Portal Hypertension Special Interest Group (SIG) 2nd Meeting

Medical School, University of Birmingham

23rd Jan 2020

Report prepared by Dr Dhiraj Tripathi and Steering Committee

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1. Introduction

The meeting was attended by 42 participants. Industry sponsors were Gore Medical, UK Medical and Sequana Medical. Dr Tripathi also thanked Samantha Jones, BASL Senior Administrator for her assistance in organising the meeting.

The SIG was introduced to all participants by Dr Tripathi who was appointed by BASL to lead the SIG for the first year and re-elected in 2019 to serve two years as SIG lead. The portal hypertension SIG is the largest of all the SIGs with a total of 213 members

Members of the steering committee were introduced:

Dr Dhiraj Tripathi (Chair), University Hospitals Birmingham
Prof Jonathan Fallowfield, University of Edinburgh
Prof Peter Hayes, University of Edinburgh
Dr Joanna Leithead, Addenbrookes Hospital, Cambridge
Dr Raj Mookerjee, University College London
Dr David Patch, University College London
Dr Vikram Sharma, Royal London Hospital
Prof Adrian Stanley, Glasgow Royal Infirmary
Dr Emmanouil Tsochatzis, University College London
Dr Abhishek Chauhan, University Hospitals Birmingham (trainee representative)
Ms Mandy Lomax (patient representative)

A description of presentations and summary of the discussions is presented thus. Slides for most presentations have been uploaded to the BASL website.

2. Active research studies

a. CALIBRE – Dr Tripathi (Chief Investigator) and Dr Ahmed (Senior Trial Manager) presented an overview of this NIHR HTA funded trial and an update:

i. Trial progress: recruitment began in January 2019 and 12 month pilot is complete. There are 55 sites open in England, Wales and Scotland. 184 patients recruited. Number of sites opened ahead of projections, however CALIBRE has not recruited to time and target. At the end of the 12 month pilot a minimum of 20 sites should be open, 240 patients recruited. There are a number of reasons for the recruitment including issues relating to CRN/research nurse resource, PI engagement, and equipoise with regards to the two therapies. Several sites have recruited poorly, and this has only been partly compensated by well recruiting sites.
ii. At present CALIBRE team are looking for more sites as funding allows for up to 66 sites and possibly more. Dr Tripathi advised the group that one patient recruited per month per site is sufficient to meet long term targets, and that CALIBRE will only succeed with engagement from all sites.
iii. CALIBRE investigators meeting is due to take place on 27th February and collaborators were encouraged to register.

b. BOPPP – Dr Patel (Chief Investigator) presented an overview of this NIHR HTA funded trial and an update:

i. Trial progress: So far 62 patients have been recruited over 22 sites since June 2019.
ii. The recruitment so far falls short of the contracted recruitment target by a significant margin. Despite opening many sites well ahead of schedule, most sites have not recruited as well as expected. This is of concern.
iii. A site had to close due to lack of research nurse support.
iv. A one page introductory patient leaflet describing both CALIBRE and BOPPP for sites recruiting to both has been withdrawn. This was due to significant differences in the protocols, in particular the consent pathways

c. ASEPTIC

Dr O'Brien (Chief Investigator) presented an overview of this NIHR HTA funded multicentre RCT. His group also lead the ATTIRE trial:

i. So far 9 sites and live and a further 4 sites have had SIVs.
ii. 4 patients recruited
iii. Recruitment may prove to be challenging

iv. Importance of stratifying according to Rifaximin

BOPPP/CALIBRE/ASEPTIC will be further discussed at the BASL/BSG research development group meeting and speciality meeting on 6th February.

d. Liver HOPE

Dr Mookerjee (PI for RFC site) updated the group on LIVEROPE which is HORIZON 2020 EU Program funded (5.6M Euro). It is a multi-centre, double-blind, placebo RCT to evaluate the efficacy of simvastatin plus rifaximin over 12m in halting the progression of decompensated cirrhosis as assessed by the time to first incidence of ACLF during treatment period.

The safety study has been published. Rhabdomyolysis was noted at Simvastatin 40mg dose (not at 20mg dose). Efficacy study will only use 20mg dose. Discussion focused on barriers to recruitment which is dropping behind target. RFH is only UK site. Important to encourage partner trusts to ensure ad1equate numbers are assessed for eligibility. Recent published haemodynamic data have not clarified position on systemic haemdynamics and cardiac function.

e. Vascular liver disease:

i. Dr Patch presented recent data on a protocol for the thrombolysis in recent portal vein thrombosis with evidence of intestinal ischaemia which has been published. Discussion focused on wider use of this protocol and patient selection. Clearly close links with specialised centres is essential.
ii. Dr Tripathi advised the group of the MASCOT study which will be presented in a future meeting.

3. Patient and public involvement and engagement (PPIE)

a. Laura Chapman (BRC PPIE Manager) and Mandy Lomax delivered a presentation providing how to write a lay summary. This stimulated lively discussion on an area that is often not given the attention it deserves.

4. Clinical guidelines

a. TIPSS – BSG/BASL/BSIR Guideline

Dr Tripathi on behalf of the Guidelines Development Group (GDG) chaired by David Patch summarised the key recommendations of the 1st ever UK

Guideline on TIPSS aimed at referring teams. The project is the culmination of 2 years of work by the Guidelines Development Group. He was delighted to inform the group that the guideline had been accepted for publication by Gut pending minor revisions.

b. Ascites guideline – BSG

Dr Palaniyappan on behalf of the GDG chaired by Prof Guru Aithal presented a short presentation focusing on research recommendations. The first draft of the guideline is nearing completion.

c. Danis stent – NICE MTEP

Dr Tripathi presented a summary of the current guidance on removable Danis stents for oesophageal variceal bleeding. This is considered an alternative to balloon tamponade in refractory acute variceal bleeding, where it can bridge patient to definitive therapies such as TIPSS. The stent can remain in place for up to 7 days and allows oral nutrition. Safety indicator balloon prevents the gastric balloon from inflating in the oesophagus and aims to reduce the risk of balloon-related perforation. It can be inserted without image guidance, allowing rapid tamponade in acute scenarios. Data is derived from 202 patients and 6 studies. A RCT suggests Danis stent may be more effective and safer than balloon tamponade. There is a lack of UK evidence. The basic unit costs £1495 excl VAT.

NICE guidance (IPG392) recommended the use of Danis stents under standard arrangements. NICE Medtech Innovation Briefing document is available with a summary of the technology, although formal guidance is in progress (NICE-MTEP).

Discussion focused on training, experience in UK, funding and complications. Several units use the stents and it has a particular role for safe transfer for definite therapies. Migration can be an issue. Removal is straightforward.

5. Service development

a. Alfapump

Dr Tripathi presented an overview revisiting the NICE Interventional procedures guidance [IPG631]: Subcutaneous automated low-flow pump implantation for refractory ascites caused by cirrhosis, The EASL guidelines on decompensated cirrhosis were also discussed. The discussion focused on 3 main areas:

a. Procedural issues
    i. Device failure

ii. Changes in design

b. Safety
   i. Renal
   ii. Infections
c. Role of albumin to minimise complications.
d. Funding - at present funding mainly through IFR route or done in independent sector. A workable funding model for the NHS would seem a priority.
e. Future studies – do we need RCTs. Efficacy vs effectiveness

b. Fontan service

Dr Patch presented an overview of the "The Fontan Nightmare!" Hepatologists are becoming increasingly involved with the care of such patients. Barts adult congenital heart disease clinic has 250 Fontan patients. Although the procedure is considered a palliative procedure many patients are living beyond expectations and developing Fontan Associated Liver Disease (FALD). It can be associated with thromboses, protein losing enteropathy, and plastic bronchitis. Pathophysiology related to congestive hepatopathy and incidence of severe fibrosis/cirrhosis in up to 70%.

Discussion focused on

I. Surveillance of patients for complications - not clear (e.g. fibrosan, varices, HCC).
II. Transitioning arrangement with paediatric hepatology
III. Ideal multidisciplinary clinic set up – there could be logistical barriers such as need for travel.

6. Research in development

a. CALIBRE and BOPPP sub-studies

Dr Mookerjee and Dr Patel presented proposals for sub-studies which involve bio-banking blood samples to explore the role of inflammation and infection in patients on NSBB. Sadly applications to NIHR EME have not been successful. It was agreed that the two trials offer an ideal to study these mechanisms, and could add significant value to the studies. Dr Patel informed the group that at KCH, there are proposals to sample blood in selected patients as part of BOPPP. Dr Tripathi and Dr Mookerjee will explore other options for CALIBRE in conjunction with the Sponsor.

b. CARBALIVE

Dr Mookerjee presented this multicentre, randomized, double blinded, placebo controlled trial to evaluate safety and tolerability of oral

administration of mesoporous carbob (Yaq-001) therapy in two dosing cohorts in patients with cirrhosis and diuretic resistance ascites. It is HORIZON 2020 EU Program funded (6M Euro). Target sample size is 56.

c. Update on grant applications

The early TIPSS grant application (REACT-AVB) led by Dr Tripathi and Dr Patch was submitted in response to the NIHR liver themed cross platform call. It will be discussed by the funding committee in March 2020 when a decision about progression to 2nd stage application will be made.

7. Future meetings

1. Steering committee meeting – tbc
2. Meeting for all SIG members – tbc