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Eradicate Hepatitis C Virus: a treatment to prevent hepatitis C in active drug users

Submission date
03/10/2012

Recruitment status
No longer recruiting

Registration date
22/11/2012

Overall study status
Completed

Last Edited
26/10/2020

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Hepatitis C virus (HCV) is a blood-borne infection that can seriously damage the liver. It mainly spreads through intravenous drug use particularly, sharing needles, and those that are already infected are at considerable risk of transmitting the virus to their sexual partners. There are good effective treatments for HCV. However treatment success is dependent on giving the correct treatment, intake of medicines regularly and with careful supervision. Active drug users are not currently offered HCV eradication treatment because they live a very chaotic lifestyle which makes it difficult for them to engage with services and to comply with the strict treatment routines and required safety follow up. This study aims to offer treatment to a group of drug users and to find out whether intensive support and regular follow up by dedicated research nurses plus giving various incentives has improved compliance with treatment and drug safety monitoring, thereby resulting in them clearing the HCV

Who can participate?
Active IV drug users, who have HCV testing that shows they are HCV positive will be asked to participate in this study.

What does the study involve?
A note of their medical history, drug use history, vital signs such as weight, blood pressure, pulse and injection sites will be recorded at the first screening visit. Depending on the strain of Hep C they are infected with they will enter one of two treatment regimes, which follows standard clinical practice, at the second visit. They will be issued with a mobile phone, asked to complete a short quality of life questionnaire, have safety blood tests done and have a urine drug screen. They may be prescribed methadone, and will be issued with a voucher for attending and some protein drinks. They will return weekly to see the study nurse for up to 24 weeks and will have urine drug screening, blood tests to check their liver and kidney function, their full blood count and viral load measured weekly for the first four weeks then fortnightly thereafter. It is to be noted that this is standard NHS clinical practice. Urine drug screening and assessment of any side effects will be noted weekly up to week 24, illicit drug use will be charted and they will be given weekly vouchers of between £5- £10, have their next weeks supply of drug therapy issued and be given a weeks supply of protein drinks. Questionnaires will be collected at their first drug administration and at weeks 6, 12 and 24. At 3 and 6 months post treatment, they will be seen by

the nurse and checked for any side effects and be given their final lot of vouchers. They will complete questionnaires at 3, 6, 18, 30 and 42 month post treatment if still contactable. All participants will receive Naloxone (an anti dote to heroin) training 3 times in this study (twice more than routine practice). IV drug users normally inject in company and it is vitally important they have the skills to provide an antidote if one of their peers overdoses, prior to the arrival of paramedics, as there is a serious risk of death from overdosing on heroin.

What are the possible benefits and risks of participating?
Possible benefits are that participants will be monitored closely during the study and will be seen by a specialist nurse at each study visits. Accessing specialist services may be an encouragement to reduce their high risk behaviour. The study may not immediately benefit all participants but if the results of the study are positive this may change the practice of managing patients with Hepatitis C who continue to inject drugs and potentially will have a great impact on other such patients in the future. There are no known risks from taking part in the study though the risks of the standard care treatment regimes for HCV infection will be explained thoroughly by the study doctors.

Where is the study run from?
The study is run from the Needle Exchange Centres in Tayside, mainly from the Cairn Centre in Dundee, UK.

When is the study starting and how long is it expected to run for?
November 2012 to February 2017

Who is funding the study?
Public Health Team, Department of Health, Scottish Government (UK)

Who is the main contact?
Steve McSwiggan
s.j.mcswiggan@dundee.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr John Dillon

Contact details
University of Dundee
Medical Research Institute
Ward 2
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY
+44 (0)1382 632 441
j.dillon@nhs.net

Additional identifiers

Protocol serial number
2012GA01

Study information

Scientific Title
Eradicate Hepatitis C Virus: A pilot of treatment as prevention in active drug users

Acronym
ERADICATE Hep C

Study objectives
Rationale:
Hepatitis C is a blood borne virus (HCV) that can seriously damage the liver. An estimated 50000 Scots have been infected with Hepatitis C. Only about one third of individuals infected with Hepatitis C are aware of it.
The main driver for spread of HCV infection is intravenous drug use. As HCV is highly infectious by the blood borne route through needle sharing, it can infect the drug user early in their habit. The outcome of HCV infection varies considerably between individuals. Some (up to 25%) are able to clear the infection spontaneously, whilst the remaining 75% become chronically infected. Within the subpopulation of chronically infected patients, some will develop serious liver disease, including cirrhosis and hepatocellular carcinoma, within a few years, whilst in others liver disease will not progress even over a period of more than fifty years.
Many who are infected are unaware of it, and often show no symptoms over a long period of time. While there is presently no vaccination for Hepatitis C, there are some good treatments. However, the effectiveness of these treatments is dependent, at least in part, on the strain (or genotype) of the virus and stage of the disease. Around 70% of patients will clear infection when treated with pegylated interferon plus ribavirin combination therapy, or triple therapy including protease inhibitors depending on genotype of virus.

With the advent of more effective therapies of shortening duration, it raises the possibility of using therapy as prevention, turning the epidemic off at source, by targeting active infected drug users who are the main source of new infections.

Current treatment pathways focus on populations drawn from those known to drug problem services and former drug users. Some older periodic drug users are tested for HCV and are offered accelerated access into opiate substitution programs and early antiviral therapy. This treatment activity will reduce the health consequences of HCV infection but have little impact on the group with active acquisition of HCV and hence the prevalence of HCV as any patients cured with anti-virals are more than replaced with new infections.

The modelling work of Martin et al, illustrates the startling possibility and impact of treating drug users to reduce the prevalence of HCV, the work shows that treating as few as 10 per 1000 drug users per year can have significant impacts on prevalence. The scale of the benefit is exponentially related to prevalence of HCV in the population, the lower the prevalence the bigger the impact. The model has some limitations, it groups all drug users together and assumes a similar risk of infection, if it were possible to access a higher risk of infection group who had a lower starting prevalence of HCV, the benefits in prevalence reduction may be even

greater than predicted. Recent unpublished work has reworked the model splitting up the drug using populations and applying Tayside specific demographics and still shows substantial reductions in prevalence.

This study will focus on tackling those drug users outside traditional services where the impact on prevalence could be even more impressive, for such a relatively small investment. This group has never been previously targeted for therapy and is believed to be too difficult to achieve the required adherence to therapy. So this study will primarily challenge this assumption.

Chronically HCV infected drug users will be recruited from Needle Exchange services in Tayside and other suitable venues and allocated to treatment dependent on the genotype of HCV. Participants will be followed up weekly for up to 24 weeks with weekly treatment injections given and a weeks supply of medications administered. They will have regular follow up until 2017 when the active patient follow up study ends.

To incentivise participants to comply with treatment regimens they will be given a small (£5-£10) value voucher for local supermarkets for attending each appointment. Protein drinks will be given and they will receive regular contact and support via a mobile phone supported by the study team to remind them of drug compliance. In addition low threshold methadone prescribing will be offered. The outcomes will be the success of treatment in this group of patients and the impact it has on the population prevalence of HCV.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Service (EoSRES), 27/09/2012, ref: 12/ES/0071

Primary study design
Interventional

Study design
Pilot open-label treatment study

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Hepatitis C infection in active intravenous drug users

Interventions
The major challenge here is to access younger infected drug users and persuade them to engage with treatment for HCV. Most of them do not regard their drug use as a problem and have no motivation to change. However they do perceive Blood borne viruses (BBVs) and HCV as a problem. The 3 stages needed to be overcome for the successful use of treatment as prevention are:
1. Diagnosis
2. Initiation on to treatment
3. Adherence to therapy

What is the evidence that this is possible and what mechanisms can we use?

1. Diagnosis:
The worry of BBV infection alone can be a catalyst for change. We have recently conducted a pilot study using BBV dried blood spot testing in needle exchange schemes where over 500 users were tested with re-contact for giving of results achieved in over 90% of those tested, this intervention did change behaviour in a large number; with those positive seeking enrolment in opiate substitution programs and those negative accessing the exchange for clean works much more frequently. Within this group a number of young infected individuals with high risk patterns of use were identified and successfully tested. The annual NESI study also attains high rates of recruitment of drug users for anonymous testing for BBVs using contingency management in the form of supermarket vouchers. We would in addition use a phone/bring a friend strategy so that most of the other users within given injecting group could be tested and those positive treated to reduce re-infection risk.

2. Initiation on to treatment:
The act of testing will have established contact and allows us to outline the benefits of treatment and the fact this is on offer without change to drug habits. The incentives for this would be:

2.1. The possibility of cure for HCV,
2.2. Low threshold opiate substitution therapy
2.3. Contingency management with supermarket vouchers.
2.4. Low threshold access to opiate substitution is widely believed to be effective at stabilising patients in the short term (which is the need in this situation). Contingency management in drug users has repeatedly been shown to be effective in short term and medium term interventions.

3. Adherence:
To improve adherence we will use a shortened course of therapy and response guided therapy. To improve the poor adherence expected with conventionally delivered therapy we will use a number of strategies: our intensified patient focussed nurse support pathway, mobile phone technologies for reminders and positive re-enforcement and contingency management. Treatment would be determined by genotype, these patients will tend to be recently infected with minimal fibrosis, so a higher proportion of early virological responders would be expected. It is to be noted that these are the standard treatment protocols within the NHS treatment services.

Genotype 1 virus would be treated with
1. PEGInterferon alpha
2. Weight based ribavirin
3. Telaprevir
For 12 weeks with a further 12 weeks of combination therapy.
Therapy would be stopped if viral load at 4 weeks or at 12 weeks of therapy are >1,000 IU/ml.

Those patients who complete 24 weeks of therapy and were not HCV PCR undetectable at 4 and at 12 weeks of therapy would be offered up to 48 weeks of Interferon/ribavirin therapy without contingency management. Patients with cirrhosis who are infected with genotype 1 virus will receive 12 weeks triple therapy with a further 36 weeks of interferon/ribavirin therapy.

Genotype 2&3 virus would be treated with
1. PEGInterferon alpha
2. Weight based ribavirin

Those who achieved an RVR (negative viral load at 4 weeks) would receive 16 weeks therapy, the rest 24 weeks.

All patients will be followed up 12 and 24 weeks post treatment to define Sustained Viral Response (SVR). All patients will be followed up annually to determine re-infection rate for the duration of the study. Trial drug therapy related side effects will be managed according to local standard clinical practice

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
To identify and treat with HCV antivirals 100 new HCV positive individuals over a 5 year period, who are active drug users using the needle exchange and other services and to determine the Sustained Viral Response rate in those patients.

Key secondary outcome(s)
1. To compare the demographic and patient response information between those refusing testing, those testing positive for HCV but declining treatment and those entering therapy.
2. To perform a health economic evaluation against standard care pathways
3. Measuring Quality of Life before, during and after therapy.
4. Determining the level of reinfection rates in the treated population over 5 years.
5. To collect marginal costs
6. To determine the rate of Adverse events in the treatment cohort compared to a matched group of standard pathway of care patients
7. Concomitant medication and drug use interactions will be assessed by questionnaire and urine toxicology screening
8. To assess the benefit of contingency management, low threshold methadone, peer/family support and mobile phone virtual support on adherence in terms of Sustained Viral Response compared to standard care pathway.
9. Patient assessment of relative importance of the adherence interventions, by focus group and qualitative interviews.
10. To determine the impact of this level of treatment over 5, 7 and 10 years on the population prevalence of HCV by comparing annual measurement of HCV chronic infection prevalence in drug users in routine dried blood spot testing in needle exchanges and as determined by the NESI project data.
11. Impact of HCV therapy on drug use will be assessed by record linkage to drug rehabilitation programs, comparing HCV treated patients to HCV negative controls from the testing program.

Completion date
28/02/2017

Eligibility

Key inclusion criteria
1. Male or female (age limit 18-70)
2. Chronic HCV positive infection
3. Genotype & PCR confirmed in addition to complying with all screening requirements

4. If female, must have negative urine test results for pregnancy during initial screening period (for trial inclusion) & immediately prior to commencing study and agree to consider / commence adequate contraceptive cover (depot injection/ implanon rod)
5. Current illicit IV drug use established through drug screening (oral swab / urine)
6. Sign and date informed consent, agreeing to study and monitoring criteria

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
94

Key exclusion criteria
1. Aggressive or violent behaviour
2. Inability to provide informed consent
3. Features of decompensated liver failure
4. Evidence of primary hepatocellular carcinoma
5. Pregnancy, breast feeding, or pre-menopausal female not using effective contraception
6. Patients with contraindications to use of interferon or ribavirin as congestive cardiac failure or known hypersensitivity to either product
7. Previous treatment with Peginterferon alpha or Ribavirin or Telaprevir
8. Participation in a drug study within the previous 30 days

Date of first enrolment
01/11/2012

Date of final enrolment
28/02/2017

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
University of Dundee
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
University of Dundee (UK)

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Government

Funder Name
NHS Scotland (UK)

Funder Name
Jansen Pharmaceuticals (USA)

Funder Name
Roche (UK)

Alternative Name(s)
F. Hoffmann-La Roche Ltd, F. Hoffmann-La Roche & Co, F. Hoffmann-La Roche AG, Roche Holding AG, Roche Holding Ltd, Roche Holding, Roche Holding A.G., Roche Holding, Limited, F. Hoffmann-La Roche & Co., Roche Holdings, Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as when the study was initially funded and set up in 2011 the researchers didn't anticipate the requirement for data sharing and so didn't plan/budget for it as they would do with studies now.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2019	27/08/2020	Yes	No