatologist, a specialist nurse, community support team and psychological support worker throughout the duration of their treatment, while the rest of 56 patients received routine care without any community or psychological support.

RESULTS: Treatment compliance was 95% in the intervention group as compared to 46% in those treated with the 'traditional' care ($p=0.009$). Overall sustained virological response (SVR) was found to be 69% in MDC group compared to 20% in those received 'traditional' care ($p=0.001$).

CONCLUSION: In conclusion, our study demonstrated that appropriate service reconfiguration for HCV infected individuals

INTRODUCTION

Hepatitis C virus (HCV) infection is a global health problem affecting more than 170 millions people worldwide^[1]. Recent estimates suggest that in the UK between 200,000 to 400,000 individuals are infected with hepatitis C. Acute HCV infection is often sub-clinical and leads to chronic infection in 60-80% of those acutely infected. Once a patient develops chronic infection, a progressive disease ensues which can lead to cirrhosis in 20-25% of patients over a 20-30 year period^[2]. Overall, the annual mortality rate of the HCV-cirrhosis is 4.0%^[3]. There have been recent advancements in the treatment of HCV infection, making it a potentially curable disease^[4]. The success of treatment is primarily measured as sustained virological response (SVR) which is absence of viraemia six months post-treatment. The combination of Pegylated Interferon and Ribavirin can achieve an SVR in about 50% of patients^[5,6]. Although the duration of this treatment is generally determined by the HCV genotype and the patient's early virological response to the antiviral regimen, the usual duration of treatment is 24-48 weeks^[4-7]. However, adherence to therapy and follow up is a major problem leading to treatment failure in a significant proportion of patients^[8]. It has been demonstrated that dedicated and organised health care services significantly improve compliance with medication across a broad range of conditions and disease severity. Improved compliance is associated with better clinical outcomes, reduced hospitalizations and overall healthcare cost and a better quality of life^[9]. Patient education, prompt management of side effects and patient support are the key factors to ensure compliance^[10,11]. The objective of this study was to compare

the treatment compliance and outcome in HCV infected patients who received a dedicated multidisciplinary service with those receiving routine care.

METHODS

It was a retrospective study of treatment outcomes in HCV infected patients at Diana Princess of Wales Hospital, Grimsby. We divided our study population into two groups. Group A included the patients who received routine outpatient care (1998-2002) and group B consisted of those who received specialised multi-disciplinary care (MDC) (2002 onwards). MDC was provided by a team comprised a hepatologist, a specialist nurse, a community support team and psychological support worker. The working strategy of this new service is outlined in table 1.

Table 1 Strategy adopted by Hepatitis C infection MDC service.

Patient education and written information about treatment.
Patient and family members involvement in treatment decisions and management of side effects.
Address co-morbidities and substance misuse issues.
Psychological support throughout treatment.
Enhanced community support, appointment reminders and frequent opportunities for communication between patient and healthcare providers.
Appropriately manage side effects using adjunctive therapies and provide patients with feedback regarding treatment efficacy.

It was an observational study, which was conducted retrospectively. All patients referred to the hepatitis clinic with a diagnosis of HCV infection and eligible for treatment (HCV antibodies positive, high viral load and/or abnormal liver enzymes) were included in this study. Information was collected from the case notes and other sources including hospital electronic result system, microbiology and pharmacy records.

Patient’s compliance was assessed by pharmacy record, counting number of dispensed prescriptions, clinic attendance, and information from community nurse visits. Viral load, at the beginning of treatment and after 12 weeks of treatment (EVR), end of treatment (EOT) and 6 months post-treatment (sustained virological response, SVR) were recorded (Table 2).

Table 2 Clinical parameters of two groups.

	Group A	Group B
Referred for treatment	N=56	N=26
Attended Clinic	50/56 (89 %)	25/26 (96 %)
Enrolled for treatment	46/56 (82 %)	24/26 (92 %)
Non compliant / Drop out	24/56 (43 %)	1/26 (4 %)
Completed treatment	22/56 (39%)	23/26 (88 %)
2 Log drop	17/22 (77 %)	22/23 (96 %)
EOT	13/22 (59 %)	20/23 (87 %)
SVR	11/22 (50 %)	18/23 (78 %)
Failed treatment	9 / 22 (41 %)	2/23 (9 %)
No documented SVR	2/22 (9 %)	3/23 (13 %)

SVR: Sustained Virological Response (Negative viral load 24 week post treatment); EOT: end of treatment viral load; Drop Out: Patients commenced on treatment but developed side effects and non-compliant with follow up.

RESULTS

82 patients were referred for treatment, 56 patients in group A, and 26 patients in Group B. Both groups were comparable as regard to the age and gender of the study participants, mean age of 40.00±1.8 years in group A, and 39.61±2.4 years in group B. There was also no statistical difference in HCV genotypes between the two groups (Figure 1).

Six patients from group A and one from group B “did not attend” (DNA) the clinic at all. Those who enrolled for treatment (group A 82% n=46/56, group B 92% n=24/26), there was a significant drop out rate in patients in group A due to poor compliance and about 24/56 patients (43%) lost follow up, refused treatment at some point or DNA from clinic and only 22/56 patients (39%) completed the treatment. In contrast, in group B a significant improvement in compliance was noted and 88% (23 out of total of 26 patients) completed the treatment (Figure 2).

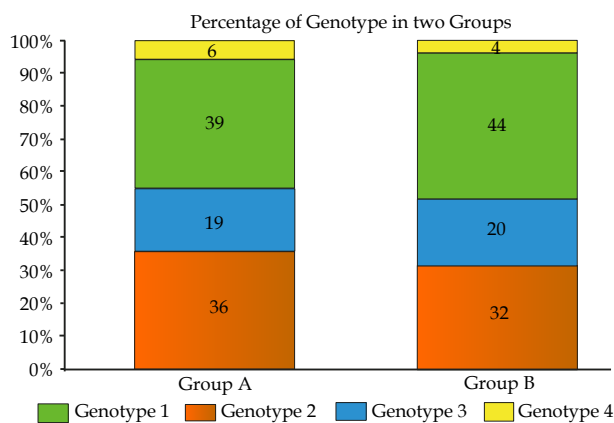


Figure 1 Graph showing comparison of Genotypes between the two groups.

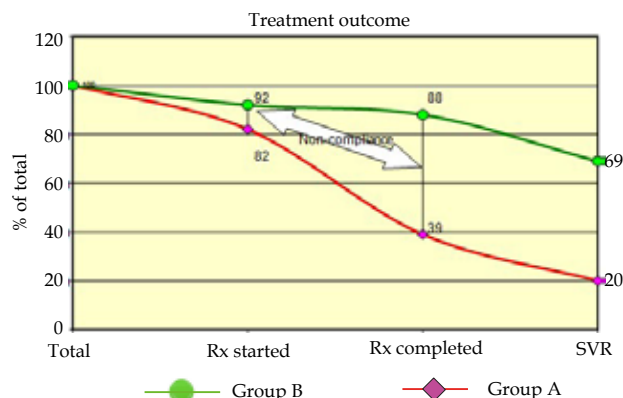


Figure 2 Comparison of Compliance and Sustained Virological response between the two groups.

All patients in group-B received combination therapy with Pegelated Interferon alpha (Viraferonpeg®) at a dose of 1.5 mcg/kg/week and Ribavarin 800 mg if weigh <65 kg or 1000 mg if weigh >65 kg in two divided doses for duration determined by their genotypes. In contrast only 58 % patients in group-A received this regimen while other patients had monotherapy with Interferon alfa at dose of 3 million units 3 times/week or in combination with Ribavarin at similar dosage.

A total of 22 patients in group-A and 23 patients in group-B completed the treatment. Analysis of those individuals who completed the treatment showed, 11/22 patients in group A (50%) achieved SVR compared to 18/23 patients (78%) in groups B (p<0.05). When compared the treatment outcomes in both groups who initially referred for treatment, there was a significant difference of SVR (69%, 18/26 patients in group-B vs. 20%, 11/56 patients in group-A, p=0.001). This difference was partly because of the poor compliance in group-A, as many patients drop out at early stages of their treatment, but it might be associated to the fact that not all patients in

group-A received combined treatment with peg interferon / ribavirin. When SVR rates were adjusted to those in both groups who received combination treatment with Peg interferon /ribavirin, it remained significantly higher in the intervention group (63% vs. 34%, $p=0.021$). Although the reason for this is not entirely clear, we suspect that even those patients in group-A, who claimed to be fully compliant with their treatment, were not actually adhering to it.

DISCUSSION

Hepatitis C is a worldwide problem, the prevalence of which varies geographically, with poorer socioeconomic areas being more affected than the developed world. The mode of infection also varies across the world and injecting drug users comprise the largest reservoir in developed countries. The overall management of hepatitis C has been revolutionized in the past two decades, with better serological and virological testing. Improved treatment modalities in the form of pegylated interferon and ribavirin offer complete eradication of the virus in about 50%-60% of patients. Despite these therapeutic advances, the outcome of treatment depends upon age, gender, genotype, degree of liver fibrosis and very importantly, treatment compliance.

The prevalence of non-compliance is underestimated and the role of physicians in understanding and promoting compliance issue is often not recognized.

Researchers have tested a variety of interventions to improve patient adherence, ranging from simple adjustments in the medication regimen to complex multidisciplinary interventions that address health system and communication barriers between patients and health care professionals^[1]. However, the overall quality of the existing literature is poor, and compared with the many thousands of trials for individual drugs, there are only a handful of rigorous trials of compliance interventions; furthermore, these provide little evidence that medication compliance can be improved consistently, with resources usually available in clinical settings, and that this will lead predictably to improvements in treatment outcomes. Various trials highlighted a number of factors influencing patient's compliance with regard to treatment especially in chronic conditions as listed below:

Factors influencing compliance

- Duration of treatment
- General side effect of treatment
- Specific psychiatric side effects related to Interferon treatment
- Lack of insight into the disease
- Lack of motivation
- Poor patient- physician relationship
- Patients unsatisfaction
- Social isolation
- Health belief and attitude
- Social isolation and social support including family support

Addressing all of these factors individually may change patients' perspective of their disease and improve adherence with therapeutic intervention leading to overall success in treatment outcomes. With regard to treatment compliance in hepatitis C, various trials have shown that patients taking 80% of their treatment are more likely to achieve sustained virological response and early compliance (i.e., within first 12 weeks of treatment) may have the greatest influence on the overall treatment success.

CONCLUSION

In summary, there is a strong relationship between adherence to treatment and successful outcome in hepatitis C management, although other factors such as viral genotypes, co-infection with HIV or Hep B and other co-morbidities also play a significant role. Adopting a multidisciplinary care strategy to improve patient compliance with treatment has a substantial role in improving the success rate of treatment outcomes and should be especially considered in the less developed areas of the world.

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