CHAPTER

116 Therapeutic Plasma Exchange and Continuous Renal Replacement Therapy as Rescue Therapy in Paracetamol Induced Fulminant Hepatic Failure

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INTRODUCTION

Patients still die from paracetamol poisoning because they are not recognized to be at risk of harm or present too late for effective treatment.

Patients who are malnourished, have been fasting, take enzyme inducing drugs, or regularly drink alcohol to excess are at higher risk of liver damage.

Patients who have ingested too much paracetamol should be treated within eight hours of ingestion whenever possible. If the time of ingestion is known, treatment can be based on blood tests taken after four hours. If the timing is uncertain or unknown, N- Acetylcysteine (NAC) should be started immediately in all patients who are at potential risk of dying due to toxic effect of paracetamol. All the patient should be considered as high risk unless factors that increase risk of harm are known to be absent.[1] A flowchart for the management of patients with paracetamol poisoning can be found and can help clinicians in the emergency department.[2] Once patient develops fulminant hepatic failure, only therapeutic option is liver transplantation.

Recently it is found that high-volume plasma exchange (HVPE)[3] which removes plasma bound toxins and continuous renal replacement therapy (CRRT), which removes water soluble toxins like ammonia can be used as rescue therapy.

Treatment with high-volume plasma exchange (HVPE) improves outcome in patients with ALF by increasing liver transplant-free survival. Total plasma exchange (TPE) corrects coagulopathy in patients with liver disease and removes hepatotoxins /cytokines. This improvement is transient but can be used as a bridge until an organ is identified for liver transplantation (LTx) or the liver itself regenerates.[4] This is attributable to attenuation of innate immune activation and amelioration of multi-organ dysfunction.

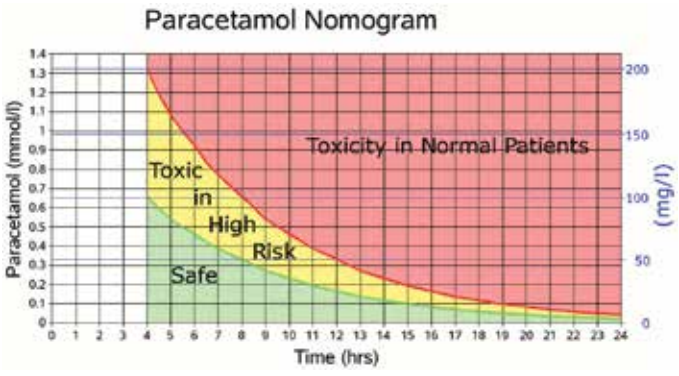

Fig. 1: This nomogram is not applicable for patient who present after 24 hours of injestion

Specific conditions in which CRRT has been proposed as the preferred modality to maintain fluid electrolyte homeostasis, water soluble solute and ammonia removal, includes combined acute renal and hepatic failure (because of the beneficial impact of CRRT on cardiovascular stability and ICP) and acute brain injury (because of the ability of CRRT to prevent cerebral edema).[5,6] Patients with acute liver failure who have suspected or proven cerebral edema should be treated with CRRT rather than intermittent renal replacement (IRRT) due to the risk for worsened cerebral edema with IRRT (even in hemodynamically stable patients).[7,8]

Both the therapy in combination can buy time and help in keeping the patient alive till hepatic failure phase (2-4 days post ingestion) is passed.[9] Once this phase is passed liver start regenerating and patient can survive without liver transplant.[9]

CASE

A 54 year male was found unconscious after consuming unknown poison. He was shifted under our care in comatose state, intubated on ventilator after 30 hours of suspected poisoning. On, arrival his Glasgow Coma Scale (GCS) was 4, pupils pin point, corneal and cough reflex present. He was hemodynamically stable (BP 160/90 mmHg), & was passing urine. He came with normal Blood counts, PT (INR) aPTT, Renal function Test, MRI brain and CSF. His SGPT was 320 IU/L, Bilirubin 1.2 mg%, and ABG (pH-7.34, PCo2- 28, PaO2 130/ 0.4 O2, HCO3-18).

On admission his toxicology screen was sent. It was positive for paracetamol, 130 mg%; after 30 hours of ingestion (Paracetamol nomogram not applicable after 24 hours of arrival); Figure 1. Other significant positive reports -PLT-80,000. SGPT 550, SGOT 600, PT (INR)1.3, pH-7.30, optic nerve diameter (OND) was 5.4mm, is marker of raised intracranial pressure(ICP). Normal OND

Adult acetylcysteine prescription (each ampoule = 200mg/mL acetylcysteine)					Please circle appropriate weight and volume	
Regimen	First Infusion		Second Infusion		Third Infusion	
Infusion fluid	200 rnLs 5% glucose or sodium chloride 0.9%		500 mLs 5% glucose or -odium chloride 0.9%		1000 mLs 5% glucose or sodium chloride 0.9%	
Duration of infusion	1 hour		4 hours		16 hours	
Drug dose	150 mg/kg acetylcysteine		50 mg/kg acetylcysteine		100 mg/kg acetylcysteine	
Patient Weight'	Ampoule volume[2]	Infusion Rate	Ampoule volume[2]	Infusion Rate	Ampoule volume[2]	Infusion Rate
kg	mL	ml/h	mL	ml/h	mL	**mL/h**
40-49	34	234	12	128	23	64
SO-S9	42	242	14	129	28	64
60-69	49	249	17	129	33	**65**
70-79	57	257	19	130	38	65
80-89	64	264	22	131	43	**65**
90-99	72	272	24	131	48	66
100-109	79	279	27	132	53	66
≥110	83	283	28	132	55	66

Fig. 2: Protocol of NAC infusion in treatment of Paracetamol

ACETAMINOPHEN-INDUCED ALF

Arterial pH <7.3 (regardless of HE)

OR all 3 of the following

- INR>6.5
- Creatinine >300 l imol/l
- HE grade 3-4

NON-ACETAMINOPHEN-INDUCED ALF

INR >6.5 (regardless of HE)

OR 3 of 5 of the following (regardless of HE)

- Age < 10 or >40 years
- Etiology, indeterminate, drug-induced
- Time interval icterus to encephalopathy > 7 days -INR>3.5
- Bilirubin >300µmol/l

Fig. 3: King's college criteria for liver transplant alert in acute liver failure

is 4.0-4.5 mm. N-Acetylcysteine infusion as per protocol was started, Figure 2.

In next 24 hour pupil became unequal, SGPT rose to 5800, pH dropped to 7.1, INR went up to 6.5, Platelets dropped to 40000, creatinine 1.30 mg%, arterial ammonia rose to 250 µmol/litre (on admission 65 µmol/litre). As per King's college criteria he needed Immediate liver transplantation to avoid impending death (Figure 3).

As patient was non affording was not willing for liver transplant, rescue therapy in form of high volume plasma exchange (HVPE) and Continuous Veno-venous hemofilteration CVVHF (35 ml/kg/hr) was offered (Figure 4). We did three cycle of HVPE and 96 hours of CVVHF.

- In CVVH, solute clearance occurs by convection
- No dialysate is used
- Typically, hourly ultrafiltration rates of 1 to 2 L/h are used
- Intravenous "replacement fluid" is provided to replace the excess volume that is being removed and replenish desired solutes, can be administered either prefilter or postfilter.
- Effective method of solute removal and
- Indicated for uremia or severe acidosis or electrolyte imbalance with or without fluid overload
- Major advantages is that solutes can be removed in large quantities, maintaining a net zero or even a positive fluid balance

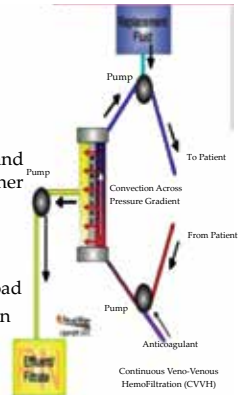

Fig. 4: Continuous Veno-Venous Hemofiltration (CVVH)

After 1st cycle of plasmapheresis & 24 Hours of CVVHF, his blood reports started improving, INR 1.5, pH 7.36, AND SGPT 860. GCS improved to 8, pupil constricted but reactive, OND dropped to 4.6 mm.

I stopped CVVHF after 48 hour and did 2nd HVPE. We again started 2nd cycle of CVVHF. After 72 hours patient woke up, but he was very irritable so we continued CVVHF for next 24 hours more (total 96 hours / 2 cycles) to control raised ICP. After this we did 3rd cycle of plasmapheresis and then monitored him for next 48 hours. He became alert and all the reports were normal after 48 hours of stopping CVVHF & Plasmapheresis. He got extubated on 6th day. He remained stable and got discharged on 11th day. So far he do not have any residual problem after 6 months.

CONCLUSIONS

PCM induced ALF has 90-95% mortality if liver transplantion is not offered immediately. Cause of death in these patients are cerebral edema, life threatening

bleeding and cardiovascular arrest. Rescue therapy (CVVHF & HVPE) was offered to keep the patient alive till hepatic failure phase of PCM induced ALF is passed. As this combination has never been documented to save this kind of patient, but this combination has potential to rescue those patients where liver can regenerate. I believe that we may try this combination to rescue viral induced AFHF. We need to explore this combination in other AFHF.

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