

Investigation and treatment of liver disease with acute onset – Local hospital protocol

- Defined as EITHER sudden onset of jaundice with evidence of liver aetiology OR incidental discovery of raised transaminases in association with symptoms suggesting acute onset
- Age of onset >3 months
- Investigate and treat as neonatal jaundice before 3 months
- Acute Liver Failure (ALF): INR>2.0 due to liver dysfunction of less than 8 weeks duration without encephalopathy or >1.5 with encephalopathy requires transfer to Transplant Centre.

Early Measures

- Ensure given vitamin K parenterally at least once and regularly by mouth thereafter.
- Ensure not hypoglycaemic with BM stix before feeds >4.0 for at least 24 hours – give IV dextrose to ensure blood glucose ≥ 4.0 mmol/l.
- Ask and record colour of urine and stool.
- Take history and perform examination especially for features of chronicity of liver disease.
- Bloods – HAV IgM, FBC, INR, DIC screen, renal, bone liver profiles, total and conjugated bilirubin levels, HBV SAg.
- If INR ≥ 2 TREAT AS LIVER FAILURE – If INR raised liver failure may be developing
- Contact SpR at Transplant Centre. Do not wait for results to make contact.
- Preliminary investigations – blood and urine cultures, urine drug screen, plasma paracetomol level if any indication, Immunoglobulins, C3, C4, auto-antibodies, pANCA, copper, zinc, caeruloplasmin, hepatitis C antibody, alpha-fetoprotein, liver ultrasound.
- Liaise with SpR at Transplant Centre to arrange transfer according to urgency depending on above information.

Investigations in Acute Liver Failure

Core investigations – prior to all investigation protocols	
Investigations	Comments
FBC, retics, film	? haemolysis/cytopenia
INR	If prolonged treat with vit K 1mg IV and repeat in 6-8 hr.
Group and save	Blood Group to be known
<input type="checkbox"/> -1-antitrypsin phenotype (from parents if transfused)	PIZZ – deficiency
Renal, lipid, bone, and liver profiles, split bilirubin, creatine kinase	Profile of liver dysfunction
Urine C&S	UTI
Blood cultures	Sepsis
HIV status	Ethics committee consent obtained for all patients – inform parents as courtesy
Liver ultrasound	Evidence and nature of liver disease

Test	Diagnosis
Glucose/BM stick 4 hourly	
SAVE INITIAL URINE toxicology screen	Drugs especially paracetomol
Hepatitis A IgM, B IgM anticore, anti Hep C antibodies, Hep C RNA	Hepatitis viruses A, B, C (URGENT to Institute of Liver Studies)
Fibrinogen (coagulation form)	HLH
Auto-antibodies, immunoglobulins,	Auto-immune hepatitis
Amylase, CK	Pancreatitis, myositis
NH ₃ (on ice)	Urea cycle disorder
Serology / PCR	Leptospirosis CMV, EBV, HSV, V-Z adenovirus, Parvovirus (PCR may be necessary) HHV6.
CXR, ECG (ECHO if indicated)	
Vitamins A,D &E	Low serum levels noted at presentation
Blood gases <i>lactate, pyruvate,</i>	PYRUVATE discuss with biochemist first

Management of ALF while waiting for transfer

- Nurse child with head elevated at 20° and no neck flexion (to decrease I.C.P. and minimize cerebral irritability)
- **DO NOT SEDATE** unless already ventilated - this may precipitate respiratory failure.
- Maintain oxygenation with facial oxygen, unless this increases the agitation.
- Maintain blood sugar between 4 - 9 mmol/l using minimal fluid volume (40 - 60 ml/kg/day crystalloid) with high dextrose concentrations e.g. 10% - 20% add K as necessary.
- Strict monitoring of urinary output and fluid balance. Catheterise if necessary. Check urinary electrolytes, urea creatinine and osmolarity.
- Frequent neuro-obs (hourly to 4 hourly as clinically indicated)
- Give one dose of Vit K (1-5 mg IV) to attempt correction of prolonged clotting time. If frank bleeding (GIT or other) occurs consider prudent use of FFP at 10 ml/kg IV OR cryoprecipitate at 5 ml/kg IV only for bleeding or insertion of monitoring devices. (FFP will mask prognostic value of INR). Factor VIIa may be used for persistent bleeding.
- CMV negative irradiated blood required for all children <1 year and agreed with haematology.
- Prophylactic Ranitidine 3 mg/kg/dose tds (max dose 50mg) IV plus oral antacid to prevent gastric/duodenal ulceration.
- IV Cefuroxime 20 mg/kg three times daily (Max dose 1.5 gram three times daily) or Tazocin 90mg/kg/dose tds (mximum single dose 4.5g) x 7 days.
- Antifungal- Fluconazole - 6mg/kg/day once daily (max 200mg/day once daily) x7-14 days
- Infants <2 should receive acyclovir IV 20mg/Kg 8 hrly for 14 days or until herpes infection is excluded.
- Patients with renal dysfunction on high WBC also require liposomal Amphotericin IV.
- Lactulose to produce 2 - 4 soft stools per day if patient conscious - omit if diarrhoea.
- Stop oral protein initially. Gradually reintroduce 0.5 g-1g/kg/24 hours.

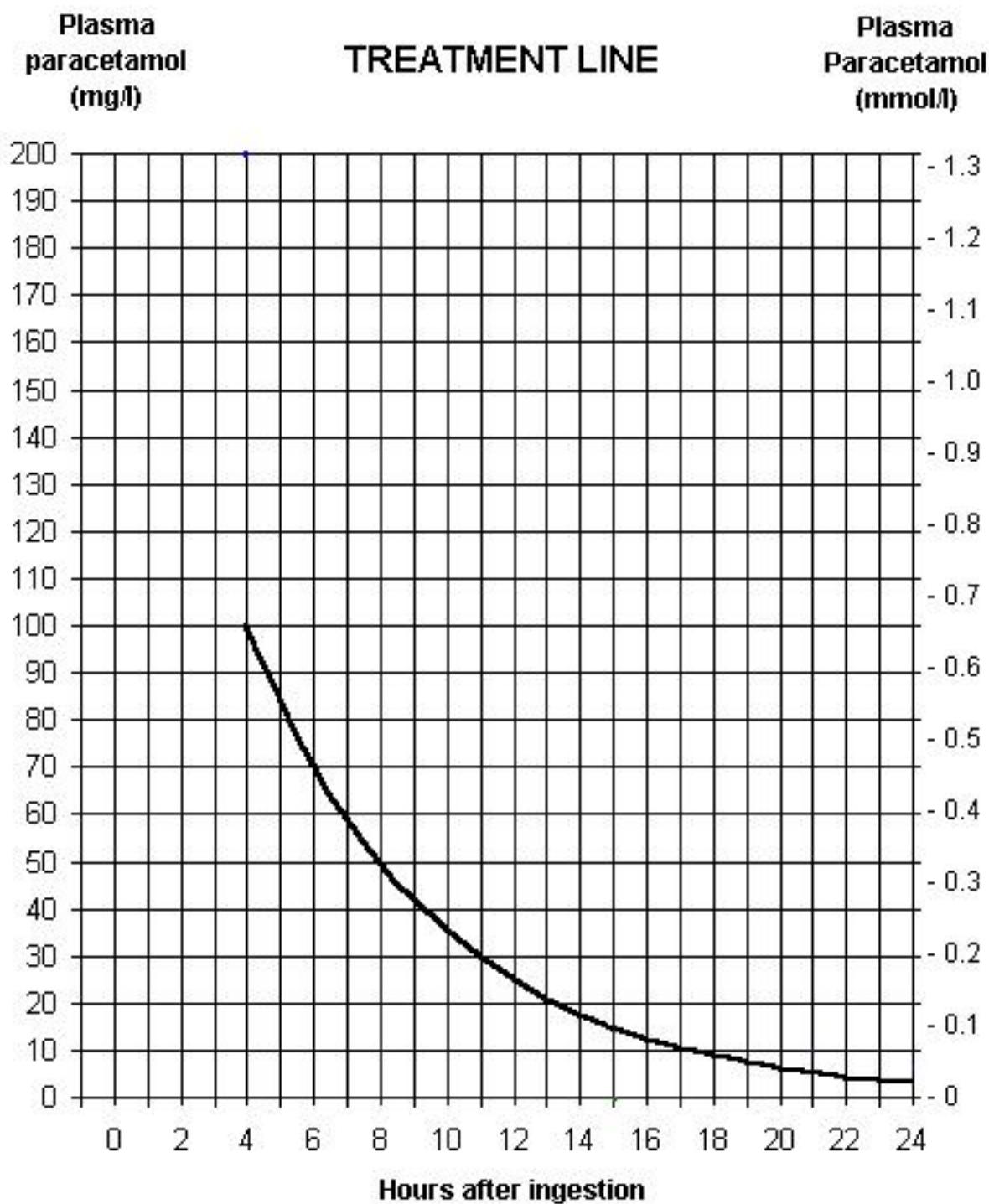
Fluid Balance

- Strict fluid balance is essential in liver failure
- Daily weights are required if the child can be moved.
- Aim for urine output not less than 0.5 ml/kg/hr
- Volume given calculated from formula (If child is not dehydrated and losses are not abnormal).

Daily Maintenance Fluid = approx 2/3 maintenance		
2/3x(100ml/Kg body weight for the first 10 Kg+50ml/Kg for the next 10Kg+10ml/Kg for each subsequent Kg)		
Fluid type	Dextrose 4 - %	Dextrose >10% or higher if hypoglycaemic (BM<4.0)
K+	1.0 - 3.5 mmol/kg/day	NIL while anuric
Na+	nil	

Paracetamol Overdose Treatment Protocol

If a Paracetamol overdose is suspected or known, the child must be treated immediately with N-acetylcysteine, at the local hospital whatever the time between the alleged overdose and the visit to the hospital. The 'High Risk Treatment Line' is used in all cases once a level is known. The N-acetylcysteine should be continued until the INR is normal (<1.2). Indication for treatment after known time since ingestion by plasma level corresponding to the High Risk Treatment Line is shown below.



Investigations

- Liver function tests, paracetamol level, INR, blood sugar, renal function tests and blood gases including lactate. Blood sugar must be closely monitored - (hourly BM stix).
- Urine drug screen should be performed as soon as possible

- INR, blood sugar, renal function and blood gases must be repeated at least twice a day and, if abnormal, three times a day. Start immediately broad spectrum antibiotics if INR abnormal and in the presence of abnormal renal function, liposomal Amphotericin i.v.
- Hypoglycaemia has to be avoided and the child should be maintained on 10% dextrose. Higher concentrations of dextrose may be needed.
- The most important prognostic parameter is acidosis on day 2. If, despite N-acetylcysteine treatment and good rehydration, the child becomes acidotic, the prognosis is poor. Acidosis is the best prognostic factor independent from all other factors. Even in the presence of a very prolonged INR, a patient who is not acidotic will have 80% chances of surviving. If the pH is <7.25, there is a 95% mortality, therefore the child should be emergency listed for transplantation.
- Other factors predicting a poor outcome are the development of grade III hepatic encephalopathy with oliguric renal failure (which usually occurs three to four days after ingestion), and/or a prothrombin time of >100 seconds, and raised plasma lactate.