Acute Liver Failure Special Interest Group Meeting
Kings Hospital London - 14th February 2020

Meeting Minutes

		Actions
Item1	**<u>Observations from Kings College Hospital (WB)</u>** WB presented a series of observations from Kings College Hospital over the years. From 1999 to 2017 there have been 1,502 admissions. Paracetamol overdose still dominates in aetiology. There has been a progressive improvement in post-transplant survival - now over 90% at one year, which is not far off the elective programme. There has also been an increase in survival for medical management alone, particularly for patients with Paracetamol induced acute liver failure. Survival is less clear in other aetiologies. The number of patients presenting with Paracetamol induced acute liver failure is decreasing, and the overall number of admissions to the Intensive Care Unit with this aetiology is decreasing. Overall survival of acute admissions is increasing, and the proportion of patients transplanted for this indication is decreasing. All centres were in agreement that fewer patients are being seen with acute liver failure overall and those secondary to intentional overdoses with Paracetamol are less common and it is more often resulting from therapeutic misadventure.	
Item 2	**<u>Report/Updates to SIG</u>** **A) Activity audit (WB)** The purpose is to identify the number of potential cases for interventional studies, to establish current activity throughout the UK and the performance of the current transplant selection criteria.	

	All patients with acute liver failure and acute liver injury were considered from 1st October 2018 to 1st June 2019. 156 cases have been submitted to date. Leeds is the only centre to have provided full 12 months data. There was partial data from Cambridge and Birmingham. We would estimate we would have around 300 cases in total per year. With the data available the median age of patients is 38, 59% are female. The dominant indication is still Paracetamol overdose, and the second is drug induced liver injury, predominantly secondary to MDMA. The overall survival is around 80% with malignancy offering the lowest chance of survival. By aetiology, all cases of Wilsons underwent transplantation, with Paracetamol overdose now having the lowest rate of transplantation. 80 patients were seen with Paracetamol induced ALF; 63 of these were not listed. Of these 50 survived with medical management and 13 died. 17 Patients were listed: 10 were transplanted and of these 5 died. 7 were not transplanted and, of these, 5 survived and two died. Of the 76 patients with non-Paracetamol induced liver failure 34 fulfilled criteria and 33 of these were transplanted, and all of these survived. One of these was not transplanted and died. 42 were not listed and of those 11 died and 32 survived. The performance of the 2017 revised criteria were then discussed (see presentation) The performance is probably sufficient but more data is awaited. **Action: To collate full years data from centres.** **B) ICP Monitoring (MB, PE-D)** A progress report was submitted from the Birmingham team after collating the data that has been submitted so far from other centres. There was ten year data and 836 patients included so far. 233 of these have complete datasets. Of the paracetamol overdose patients less intracranial bolts are being inserted,	**WB**

	but cerebral deaths would seem to be consistent. In 2018 there was only 1 intracranial bolt inserted. In the non-Paracetamol induced patients the incidence of bolts is also very low Of the 52 patients bolted, there was a bleed post bolt in 13% of patients and all of these subsequently died. It would appear that intracranial pressure monitoring is not linked to the rate of transplant or survival, or cerebral deaths, although it is acknowledged that complete datasets are still needed. Mortality would appear to be higher in bolted patients (54% versus 26%) but this may also reflect a sicker cohort. It was also acknowledged that it could be difficult to categorise HE severity, particularly if grade 0 at referring hospital and the patients were then intubated. Different strategies were discussed and will be taken forward outside this meeting as to how best to address this. It was also noted that nearly half of bolted patients were not CT scanned, and so it is possible that complications were missed. It is also difficult to ascertain the number of cerebral deaths accurately - of 229 patients no cause of death was given. There was wider discussion about narrowing the dataset to make it more achievable. It was also proposed that potentially year 10 data could be compared to the last 5 years to help data interpretation and collection. **Action: The ICP working group will take the dataset completion issues and consider these outside of the meeting. Aim for full dataset presentation at next meeting.** **C) Plasma exchange (JM/BA/AD)** A progress report was presented by JM and AD regarding the work of the plasma exchange (PEX) sub-group. Questions to be addressed include the indication for PEX, replacement fluid used and transplant free survival with PEX for those meeting criteria who both are and are not transplanted, the change in composite organ failure scores,	**ALL**

	and also to look at associated complications including infections. So far data has been submitted from the Royal Free, Kings, Leeds and Newcastle. Birmingham is planning to send further data. Currently Edinburgh and Cambridge are not plasma exchanging patients. Kings are currently kindly providing control data, and Birmingham and Edinburgh have both offered to collect control data. The variables will be sent through to them (by JM). There would appear to be a signal at the moment with this limited dataset - those patients who completed at least three sessions had a transplant free survival benefit (P = 0.04). This was with all aetiologies. This however possibly reflects a less sick cohort however. Most centres would appear to be doing standard volume exchanges rather than high-volume. It was mentioned that Fin Larson and the group in Barcelona have offered to contribute data if we wish. So far there appeared to be no difference in the APACHE and SOFA scores. More Paracetamol overdose patients had received PEX than non-PODS which could be a confounder. Action: The PEX working group will take the dataset completion issues and consider these outside of the meeting. Aim for full dataset presentation at next meeting. WB to approach FSL / JF for possible data contribution	**JM** **ALL** **WB**
Item 3	**<u>Point of care Ammonia demonstration (LB)</u>** LB demonstrated the Fuji film/Fuji analyser for point of care Ammonia testing. It was explained this was a dry slide technology, and there has been a kind offer to provide point of care Ammonia analysers to recruiting centres. The patient ID is inputted (or scanned). 10 microliters of whole blood or plasma can be put onto the side. Two minutes after pressing start the result will be available. It measures	

Item 4	between 7 to 357 micromoles per litre. Fujifilm will collate the data. Louise would be grateful for a key contact from each site [email removed]. Action: WB to link Louise to centre representatives **Observational/interventional studies.** **Ammonia: nutrition and filtration (WB)** Literature was presented regarding Ammonia in ALF patients. A study was proposed - a prospective, observational study of enteral nutrition in acute liver failure. Patients would be recruited with acute liver injury/acute liver failure and ammonia over 100. Patients would be fed as normal and ammonia would be measured before and during enteral nutrition. Outcomes such as length of stay and complications, for example sepsis, would be looked at. The pros would include that this is a real clinical issue, it is cheap and practical study and there is minimum risk. There are also minimal regulatory concerns. The con could include that a standard feed might be required. Another study was presented investigating controlling ammonia with different modes of haemofiltration. The proposal was a prospective renal replacement therapy in acute liver failure, investigating specific modes of renal replacement therapy and their association with lowering the arterial ammonia. This would primarily include CVVHF and standard medical therapy versus CVVHDF and standard medical therapy, and looking at the change in ammonia in 12-24 hours as well as secondary measures of HE severity including length of stay and complications including sepsis and intracranial hypertension. This could lend itself to ancillary studies as well. The pros would be that this includes minimal deviation from standard practice, and the cons would be that it would require standard renal replacement technology in all the centres, and standard ways of ammonia monitoring.	**WB** **WB**

	Action: WB to contact centres for detail on nutrition and RRT practice as a preliminary to completing REC submission. **Birmingham proposal (MB)** The role of angiotensin II for vasopressor support was presented. This would be a two stage randomisation trial. This would involve looking at albumin initially, and then at the second stage of randomisation angiotensin II. Outcomes would include survival. It was discussed as a wider group whether we should expand to include all liver disease to help the sample size. Grifols potentially could be approached for funding. It appears that angiotensin II has recently been discontinued and MB will explore further why this might be, and also look to calculate a sample size. **Action: MB to explore availability of agent and will discuss further at the next meeting**. **Edinburgh studies (KS)** An update was provided on the surviving ALF study. This was a large data linkage study to look at what happens in the longer term in patients who have survived ALF compared to matched populations, in respect of mortality and health care utilisation. There are 700 survivors. It would seem that this is not an ITU survivorship issue. Liver transplant doesn't appear to impact on longer term survival. KS is keen to roll this out across the UK. Only basic identifiers would be needed - NHS numbers, post codes, sex, and when the patient was admitted. For now it is encouraged that individual centres keep this information which can be used at a later date. We would hope for around 3,000 survivors. KS also updated on the European Registry data. Data is still needed from Cambridge, Birmingham and UCL. A Research Fellow can come to the respective centres to help collect data as needed.	**MB** **VH/VS**

	Genotyping ALF patients was also discussed. MB mentioned a study led by Ken Bailey in Edinburgh. We believe that CRN approval is obtained. **Action: KS will approach KB with a view to seeing if acute liver failure could be included. He could be invited to the next SIG.** **Final conclusions** - all centres with outstanding data are encouraged to submit. **<u>Next venue will be Leeds on 18th June 2020</u>**.	**KS**