RESEARCH

Improving access to treatment for patients with chronic hepatitis C through outreach

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ABSTRACT

Background Chronic hepatitis C infection (HCV) is common in injecting drug users and is a major cause of liver disease. Antiviral treatment can 'cure' HCV, but is frequently associated with side effects and requires regular monitoring. Non-attendance at hospital appointments is frequent. To try and improve attendance and increase the number of current and previous injecting drug users treated we developed three outreach clinics.

Objective To review the outcome of patients referred to the outreach clinics.

Methods Retrospective service review of three clinics at drug treatment centres in Newcastle and Northumberland. Data was collected on attendance rates, patient demographics, treatment rates and outcomes.

Results 141 referrals were received across the three sites with an overall attendance rate of 75% (106 patients, 79% men and median age 36), which compared favourably with that at our hospital (50%). All patients were on methadone/subutex. 45% were infected with Genotype 1 HCV. 10% were cirrhotic. To date, 30% have started treatment and 21% are waiting to start or are still in workup. 13% elected to delay treatment due to early stage disease and 11% were not ready for treatment on psychological or social grounds. Only 12% failed to attend follow up after initial assessment. To date, 24 patients have completed full courses of treatment with sustained viral response in 13 patients. Results are awaited for seven patients.

Conclusions The development of outreach clinics for HCV in drug treatment centres can substantially improve clinic attendance and increase access to treatment in this marginalised group.

INTRODUCTION

Chronic hepatitis C virus infection (HCV) is common, affecting approximately 300 000 individuals in the UK and is a major cause of end stage liver disease and liver cancer.¹ The main risk factor for HCV infection is injecting drug use (IDU), which accounts for approximately 85% of cases. Following exposure to HCV, chronic infection develops in approximately 55–85% of subjects resulting in chronic hepatitis and fibrosis that may progress to cirrhosis.² The rate of progression of HCV-associated liver fibrosis is variable, with 4–24% developing cirrhosis after 20 years of infection.³ The development of cirrhosis is associated with increased risk of morbidity and mortality from complications of portal hypertension and hepatocellular carcinoma (HCC).⁴ In patients with HCV cirrhosis, the risk of liver cancer is approximately 4% per year and HCV cirrhosis is one of the main indications for liver transplantation in the UK and elsewhere.

Antiviral treatment for hepatitis C is effective and can 'cure' the infection, which leads to improvement in liver histology, reduces the incidence of cirrhosis and reduces liver related mortality.¹ Overall, a sustained viral response (SVR; HCV RNA negative 6 months post-treatment='cure') occurs in approximately 55% of HCV-infected subjects treated for 48 weeks with polyethyleneglycosylated interferon- α (PEG-IFN α) and ribavirin (RBV).^{5–7} HCV genotypes 2 and 3 are very responsive to treatment with PEG-IFN and RBV and approximately 80% of treated subjects achieve an SVR.^{5–7} However, only approximately 45% of patients with HCV

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genotype 1 will achieve an SVR with PEG-IFN and RBV.^{5,6} The addition of a protease inhibitor, boceprevir or telaprevir, to PEG-IFN and RBV significantly increases SVR rates to around 70% for subjects infected with HCV genotype 1, and this has now become the new standard of care for patients with genotype 1 HCV.⁸ One of the major limitations of interferon-based treatments for HCV is the high frequency of side effects such as depression, flu-like symptoms, fatigue and myelosuppression, which necessitates regular monitoring during treatment and frequent visits to hospital.⁹ This factor deters many patients from accessing treatment for hepatitis C. Indeed the overall uptake of HCV treatment in the World Health Organisation European region is estimated at only 1–16% and critical steps are needed to try and improve access and uptake of treatment.¹⁰

The majority of patients infected with HCV acquire it from IDU and many patients who are referred for treatment of HCV regularly use drugs or are in opiate replacement programmes and have chaotic lifestyles.^{11,12} In addition, the frequency of psychological co-morbidity is very high in this population. This group often feel marginalised in society and feel stigmatised by the illness they have.¹² As a result, non-attendance rates at clinic appointments for HCV treatment can be very high (approximately 50% for new patient appointments in our Freeman Hospital HCV clinic).

In the UK, more than 200 000 subjects attend drug treatment centres and more than 60% of these are current or previous IDUs and between 36–49% are HCV antibody positive.¹³ Subjects who are on opiate replacement are required to attend drug treatment centres regularly to collect opiate prescriptions. This, therefore, might be an ideal environment to offer treatment for HCV. Given that data from the Health Protection Agency (HPA) estimates that there are 2000 undiagnosed cases in the Newcastle, North Tyneside and Northumberland areas, of whom 335 would be expected to have moderate fibrosis and 39 would be expected to be cirrhotic, it is important to adopt novel strategies in HCV management.¹ In order to try and increase access to treatment for HCV and improve clinic attendance, we developed three outreach clinics at drug treatment centres in our region. The aim of this service review was to assess the outcomes of patients referred to and treated in these outreach clinics.

METHODS AND DESCRIPTION OF OUTREACH SETTINGS

This was a retrospective service review of three outreach clinics in Newcastle upon Tyne and Northumberland. Data was collected on the number of patients referred to each clinic, attendance rates, demographics, treatment rates and outcomes of treatment.

Plummer court outreach clinic

Plummer Court addiction service is a psychiatry-led service in Newcastle upon Tyne that offers a full range

of addiction services. The HCV outreach clinic started in June 2008. A consultant (AP) and hepatitis C specialist nurse (CM) conducted a clinic on the premises once a month.

Bridge view drug outreach clinic

An HCV outreach clinic was started in October 2010 at Bridge View drug treatment centre, a general practitioner (GP) led addiction service. The centre currently has 553 clients and 6 monthly testing for blood borne viruses is offered to all those still injecting. Patients who were hepatitis C positive and considered stable enough socially and psychologically were referred by the clinic's specialist nurse. Once again a consultant (SMcP) and hepatitis C specialist nurse (CM) conducted a clinic once a month.

Blyth outreach clinic

Another clinic was held in a GP surgery associated with the harm reduction service in Blyth, Northumberland from November 2010. This area has been shown to have a higher than average rate of HCV positivity according to data from the North East Health Protection Agency. Monthly clinics were conducted by SMcP and CM.

In all three clinics, patients were worked up for treatment in the individual centres although they were required to attend the Freeman Hospital once for a Fibroscan and liver ultrasound scan. All treatment and monitoring was delivered in the outreach settings. There was no specific additional resource allocated to setting up these outreach clinics.

RESULTS

Outreach clinics improve attendance rates among a challenging group of patients

Table 1 shows the demographics of patients referred to all three outreach clinics to date. There were 141 referrals in total across the three sites with an overall attendance rate of 75.2% (106 patients). This compares favourably with the overall new patient attendance rate of 50% at our Freeman hospital clinic. Indeed an audit of the Bridge View service for the first 9 months of 2010 (prior to setting up the outreach clinic) showed that only nine patients were referred to secondary care (compared with 46 in the first 15 months of the outreach clinic) and only three patients attended (33% attendance). Attendance rates were poorer for Plummer court outreach clinic (PCOC) reflecting the fact that patients attending this psychiatry run unit often have multiple addictions; this is reflected in the higher rates of alcohol excess (29%) in this cohort of patients compared with those from Bridge view drug outreach clinic (BVOC) (3%) and Blyth outreach clinic (BOC) (13%). We do not have any specific data regarding the percentage of HCV positive individuals who attended all three outreach settings who were actually referred to our

Table 1 Demographic data for patients seen in the outreach clinics

	BVOC	BOC	PCOC
Established	Oct 2010	Nov 2010	Jan 2008
Pts referred	46	30	65
Pts attended	38 (83%)	24 (80%)	44 (67%)
% Male	87%	75%	75%
Age	36 (27–64)	37 (23–53)	36 (19–48)
G1	15 (40%)	9 (40%)	24 (55%)
Cirrhosis	3 (8%)	1 (4%)	7 (16%)
Methadone use	100%	83%	84%
Subutex use	0%	17%	16%
Significant psychiatric history	18 (47%)	17 (71%)	N/A
Ongoing IDU	9 (24%)	2 (8%)	1 (2%)
Alcohol excess	1 (3)	3 (13%)	19 (29%)
Co-infection	1 (HBV)	0	1 (HBV)

BOC, Blyth outreach clinic; BVOC, Bridge View outreach clinic; IDU, injecting drug use; PCOC Plummer court outreach clinic.

services. However, the referral protocols were intentionally made very easy and we would estimate that 70–80% of all HCV positive individuals were referred.

The majority of patients referred were men (79% across the three sites) and of relatively young age (median 36 years old). The patients were universally on methadone or subutex and there were significant levels of previous psychiatric history (defined as current or previous treatment with antidepressant or antipsychotic drugs) in the two centres where data was available. The high level of psychiatric history (71%) in BOC is understandable given that these patients were referred from a harm reduction service. Forty per cent of patients from BVOC and BOC were infected with genotype 1 HCV and this figure rose to 55% for PCOC patients. There were only two patients of the 106 seen who were co-infected; both with hepatitis B. There were 12 individuals referred to the three clinics who were still actively injecting drugs. There were 11 patients (10%) with cirrhosis (diagnosed on imaging, fibroscan >15 KPa or histology). This suggests that among this group of patients who do not access traditional avenues of healthcare there is quite a substantial burden of serious chronic liver disease.

Significant numbers of patients in outreach settings are suitable for treatment

Table 2 summarises the treatment outcomes for the 106 patients who attended clinics across the three outreach settings. In total, 32 patients (30%) started treatment with a further 6 (6%) were due to start at the time of writing. Sixteen patients (15%) were still in workup meaning in total that 51% of patients seen in these outreach settings were potential treatment candidates. In our experience, this is higher than the percentages that are treated in our traditional hospital

Table 2 Outcomes for the 106 patients who were seen in the outreach clinics

	BVOC	BOC	PCOC
Started on Rx	10 (26%)	10 (42%)	12 (27%)
Waiting to start Rx	2 (5%)	3 (8%)	1 (2%)
Still in workup	7 (18%)	5 (21%)	4 (9%)
Spontaneous clearance	1 (2.5%)	1 (4%)	4 (9%)
Delay treatment	8 (21%)	1 (4%)	5 (11%)
Not ready (Psych or social)	3 (8%)	3 (12%)	6 (14%)
DNA after initial review	5 (13%)	1 (4%)	7 (16%)
Decompensated cirrhosis	1 (2.5%)	1 (4%)	2 (5%)
Prison	1 (2.5%)	–	3 (7%)
Died	–	–	1 (2%)

BOC, Blyth outreach clinic; BVOC, Bridge View outreach clinic; DNA, Did Not Attend; PCOC, Plummer court outreach clinic.

setting where over the last 2 years, only 37% of new patients seen were deemed suitable for treatment. A clinical decision to delay treatment (due to early stage of the disease) was made in 14 patients (13%). Twelve patients (11%) were assessed as not being ready for treatment on psychological or social grounds. Once again this compares favourably with the situation in tertiary care where 17% of patients seen were assessed as not being ready on the same grounds. Only 13 patients (12%) failed to attend any further follow up after their initial assessment; a substantial reduction compared with Did Not Attend (DNA) rates of 25% in our secondary care clinics. Six patients (5%) spontaneously cleared the virus during follow up.

Four of the 11 cirrhotic patients seen had evidence of decompensation on assessment with two patients diagnosed with HCC. One of these has since died from multifocal disease.

Comparison of the three different sites suggests that patients from the psychiatry referral service at PCOC were more difficult to get into treatment with only 36% of patients started on treatment, awaiting treatment or currently being worked up for treatment. This compares with 49% and 81% at BVOC and BOC, respectively. This might be due to the higher prevalence of alcohol excess in the first group as shown in table 1.

Satisfactory treatment completion rates are achieved in outreach settings

Table 3 summarise the outcomes for the 32 patients who started treatment across all three outreach settings. All patients were treated with PEG-IFN and RBV as this review was conducted prior to approval of the protease inhibitors. Twenty-four patients have completed a full course of treatment with SVR seen in 13 patients. Results are awaited for a further seven patients and another three patients (all from PCOC) have been lost to follow up. Eight patients had treatment stopped early; two had viral breakthrough on treatment due to poor compliance, one DNA further

Table 3 Outcome for the 32 patients who were started on treatment across all three outreach settings

	BVOC	BOC	PCOC
SVR	4	5	4
Completed—awaiting results	1	4	2
Viral breakthrough	2	1	—
Stopped for side effects	1	—	—
Non-responder	1	—	3
Relapser after completion	1	—	—
Lost to follow up after completion	—	—	3

BOC, Blyth outreach clinic; BVOC, Bridge view drug outreach clinic; PCOC, Plummer court outreach clinic; SVR, sustained viral response.

follow up and one developed pneumonitis which improved on cessation of treatment. This 12.5% discontinuation rate on treatment in this difficult to treat group of patients was similar to the rates we observed in our secondary care clinics where a recent audit showed that 16% of patients on treatment discontinued this because of side effects. Only four patients of the treatment cohort failed to respond to PEG-IFN and RBV treatment and all four had genotype 1 HCV. Our overall SVR rate in this cohort (excluding those awaiting results and those lost to follow up) was 13 out of 22 or 59%.

Patients expressed a strong preference for assessment and treatment in outreach settings with high satisfaction levels for the service delivered

We carried out a questionnaire-based patient survey of patients attending BVOC. Compliance with filling these out was poor and only six fully completed questionnaires returned. All six patients said they preferred being seen in an outreach setting with 50% of them describing the setting as excellent and 50% as good. None thought it was fair or poor. Similarly, 50% reported their overall satisfaction with the service to be excellent and 50% graded this as good.

DISCUSSION

Recent years have seen increased emphasis placed on delivering care in the community closer to where patients live. This was one of the political priorities identified in the *Darzi* report in 2008.¹⁴ The treatment of viral hepatitis in the community provides an ideal opportunity to provide care closer to home as it is mainly done in an outpatient setting albeit with close monitoring of the patients throughout. This is particularly relevant for ex-IDU infected with HCV as their attendance rates and compliance with treatment in secondary settings is often poor. Indeed in a historical cohort from Newcastle, Jowett *et al*¹⁵ reported that of 237 referrals seen in secondary care only 50 patients were started on treatment; a conversion rate of 21%. Similarly, Irving *et al*¹⁶ showed that of 125 patients in a similar cohort referred to secondary

care only 68 (55%) attended. The conversion rate for treatment was even poorer at 10% of those attending. It is important to note that this historical data was in the era when liver biopsy was used to stage the disease.

However, there is good evidence that once involved in treatment ex-IDU patients on stable methadone programmes have equivalent SVR rates to other populations.¹⁷ It is, therefore, important to improve access of this group to treatment to prevent development of significant chronic liver disease in the future.

The concept of outreach clinics for hepatitis C is not new. Treatment of patients in prison has been especially well documented. As far back as 2003, Skipper *et al*¹⁸ reported on their experience of setting up an outreach clinic in the Isle of Wight prison cluster although they only managed to treat six patients. Moriarty *et al*¹⁹ reported setting up an outreach clinic in a drug and health development project in Wellington, New Zealand in 2001. This was a very similar set up to the one we report here. Once again the numbers were small and they only report treating five patients.

A recent important paper published in the *New England Journal of Medicine* demonstrated that treatment across 21 rural and prison sites in New Mexico had SVR rates that were equivalent to those seen at a University hospital specialist clinic.²⁰ This did rely on state-of-the-art telemedicine technology to provide training and support from specialists in the University hospital to the primary care physicians treating the patients. This paper does suggest an alternative model of outreach treatment for viral hepatitis that could potentially be transferable to the UK. It would, however, require significant cooperation between primary and secondary care as well as substantial infrastructure investment.

Another interesting study based in Dundee was reported by Tait *et al*²¹ in 2010. They report outcomes of treatment of patients infected with HCV before and after the establishment of a managed care network (MCN) in 2004. Establishing the MCN resulted in increased engagement with the service and more patients were treated (133 over a 3 year period) with increasing SVR rates. Nurse outreach clinics formed part of the MCN although the data was not broken down into patients that were treated in secondary care versus those treated in outreach settings. Of the 133 patients treated only 42 had used IV drugs in the last 1 year and no data on methadone/subutex use was presented.

There are several unique aspects to the model of care we present in this study. All of our patients were either current or ex-IDU as reflected by the universal use of either methadone or subutex among the patients seen in the clinics. Our findings represent 'real world data' for the treatment of HCV in this difficult population and illustrates that more than 50%

of ex-IDUs seen in an outreach setting can be treated by removing some of the traditional obstacles associated with treatment in secondary care. This is reflected in the attendance rates in our clinics with 75% of patients with new appointments being seen. This reflects very favourably with the historical data discussed above. In addition, to date, we have managed to get 50% of those started on treatment through the complete course; something which has been traditionally difficult in this group. A further strength of our data are the findings of the patient satisfaction questionnaires, which although limited in number, demonstrate a universal desire for these patients to be treated in outreach settings.

The HPA report published in 2011 specifically states that all UK countries should develop plans to improve access to treatment services, for example, by providing care in non-traditional settings.¹ The looming era of interferon free regimens will only serve to enhance access by allowing patients who have traditionally been excluded due to psychiatric co-morbidities. Adopting our model of outreach clinics around the country will, in our opinion, deliver this. As HCV treatment becomes more effective in the direct acting antiviral era, it will become critical to achieve SVR in a high proportion of the ex-IDU population thereby reducing the chances of future transmission if individuals return to drug use. Achieving this will also have significant health economic benefits by reducing the numbers of patients who develop decompensated liver disease and HCC in the future. We have managed to deliver this improvement in service by engaging with our partners in primary care and in drug addiction services. This has occurred without the need for a large capital investment and we, therefore, believe that this model is easily transferable and should be adopted widely around the UK and elsewhere.

Key messages

- ▶ Outreach services for difficult to reach hepatitis C patients vastly improve attendance rates
- ▶ Up to 50% of patients seen in these settings are eligible for treatment of their hepatitis C
- ▶ Treatment can be delivered locally with good sustained viral response rates

Contributors AME, AP and SMcP conceived the idea of the paper and collected the data. CM, AH, GB, AP and SMcP provided clinical care. AME wrote the initial and subsequent drafts of the paper and AP and SMcP provided input and guidance throughout.

Competing interests None.

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