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Intravenous Lipid Emulsion Therapy In Paediatric Poisoning

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ABSTRACT:

Lipid emulsions are traditionally used as a part of total or partial parenteral nutrition. However in the past few years role of lipid emulsions has been identified in the management of poisoning and overdose caused by the lipophilic agents. Although most of the evidence comes from the various case reports. We are reporting 2 cases of poisoning in the paediatric age group. In both the cases multiple poisoning agents were involved with tricyclic antidepressants being the common agent in either case. Lipid emulsion therapy was used as an adjunct in addition to the traditional poisoning management. Both the girls recovered completely without any neurological deficit. The sequence of events observed provides a considerable evidence regarding the role of ILE therapy in the successful management of both the cases. However more research is required in the area to develop definitive guidelines regarding the use of Intravenous lipid emulsions in paediatric poisoning caused by lipophilic agents.

Keywords: Lipid emulsion therapy, Paediatric poisoning, Tricyclic antidepressants poisoning.

INTRODUCTION:

Lipid emulsions are originally used as a part of total or partial parenteral nutrition in patients unable to take orally. However role of lipid emulsions in the treatment of poisoning has been observed in last few years in animal models as well as in humans[1]. In 2006 first case report proving the role of intravenous lipid emulsion therapy as a treatment option for acute drug poisoning was published[2]. After that various other cases and subjective reports also supports the role of intravenous lipid emulsions in the treatment of toxicity caused by various drugs and pesticides[3,4,5].

Intravenous lipid emulsion is an accepted therapy for the treatment of severe cardiac toxic effects caused by local anesthetics and is being studied as therapy for hemodynamically unstable patients poisoned with several lipophilic medications like TCAs, calcium channel blockers, barbiturates[6].

Here we report two cases: A 6 year old female, case of accidental poisoning and an 11 year old female, a case of suicidal poisoning. Multiple drugs were involved in either case with tricyclic antidepressant being a common drug. In both the cases lipid emulsion therapy was also used in addition to the recommended management of poisoning with specific agents.

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CASE STUDY:

CASE 1: A 6 years old female was brought to Pediatric ER at 9.30 am when her mother found her unconscious with frothing at her mouth.

On examination the child was unconscious with GCS of 4/15(E1M2V1), tachycardia with heart rate of 130/minute, shallow breathing, constricted and nonreactive pupils, oxygen saturation of 78% in room air and RBS was 53mg/dl. ECG showed sinus tachycardia with no other abnormality. ABGs showed uncompensated metabolic acidosis. The urine toxicology report was positive for opiate and tricyclic antidepressants.

Naloxone at 0.1mg/kg was given, after a single dose of naloxone the GCS improved to 9/15(E4M3V2) and the pupils were now bilaterally equally reactive to light.

Sodium bicarbonate infusion was started as a part of traditional management of TCA poisoning treatment protocol so as to maintain alkaline PH. No further improvement was noted for next 2 hours in the GCS and patient was still having tachycardia, so it was decided to start intravenous lipid emulsion therapy. As no pediatric dosage has yet been recommended we followed the adult dosage regimen for ILE therapy. Initially 2 boluses were given at 1.5ml/kg, each over 3 minutes and 5 minutes apart. Still no improvement was noted so lipid emulsion infusion was started. It was continued for next 6 hours. ABGS showed improvement gradually as well as the patient regained GCS of 13/15(E4M5V4) and the tachycardia improved after 2 hours of starting ILE infusion. Patient was clinically and hemodynamically stable in the next 12 hours. Serum amylase and serum triglycerides levels were found to be normal after the therapy.

During her ICU stay she did not develop any hemodynamic instability or seizure disorder.

CASE 2: An 11 years old girl was bought with complaint of unconsciousness for past 5 hours.

Examination revealed that she had a GCS 4/15 (E1V1M2), with mid dilated, sluggishly reactive pupils. her pulse rate was 90/min, respiratory rate of 30breaths/min, BP was 115/60. Her planters were bilateral up going but deep tendon reflexes were normal. ECG was normal. ABGs showed metabolic acidosis and urine toxicology was positive for benzodiazepines, barbiturates and tricyclic antidepressants.

The patient was given flumazenil as an antidote for benzodiazepine poisoning. It was given in 3 divided doses with a gap of 1 minute along with GCS monitoring. GCS improved to 8/15(E2M4V2).Sodium bicarbonate infusion was maintained. Lipid emulsion therapy was given initially as 2 boluses at 1.5ml/kg over 3 minutes and 5 minutes apart. The GCS of the patient improved to 12/15(E4M5V3) after the second bolus. The lipid infusion was continued for next 6 hours. ABG showed improvement and were completely normal in next 3 hours after starting infusion. The patient regained full GCS of 15/15 with down going planters which were initially up going after 4 hours of starting infusion. Serum amylase and triglyceride levels were monitored after the therapy, no abnormality was observed. Psychiatric consult was done which revealed that the child has pressures for performing well in studies from the family, which lead to the suicide attempt. She was advised psychotherapy and she improved on follow-up.

More than 1 kind of drug was involved in both the poisoning cases with TCA being the common agent. In both the cases amount of the drug ingested is unknown. We observed that the use of lipid emulsion therapy hastened the recovery in either case with no major side effects.

DISCUSSION:

Lipid emulsion therapy is well known for the purpose of total and partial parenteral nutrition. Its role has also been proved in the treatment of cardiac toxicity caused by local anesthetics. There is an emerging role of lipid emulsion in the management of acute poisoning as well; although the data available is based mainly on the case reports.

According to the scientific literature how lipid emulsion works in management of poisoning is not fully understood. However, there are various mechanisms by which the lipid emulsion is believed to be beneficial in the management of poisoning. Two most likely possibilities are:

1. Intravenous lipids act as a 'lipid sink'. Lipophilic agents are easily absorbed by or easily attached to lipids but are not absorbed by water. The practical effect of this characteristic is that a highly lipid-soluble drug or chemical will not remain in the intravascular compartment but will pass through cell membranes and reach binding sites in the tissues. A bolus of intravenous lipid may provide an intravascular lipid sink that attracts and absorbs highly lipid-soluble drugs or chemicals before they reach the tissues, or the lipid will actively pull drugs or chemicals from tissue binding sites[7].

2. The second possibility involves fatty acid metabolism. Under normal circumstances, the myocardium uses fatty acids for energy. Local anesthetics inhibit fatty acid metabolism in the heart, and experiments in animals have indicated that intravenous lipid may reverse the cardiac toxic effects caused by high doses of bupivacaine by providing an exogenous energy source for the myocardium. This mechanism supports the already accepted theory of the role

Table 1: Comparison of the two cases.

	CASE 1	CASE 2
AGE , WEIGHT	6years, 18 kg	11 years, 35 kg
DRUGS	TCA, Opioids	TCA, Benzodiazepines, Barbiturates
DOSE	Unknown	Unknown
TIME OF PRESENTATION AFTER POISONING	More than 12 hours	Around 8 hours
TOXICITY ONSET	Loss of consciousness(GCS 4/15), metabolic acidosis, tachycardia, shallow breathing	Loss of consciousness(GCS 4/15), metabolic acidosis
TREATMENT	Naloxone at 0.1mg/ kg, Sodium bicarbonate infusion, Intravenous lipid emulsion therapy at 1.5ml/ kg as 2 boluses 5 minutes apart and then an infusion for 6 hours at 0.25 ml/kg/min.	Inj Flumazenil 1 mg in 3 divided doses. Sodium Bicarbonate infusion, Intravenous lipid emulsion therapy at 1.5ml/ kg as 2 boluses 5 minutes apart and then an infusion for 6 hours at 0.25 ml/kg/min.
TOXICITY REVERSAL (Time of onset)	GCS improved to 13/15, improvement in ABGS noted after 2 hours of starting lipid infusion.	GCS improved to 12/15 after the second bolus, metabolic acidosis resolved completely in 3 hours of starting infusion. GCS 15/15 after 4 hours of infusion.

of lipid emulsion in reversal of severe cardiac toxic effects of local anesthetic[8].

ACMT guidelines suggest the following dose for lipid resuscitation therapy:

Dose of lipid emulsion is 1.5ml/kg bolus given over 2-3 min, it can be repeated after 5 min to a maximum of 3ml/kg.For the purpose of continuous infusion dose is 0.25ml/kg/min till the patient becomes hemodynamically stable preferably through a central line[9].

Most of the published case reports on the subject describe adults, only a few cases regarding children and adolescents have been reported. The first pediatric case report published in 2011 where ILE therapy was used in case of acute poisoning. It reported a 20 month old girl who ingested a large amount of TCA and presented with seizures and hemodynamic instability. She did not respond to the traditional poisoning management protocol; Intravenous lipid emulsion therapy was administered, which resulted in successful recovery of the patient[10].

An article published in 2013 reviewed all the case reports published regarding the use of ILE therapy in children and adolescents. It concluded that almost all the cases showed a beneficial effect of ILE therapy with side effects observed only in 1 case report. The dosage regimens were not well defined though[11].

TCA is lipophilic drug, and when taken in excessive amounts it has cardiovascular and central nervous system side effects. In both our cases, mainly neurotoxicity was noted. Lipid emulsion therapy was used and it demonstrated rapid recovery in both the cases. Although due to multi agent poisoning and multiple therapies given, it is impossible to attribute the success in saving lives exclusively to Lipid Emulsion therapy; however the sequence of events observed in toxicity reversal proves a substantial role of ILE in the favorable outcome observed in both the above cases.

Lipid emulsion therapy is a promising therapy and a cheaper option in the cases of acute poisoning with lipophilic agents where a specific antidote is not available for the chemical[12]. Jeffrey Brent a renowned medical toxicologist, gave a remarkable statement in this regard in an editorial published few years back "It is fair to say that based on what we known so far, no patient dying of cardio toxic drug poisoning should do so without a trial of lipid rescue"[4,13]. We can suggest that the statement is well-thought-out in terms of lipid rescue for neurotoxic effects of lipophilic drugs as well; at least in both our cases. More research is required into the subject and proper guidelines need to be developed for pediatric usage.

CONCLUSION:

This is the first ever reported use of successful intravascular Lipid Emulsion therapy in the management of life threatening effects of poisoning with multiple agents, with TCA being the common agent in both the cases in a Public Sector Pediatric Tertiary Care setting in Pakistan. This case report add to the increasing evidence of the role of Lipid emulsion therapy in the treatment of acute poisoning with lipophilic agents and also proves pediatric safety profile.

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