BASL Alcohol-related Liver Disease Special Interest Group (ArLD SIG)

First Meeting

St Mary's Hospital, Imperial College

9th January 2019

Introduction

The ArLD SIG was convened and initially the purpose of the group was outlined as specified in the BASL/BSG Special Interest Groups paper. Primarily the ArLD SIG exists to foster, promote and encourage collaborative research and clinical trials in ArLD. An integral part of the SIG will be to develop databases in aspects of ArLD. The SIG will be open to questions from Pharma in ArLD and will be responsible for responding on behalf of BASL to enquiries from national bodies such as NICE and HTA. The SIG would aim to provide input into any relevant guideline development.

Co-opted members of the group currently include Julia Verne, Public Health England, and Colin Drummond, Addiction Psychiatrist. It is noted that currently there is no patient representative despite approaching the British Liver Trust. This will be addressed.

Ewan Forrest is the current nominated Chair of the SIG as appointed by the BASL Committee. There will be an election for the first elected Chair in September 2019.

Areas of Discussion:

1) There was an enthusiasm for the SIG to be involved in establishing Clinical Standards for areas of ArLD as well as encouraging research and developing guidelines.
2) The SIG agreed not to pursue Pharma sponsorship of meetings at this time.
3) The SIG was identified as the natural successor to the BASL Trial Development Group.
4) There was an acknowledgement of the multi-morbidity nature of ArLD and the importance of being aware of the social, psychiatric and general medical aspects of alcohol-related problems.
5) A series of 'workstreams' within ArLD were identified to which members of the SIG can attach themselves
6) It was noted that a 'liver themed' call from the NIHR is expected in 2019, therefore the SIG is in a good position to identify suitable projects for submission.

Alcoholic Hepatitis: Prof Mark Thursz

Through the success of the STOPAH Trial and the MRC Stratified Medicine Grant for Minimising Mortality in Alcoholic Hepatitis, this area of ArLD research is well developed in the UK. Active studies include the ISAIAH Phase 2 Trial looking at moderate Alcoholic Hepatitis using an IL-1β antagonist. Recruitment has just begun and will focus on a limited number of centres (approx. 16).

In development is the PROCESSAH Trial which is to study GCSF in severe Alcoholic Hepatitis. A submission to EME is planned in March.

A pharmacokinetic study of Obeticholic Acid in mild Alcoholic Hepatitis is also planned supported by Intercept (MAFIA).

MICAH is a non-interventional study looking at Biomarkers in Alcoholic Hepatitis. The protocol is being finalised with a view to Ethics submission and approvals by the second quarter of 2019. A total of 1000 patients are to be recruited from 40 UK centres.

Afimmune is setting up a study in the UK which is already active in the USA.

Faecal transplant in Alcoholic Hepatitis is also being explored but no formal proposal or protocol is available as yet.

Management of Alcohol Withdrawal Syndrome in ArLD: Ewan Forrest

In contrast to Alcoholic Hepatitis, the management of AWS in ArLD patients is lacking any substantial evidence base. Guidelines suggest using shorter acting benzodiazepines and using symptom-triggered approaches rather than fixed-dose regimens. The applicability of AWS treatment in general to those with ArLD is uncertain. In addition, throughout the UK there are widely differing approaches to AWS management.

The SIG discussed this gap in evidence and the best means to start addressing the issue. As the baseline of evidence was essentially 'zero', it was felt that an initial survey of UK Clinical Practice would be helpful. Colin Drummond informed the SIG that there had been a recent audit of AWS management in the Mental Health sector. It was felt that a survey derived from this could be applied to ArLD patients. A group will be established within the SIG to formulate this survey. The aim would be to circulate to BASL/BSG members, and possibly to professional bodies representing Acute Medicine and A&E staff.

Management of Alcohol Dependency in ArLD: Colin Drummond

Whilst there has been a lot of work on approaches to manging Alcohol Dependence, very little has been specifically targeted upon patients with ArLD. Again there is the question of the applicability of these approaches to the ArLD patient.

Pharmacotherapy has been studied with some recent emphasis upon Baclofen. However there remains inadequate evidence to inform clinical practice.

Different psychosocial interventions have been studied and in particular Assertive Outreach for 'high cost' patients with Alcohol Dependence has been shown to improve outcomes and reduce cost. However in these initial studies, only a minority of patients had ArLD.

The management of Alcohol Dependence in ArLD is an area which would appear ripe for a program grant. The potential for collaboration between Hepatology, Psychiatry and Public Health is attractive. An initial approach could be the collation of a comprehensive Evidence Review of management in ArLD patients.

The Role of Biopsy in ArLD: Richard Parker

Practice regarding biopsy in ArLD varies in the UK but in general it is carried out only in selected cases. Despite the prevalence of ArLD, knowledge of its natural history relative to histological features is not well established.

WALDO is a study which seeks to address this question. The intention is to identify ArLD patients from pathology records and then determine total mortality as well as liver-related and non-liver-related outcomes. The study has approval and interested parties can indicate their willingness to participate. It was also noted that software to scrutinise pathology reports for features of ArLD was available (Jonathan Fallowfield, Edinburgh). This could be used to identify patients although the patients would need to be differentiated from NAFLD patients with similar histological features.

Identification of ArLD Hospital Episodes: Steve Hood

Estimation of the extent of ArLD hospital episodes is largely based upon standard coding which is open to misclassification. The result is a significant underestimation of the burden of ArLD. In the North West of England an algorithm has been formulated deriving information from 83 diagnostic codes rather than the usual 6 to inform about an alcohol-related hospital admission. This is able to more accurately chart the impact of ArLD hospital episodes over time and allows for a more detailed assessment of socio-economic factors.

This Connected Health Cities Algorithm is available for application throughout England and could also be applied to Scotland and Wales.

The SIG was also seen as a resource for Public Health England. The aim would be to establish a 'virtual coding committee' via email contact. This would allow uncertainties regarding the significance/ relevance of diagnostic coding in regard to ArLD to be discussed and clarified.

Early Community Diagnosis of ArLD: Nick Sheron

It is clear that there are many missed opportunities to recognise ArLD at an early stage. The merit of such early diagnosis is that these high risk patients can be targeted for medical and addictions intervention to prevent progression and reduce mortality/ morbidity. Work carried out through the LOCATE study has shown that such screening is feasible using standard blood tests and liver stiffness measurement.

A program grant to support the POLEMMIC trial is in progress. This will be based in Primary Care and will be carried out as a cluster study. When funding is hopeful approved, liver centres will be asked to support this initiative.

Transplantation for ArLD: Mike Allison

There was a general feeling at the SIG that there was still a lack of transparency and perhaps lack of equity regarding liver transplantation for ArLD patients. There is no formal record of those turned down for transplantation for ArLD and the reasons given. It was suggested that this should information should be collected. This could be broached with new chair of the Liver Advisory Group.

There was particular discussion regarding the role of liver transplantation for Alcoholic Hepatitis. The previous Clinical Evaluation has been closed mainly due to lack of referrals. There remains concern about our ability to identify those at greatest risk of mortality, and therefore risk transplanting someone whose liver may have the potential to recover. A recent BASL/BSG survey of attitudes to transplantation for Alcoholic Hepatitis has been carried out and the details will be circulated to members of the SIG.

Refining the threshold of the Lille score to increase specificity, or the introduction of a novel score (such as the Bayesian Variable Selection model derived from STOPAH data) may improve patient selection. Further discussion with the LAG is ongoing with the aim to see if a modified Clinical Evaluation might be established.

The SIG also felt that the work from the Connected Health Cities project might provide further information about the burden of ArLD relative to transplantation rates.

Other areas of ArLD Interest

The interaction between ArLD and Obesity attracted much discussion. Subsequent to the meeting, the chair has heard from Gautam Mehta regarding a NIHR RfPB application on this topic. Further details will be circulated to the SIG in due course.

There is already established in Yorkshire a study to look at a cohort of patients at risk of ArLD prospectively. (ALLHEAL). This could be rolled out throughout the rest of UK and is open to interested parties.

ACTIONS

1. Patient Representation: possible representatives were identified by Andrew Fraser, Glasgow, and Steve Ryder, Nottingham. These will be followed up. Ewan Forrest will approach the British Liver Trust again. Other members of the SIG are invited to indicate if they have suggestions for patient representatives
2. Further details of the studies described above will be circulated to the whole SIG.
3. SIG members are asked to review the various workstreams and identify with which they may wish to be more specifically engaged. This particularly applies to those areas where there is the need to develop programs of investigation: transplantation, AWS, dependency.
4. SIG members should also note interest in participating studies which are either in advanced stages of development or already established: MICAH, WALDO, ALL HEAL, Connected Health Cities coding project, Public Health England coding email group