

UK LIVER TRANSPLANT GROUP RECOMMENDATIONS FOR LIVER TRANSPLANT ASSESSMENT IN THE CONTEXT OF ILLICIT DRUG USE

1 Introduction

Liver transplantation is an established treatment option in the UK where patients have a likelihood of poor survival or impaired quality of life secondary to chronic liver disease. Current requirements are for a prognosis of greater than 50% survival at 5 years excluding liver disease.

Due to the potential risk of recurrent disease or poor compliance leading to graft loss, clear guidelines have been laid down by United Kingdom Liver Advisory Group (LAG) for careful assessment of psychosocial and substance use factors for patients with a diagnosis of alcohol related liver disease (ALD). With the increasing number of assessments for patients with viral hepatitis C (HCV) secondary to intravenous drug use IVDU and the frequent relationship between drug and alcohol use, there is a growing requirement for assessment of illicit drug use and, in particular, to consider poly-substance use and drug dependence due to the potential for both direct effect upon the liver and also indirect consequences such as poor programme compliance or initiation/resumption of harmful alcohol use. These guidelines are complementary to those for patients with ALD.

It is acknowledged that these are clinical guidelines and should be utilized accordingly. They are neither exhaustive nor prescriptive and should be interpreted in a considered way by the treatment team at a local level. These guidelines cannot account for all clinical situations so interpretation of the guidelines must be done in the light of individual cases. It must be remembered that, in the interests of equity and justice, all Units should work to the same criteria.

These guidelines were developed at a Consensus meeting held in Birmingham, attended by representatives from all the designated Liver Transplant Units in the UK. The report includes feed-back from all Units and the NTA.

2 Assessment

Patients admitted for a transplant assessment irrespective of diagnosis should be screened for current and past illicit substance use as part of the clinical interview. This should include misuse of over the counter medications (OTCs) and apparent misuse of pain relief medication

- Any patient considered to have a significant drug taking history should be assessed by a specialist in substance misuse; the term 'significant' must be interpreted by the clinical, multi-disciplinary team
- Adequate time and resources should be made available to allow this specialist to undertake this process

- Assessment should include problematic or dependent use as well as recent use. It should also identify substance use and stability within the patient's wider social support network, and take into account mental health and criminal justice issues as appropriate
- Services should endeavour to develop and implement joint screening and assessment protocols between hepatology and substance misuse services to ensure effective care pathways are in place.

2.1 Contraindications

Contraindications to listing for transplantation include the following:

- I. Current ongoing intravenous use of illicit or non-prescribed substances
- II. Two or more recent (within 2 years) incidences of unexplained and significant non compliance with treatment – not necessarily confined to the management of liver disease
- III. Current failure to comply with the assessment and treatment process for transplantation, including refusal to provide consent for gaining access to information pertaining to drug treatment and prescribing
- IV. Recent past history of cross dependency (substituting from one drug to harmful/problematic use of another), within the last 2 years; this requirement could be relaxed for patients who have switched drugs within 2 years but have been stable since maintaining engagement in substance misuse services
- V. Length of abstinence should be 2 years ideally, but not less than 6 months, where a patient has been dependent on a drug. The patient should have the opportunity to engage in an optimum substance misuse treatment programme.

2.2 Potential Contraindications

Potential contraindications allow issues of concern to be factored in without necessarily attempting to weight issues against one another in the absence of good evidence. The importance of potential contraindications should be discussed between the transplant team and substance misuse specialist and interpreted with clinical judgement on a case by case basis.

- I. Current legally prescribed intravenous drug use (i.e. Diamorphine or Physeptone). Some patients are long term yet stable IVDUs and their use of prescribed IVDU opiates is as part of a long term agreed treatment plan. Others may be more recent presentations who have failed on an optimum treatment programme but are a high risk group. Assessment here needs to be done by a specialist
- II. Insufficient social support network to remain abstinent from illicit drugs, and where it is not possible to work with the patient to facilitate a suitable and acceptable social support package

- III. Lack of motivation to move away from drug using culture/area, within the confines of opportunity
- IV. Current illegal drug use
- V. Past history of cross dependency (substituting from one drug to harmful or problematic use of another, within the last 2-5 years)
- VI. Reluctance to agree to drug treatment and after-care or to sign a treatment agreement
- VII. Active ongoing alcohol use in the presence of HCV, where there is clear evidence of medical advice to become abstinent.

3 Transplantation and Substitute Prescribing

The recommendations regarding this area are given in the context of limited research data. Small studies are favourable to consideration of transplantation whilst on a substitute prescription e.g. Methadone maintenance therapy (MMT).

Analgesia post transplantation will need careful consideration and may require an agreed plan between the anaesthetist, pain team and substance misuse specialist. Awareness of potential issues relating to patient controlled analgesia (PCAs) will also be required, and risk factors should be assessed and a local management plan effected accordingly. The potential for misuse should be balanced with the knowledge that opiate tolerant patients are likely to need higher doses than an opiate naive person.

3.1 Methadone

MMT is a safe, well evidenced treatment for patients unable to become opiate free. It is commonly a long term treatment. Patients on a stable MMT should be offered assessment for transplantation where medically indicated. Stability - individually measured as a continuum, not an absolute - indicates abstinence from other illicit drug use (predominantly other opiates, stimulants – including cocaine and crack cocaine). There should be treatment engagement with a drug treatment service and the patient should have an agreed care plan and a named key worker (though it should be acknowledged that it is now common practice to transfer stable patients to GP management. MMT patients should not be asked to reduce their methadone simply for the purpose of transplantation as this has the potential to destabilise them and provoke a relapse to other drug use.

Evidence suggests the likelihood of a prolonged ITU stay post transplant and the requirement for larger doses and longer treatment for post-operative analgesia.

3.2 Buprenorphine

The same requirements apply in the context of substitute prescribing as for MMT (as in 3.1). Due to its method of action as a partial opioid agonist-antagonist there will be issues around peri-operative analgesia. Where possible, conversion to methadone peri-transplant will assist with this issue. This should be undertaken in consultation with a substance misuse specialist.

3.3 Prescribed I/V Diamorphine or Physeptone

Where clinically possible, conversion to oral substitution therapy should be considered, in view of concerns including venous access and sepsis. This decision needs consideration and team discussion incorporating the patient and substance misuse specialist.

3.4 Benzodiazepines

Careful assessment should be made where there is past or current significant use of benzodiazepines – whether prescribed or illicit – and the context of this use. Replacement of opioids and alcohol with benzodiazepines can occur, and thus their use might mask a relative risk to relapse. It is worth noting that benzodiazepines are also associated with high risk behaviours and cognitive and memory impairment, and so their use may actively trigger relapse.

4 Drug Screening

Drug screening should be arranged where there is concern about concurrent illicit drug use. Where a patient is on MMT they should be undergoing drug screening as part of their programme with the substance misuse team, and consent to obtain drug test results from the substance misuse team should be given. A positive screen for illicit drugs (except cannabis) prior to transplant is a contraindication to listing. Post transplant a positive screen is a clear prompt for intervention and support. Whether drug testing is via mouth swab or urinalysis, and whether it is a supervised process or not will depend on the practice of individual units.

4.1 Drug Screening and Alcohol Agreements

These should be undertaken on the basis of past history or where there is perceived risk of alcohol being used to substitute for other drugs (commonly opioids). This approach to testing requires each unit to consider its approach to the process of screening questions for alcohol and drug use and referral to the substance misuse specialist. Blood alcohol levels can be taken during blood tests or randomly requested. A “drugs of abuse” screen can be undertaken with a urine sample via the toxicology laboratory. All patients assessed for transplant listing should give explicit consent to future drug and alcohol testing from this period onward, as considered appropriate by the unit.

5 Treatment Agreement

A treatment agreement is recommended as a useful process for a number of reasons. It can outline a statement of intent including treatment engagement, commitment to the programme and consent to share appropriate information with relevant agencies. Any potential consequences to non-concordance with the treatment agreement (e.g. non-attendance, refusal of or positive drug screens) should be made clear in the agreement. Past behaviour documented in a comprehensive assessment is a better guide to stability and engagement than the signing of a treatment agreement. Consent should be part of a treatment plan.

6 Post Transplant Follow-up

It is recommended that follow-up with the local drug/support services – where required - is explicit in the agreement and should also form part of the care plan at the substance misuse service. Follow-up within the transplant programme should also clearly monitor and document substance use – preferably with monitoring by a substance misuse specialist – and the transplant team should actively encourage referral to and engagement with substance misuse services in the event of a relapse. This is likely to be expedited more successfully where contact with local substance misuse services has already occurred. As stated above, good data collection for the purpose of clinical audit is necessary to inform this area of transplantation.

7 Predictors of relapse

Research data in this field is currently limited. Guiding principles require referring to good practice and clinical “common sense”. Dependence on substances such as opioids and alcohol is a relapsing condition and harmful patterns of drug use may be repeated, however behaviour change can occur and be sustained though may take many years and numerous treatment attempts. Reasons for abstinence as well as relapse are numerous and individual.

8 Outcome Monitoring

In order to monitor the outcome of transplant listed patients with a significant illicit drug history, appropriate clinical data should be recorded. Consent for this to occur should be given at the same time as the drug and alcohol screening.