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Extracorporeal treatment in children with acute severe poisoning

Xiaomei Sun, MD[a,b], Xiuying Chen, BM[a,b], Jing Lu, MM[a,b], Yuhong Tao, MD[a,b], Lijuan Zhang, MD[a,b], Liqun Dong, MD[a,b,*]

Abstract

Acute poisoning in children is a clinical emergency. Prompt and effective treatment is critical for life-threatening poisoning. Extracorporeal treatment (ECTR) is a practical option for enhancing the elimination of poisons.

We conducted a retrospective observational study on 338 children with severe acute poisoning who received ECTR during hospitalization from January 2010 to December 2017. The poisonous substances, utilization of ECTR, adverse reactions to ECTR, and outcomes were recorded.

The top 3 poisoning categories, in order of frequency, were found to be pesticides (57.99%), biotoxins (25.15%), and pharmaceuticals (14.20%). Paraquat (35.21%), an organic heterocyclic herbicide with high toxicity to humans, was the most common toxic substance. The main modalities of ECTR use were hemoperfusion (50.59%) and therapeutic plasma exchange (42.60%), followed by continuous renal replacement therapy (4.44%) and hemodialysis (1.18%). There were also 4 patients (1.18%) with a combination of ECTR performed. Adverse events of ECTR included errhysis and hematomas around the catheter exit site, oral cavity bleeding, allergic reactions, hypothermia, hypotension, and blood coagulation. The adverse reactions were mostly mild to moderate and were manageable. During the study period, there were 295 patients (87.28%) who were cured, 9 (2.66%) who experienced some improvement, and 34 (10.06%) who died.

ECTR modalities were found to be clinically effective approaches to the treatment of poisoning by pesticides, biotoxins, and pharmaceuticals, indicating they are important modalities in toxicology and treatment, and are well tolerated by children.

Abbreviations: CRRT = continuous renal replacement therapy, CVVH = continuous veno-venous hemofiltration, CVVHDF = continuous veno-venous hemodiafiltration, ECTR = extracorporeal treatment, HD = hemodialysis, HP = hemoperfusion, MODS = multiple organ dysfunction syndrome, TPE = therapeutic plasma exchange.

Keywords: children, extracorporeal treatments, severe poisoning

1. Introduction

Acute poisoning in children is still a significant public health problem and remains a persistent cause of injury-related morbidity and mortality throughout the world. According to the World Health Organization Global Burden of Disease project, approximately 45,000 children and young adults die each year as a result of acute poisoning.[1]

Most substances are non- or minimally toxic in pediatric poisonings, but a few are severely toxic, requiring immediate and appropriate medical intervention to prevent severe harm or death.[2,3] Severe poisoning is defined as exposure to a poison causing a significant clinical effect that can be lethal (eg, massive salicylate ingestions, paraquat), may cause irreversible tissue damage (eg, methanol-induced blindness), or may cause minor end-organ damage (eg, lithium-induced tremors).[4,5] Supportive care, along with antidote when available, continues to be the cornerstone of therapy.[2,3,6] When the patient has developed life-threatening manifestations of poisoning, and alternative treatments are not available, timely consideration of extracorporeal treatment (ECTR) is indicated if the poison is considered dialyzable.[7]

The goal of ECTR is to maximize poison elimination [7,8] or harmful metabolites [9] from the body by diffusion, convection, adsorption, and centrifugation. ECTR includes hemodialysis (HD), continuous renal replacement therapy (CRRT), extensive dialysis, peritoneal dialysis, hemofiltration, hemodiafiltration, hemoperfusion (HP), therapeutic plasma exchange (TPE), and albumin/"liver" dialysis.[4] Modalities grouped under the heading of CRRT include continuous veno-venous hemofiltration (CVVH) and continuous veno-venous hemodiafiltration (CVVHDF).[10] Whether extracorporeal removal is possible depends on the characteristics of the toxin itself and of the

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[a] Department of Pediatrics, [b] Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China.

[*] Correspondence: Liqun Dong, Department of Pediatrics, West China Second University Hospital, Sichuan University, Chengdu, Sichuan 610041, China (e-mail: dongliqun@scu.edu.cn).

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elimination technique used.[11] For biotoxins, ECTRs are mainly used to remove the toxic metabolites produced by the biotoxins, attenuating organ damage.[9]

The purpose of this study is to describe severe poisonings in children who underwent ECTR; investigate the substances involved in acute severe poisoning exposures; evaluate the safety of ECTR in children and explore the principles of selecting 1 modality of ECTR over the others in cases of severe poisoning.

2. Materials and methods

2.1. Ethics

This study was conducted at the West China Second University Hospital of Sichuan University, with full ethical approval from the Hospital Ethics Committee. All procedures adhered to the Declaration of Helsinki. Because this study was a retrospective investigation of existing data, written informed consent from patients was not required. All information gathered from patients was anonymized and securely protected. All data were only available to the investigators.

2.2. Patients

The patients or their families provided the patient's medical history. We retrospectively reviewed the medical records of acute poisoning patients admitted to the Pediatric Department between January 2010 and December 2017. The inclusion criteria were:

(1) a clear present history of severe acute poisoning;
(2) patient age below 18 years;
(3) hospital admission within 24 hours of poisoning; and
(4) treatment with ECTR while hospitalized.

The exclusion criteria were:

(1) iatrogenic poisoning;
(2) a previous history of renal dysfunction; or
(3) peritoneal dialysis.

Clinical evidence of severe poisoning included hypotension, coma, metabolic acidosis, respiratory depression, dysrhythmias, or cardiac decompensation.[12]

The treatment outcomes were categorized as curative, improved, and dead.

2.3. Treatments

2.3.1. Conventional treatments. Readily available literature offers excellent summaries of the general approach to the treatment of poisoned children.[2,13–15] For most cases of ingestion poisoning, gastric lavage and activated charcoal were used as the conventional initial treatments. Diuresis and other symptomatic treatments were performed next. Water-electrolyte imbalances were corrected. Conventional treatments were performed promptly and completely in each case before ECTR used. For example, prescribing sodium bicarbonate and norepinephrine were required in the case of amitriptyline poisoning with refractory hypotension.[16] Oral activated charcoal, N-acetylcysteine, silibinin, antioxidant drugs, and other supportive measures were used to treat amanita poisoning.[17] Special antidotes such as atropine injection in organophosphate poisoning patients and antivenom to neutralize snake venom were promptly used.

2.3.2. Indications of ECTR. The cases in which physicians must decide whether to use ECTR include patients who have been exposed to a highly toxic substance that is likely to cause serious morbidity or mortality, such as paraquat; patients who demonstrate progressive clinical deterioration despite appropriate clinical management, presenting with intractable hypotension, hypoventilation, heart failure, seizures, metabolic acidosis, or dysrhythmias; and patients whose normal route of elimination of the intoxicant is impaired (liver or kidney dysfunction).[10,18] When these situations occurred or appeared likely to be so, ECTR was taken into consideration as soon as possible. In all cases, because delayed treatment initiation in patients with severe poisoning is associated with significant permanent morbidity and mortality, regardless of treatment,[19] treatment was started as quickly as possible after determining that the cause of illness is acute poisoning.

2.3.3. ECTR. A temporary veno-venous vascular access was established with a flexible double-lumen catheter (GDK-612.5P/812.5P/1115; Baxter International Inc, Deerfield, Illinois) via the femoral vein. The courses of each ECTR were made on a case-by-case basis at the clinician's discretion. The blood flow rate was 3 to 5 mL/kg/min.

The HD was implemented for 2 to 4 hours once daily using a FX5 (15 kg$\leq$ weight $<$30 kg) or FX8 (weight $\geq$30 kg) dialyzer (Fresenius SE & Co KGaA, Germany). Nadroparin calcium (Fraxiparine, manufactured by GlaxoSmithKline, UK) was used as an initial dose of 67 IU/kg and did not require a maintenance dose.

The HP apparatus includes the activated charcoal adsorbent HA100 (15 kg$\leq$ weight $<$30 kg) or HA160 (weight $\geq$30 kg) (Zhuhai Lizhu Medical Bio-Material Co, Ltd, China). The HP was performed for 2 to 4 hours once daily. Heparin sodium was administrated at a total dose of 1 mg/kg during each session.

The CRRT (CVVH or CVVHDF) was implemented at the bedside with Gambro Prismaflex M60 set (weight $<$25 kg) or M100 set (weight $\geq$25 kg) (Baxter International Inc). The CRRT was given as a 12 to 24 hours daily treatment. Fraxiparine was administrated at an initial dose of 60 to 80 IU/kg, followed by an additional dose of 6 to 8 IU/kg/h.

TPE was performed using the Gambro Prismaflex TPE 1000 set (weight $<$25 kg) or the TPE 2000 set (weight $\geq$25 kg) (Baxter International Inc) every other day, for approximately 2 to 2.5 hours during each session. The replacement fluid was homotypic fresh frozen plasma with a total volume of 1.2- to 1.5-fold of the patient's plasma volume. Fraxiparine was used at a single dose of 60 to 80 IU/kg.

The safety of the ECTR was assessed according to the following complications:

(1) hemorrhage,
(2) infection,
(3) allergy,
(4) hypothermia,
(5) hypotension, and
(6) blood coagulation.

2.4. Statistical analysis

SPSS 22.0 (IBM, Armonk, NY) was used for all the statistical analyses. Continuous variables are expressed as mean $\pm$ standard deviation. Categorical variables are reported as percentage. Statistical significance was defined as $P < .05$.

Table 1

Characteristics of the patients.

	Total (n = 338)	Deaths (n = 34, 10.06%)
Sex		
Male	160 (47.30%)	16 (47.06%)
Female	178 (52.70%)	18 (52.94%)
Age, yr		
0–3	80 (23.67%)	2 (5.88%)
3–6	78 (23.37%)	5 (14.71%)
6–10	45 (13.31%)	3 (8.82%)
10–18	135 (39.94%)	24 (70.59%)
Area		
Country	262 (77.51%)	29 (85.29%)
Suburb	59 (17.46%)	4 (11.76%)
Cities	17 (5.03%)	1 (2.94%)
Reason for exposure		
Unintentional	240 (71.01%)	10 (29.41%)
Intentional	98 (28.99%)	24 (70.59%)
Age for those with intentional use, yr	12.2 ± 1.4	
Age for those with unintentional use, yr	5.6 ± 3.4	

3. Results

3.1. Patient characteristics

A total of 338 patients were included in this study, 160 were boys, and 178 were girls, with a mean age of 7.5 ± 4.2 years (range: 0.83–17 years) (Table 1). The age distribution showed 2 peaks: 1 at 2 years with 39 patients (11.54%) and another at 13 years with 45 patients (13.31%). Unintentional exposure was found to be caused by misuse (149 patients), food poisoning (31 patients), and envenomation (60 patients) in 240 patients (71.01%); intentional exposure, which here refers to suicide attempts, was confirmed in 98 patients (28.99%). There were no intentional exposures among patients ≤8 years.

3.2. Substances in exposure

The substances encountered by patients are shown in Table 2. The top 3 types of poison were, in order of frequency, pesticides (57.99%), biotoxins (25.15%), and pharmaceuticals (14.20%). Paraquat (35.21%), an organic heterocyclic herbicide with high toxicity to humans,[12] was the most common substance. Wasp stings represented 35.29% of biotoxin, followed by snake bites (21.25%) and insect bites (16.25%). Antipsychotic and antiepileptic agents were the most common 2 agents in pharmaceutical poisoning.

Table 2

Substances involved in poisoning exposures.

Substances	Total (n = 338)	Deaths (n = 34)
Pesticides	196 (57.99%)	27 (79.41%)
Paraquat	119 (35.21%)	22 (64.71%)
Organophosphorus	39 (11.54%)	1 (2.94%)
Rodenticides	26 (7.69%)	2 (5.88%)
Other pesticides	12 (3.55%)	2 (5.88%)
Biotoxins	85 (25.15%)	6 (17.65%)
Wasp stings	30 (8.88%)	4 (11.76%)
Snake bites	17 (5.03%)	0
Insect bites	13 (3.85%)	0
Mushroom	12 (3.55%)	2 (5.88%)
Plants fruits	8 (2.37%)	0
Fish gall bladder	5 (1.48%)	0
Pharmaceuticals	48 (14.20%)	1 (2.94%)
Antipsychotic	11 (3.25%)	1 (2.94%)
Antiepileptic	11 (3.25%)	0
Sedative-hypnotic	4 (1.18%)	0
Miscellaneous drugs	22 (6.51%)	0
Industrial products	3 (0.89%)	0
Others	6 (1.78%)	0

The main substances involved in unintentional poisoning were pesticides (106 patients, 44.17%), biotoxins (85 patients, 35.42%), and pharmaceuticals (40 patients, 16.67%). The poisons associated with suicide attempts were pesticides (90 patients, 91.84%) and overdoses of pharmaceuticals (8 patients, 8.16%).

3.3. Clinical presentation

Sixteen cases (4.73%) developed hypoventilation and required ventilator-assisted ventilation, 20 patients were in a coma (5.92%) and 22 patients (6.51%) presented seizures. Liver dysfunction occurred in 79 patients (23.37%), acute kidney injury in 74 patients (21.89%), myocardial injury in 49 patients (14.50%), and cardiac dysrhythmias in 12 patients (3.55%). A total of 12.43% patients (42 patients) with multiple organ dysfunction syndrome (MODS) were observed.

3.4. Utilization of ECTR

ECTR was used in all 338 patients for a total of 1350 extracorporeal sessions. In most cases, ECTR was used for primary toxin removal (83.14%) (Table 3). Each patient underwent 2 to 6 sessions. The interval between patients' admission and the use of ECTR ranged from 2 to 24 hours. The principal modality of ECTR was HP (171 patients, 50.59%), followed by TPE (144 patients, 42.60%), CRRT (15 patients, 4.44%), and HD (4 patients, 1.18%). There were also 4 patients (1.18%) with a combination of ECTR performed, including 3 patients treated with HD + HP and 1 patient with TPE + CRRT.

3.5. Outcomes

There were 295 patients (87.28%) cured, 9 (2.66%) improved, and 34 (10.06%) dead. The most common substance causing death was paraquat (22 patients, 64.71%), followed by wasp venom (4 patients, 11.76%) and mushrooms (2 patients, 5.88%) (Table 4). Correspondingly, the mortality rate in the present study was 18.49% (22/119) for paraquat, 13.33% (4/30) for wasp venom, and 16.67% (2/12) for mushrooms.

Among 98 patients with intentional exposure, 24 died, including 21 who died of paraquat poisoning. Among 240 patients of unintentional exposure, 10 died including 1 of paraquat poisoning, 1 of organophosphorus poisoning, 2 of rodenticide poisoning, 2 of mushroom poisoning, and 4 of wasp stings. The mortality of patients with intentional exposure (24/98, 24.49%) was significantly higher than that of patients with unintentional exposure (10/240, 4.17%) ($P < .001$).

3.6. Adverse reactions of ECTR

Femoral catheters were placed in 338 patients and no catheter-associated infections were observed. Sixteen patients (4.73%) had catheter-related errhysis or hematomas that disappeared upon compression. The adverse reactions that occurred during

Table 3

Modalities of ECTR for children with acute poisoning.

		HD (n = 4)	HP (n = 171)	TPE (n = 144)	CRRT (n = 15)	Combination (n = 4)
Reason for ECTR						
Primary toxin removal		2	171	101	7	0
Secondary complication treatment		2	0	43	8	4
Substances						
Pesticides		**0**	**106**	**84**	**4**	**2**
Paraquat		0	54	60	3	2 (HD + HP)
Organophosphorus		0	31	8	0	0
Rodenticides		0	9	16	1	0
Other pesticides		0	12	0	0	0
Biotoxins		**1**	**26**	**49**	**7**	**2**
Mushroom		1	4	5	0	1 (PE + CRRT) 1 (HD + HP)
Plants fruits		0	4	4	0	0
Fish gall bladder		0	0	2	3	0
Insect bites		0	11	2	0	0
Snake bites		0	1	15	1	0
Wasp stings		0	6	21	3	0
Pharmaceuticals		**3**	**35**	**7**	**3**	**0**
Antipsychotics	Clozapine	0	4	0	1	0
	Ziprasidone	0	1	0	0	0
	Penfluridol	0	0	3	0	0
	Amitriptyline	0	1	0	1	0
Antiepileptics	Carbamazepine	0	5	0	0	0
	Valproic acid	3	0	0	0	0
	Lamotrigine	0	2	0	0	0
	Phenytoin sodium	0	1	0	0	0
Sedative-hypnotics	Clonazepam	0	3	0	0	0
	Zolpidem tartrate	0	0	1	0	0
Miscellaneous drugs	Digoxin	0	3	0	0	0
	Isoniazide	0	1	0	0	0
	Euthyrox	0	0	1	0	0
	Vitamin D	0	1	0	0	0
	Metformin	0	0	1	0	0
	Other	0	13	1	1	0
Industrial solvents		**0**	**1**	**1**	**1**	**0**
Other unspecified/miscellaneous		**0**	**3**	**3**	**0**	**0**

CRRT = continue renal replacement treatment, HD = hemodialysis, HP = hemoperfusion, TPE = therapeutic plasma exchange.

ECTR sessions are shown in Table 5. A total of 107 adverse events (7.03%) were recorded in 1350 ECTR procedures, including oral cavity bleeding, allergies, hypothermia, hypotension, and blood coagulation. The incidence of adverse reactions in HP was the highest (8.72%), followed by TPE (7.50%), HD (4.76%), and CRRT (3.08%). Exactly 3 ECTR sessions were not completed (0.89%) due to blood coagulation. All the other sessions were successfully completed without death or life-threatening adverse events.

Anaphylaxis was alleviated after an intravenous drip of hexadecadrol. Hypothermia was relieved after the temperature in the room was raised and the patient was supplied with forced-air and electric heating pads. Hypotension was normalized after standard saline infusion.

Table 4

Outcomes of the patients.

	Total (n = 338)
Cured	295 (87.28%)
Improved	9 (2.66%)
Dead	34 (10.06%)
Paraquat	22 (64.71%)
Wasp venom	4 (11.76%)
Mushrooms	2 (5.88%)
Rodenticides	2 (5.88%)
Other pesticides	2 (5.88%)
Organophosphorus	1 (2.94%)
Antipsychotic drugs	1 (2.94%)

4. Discussion

Poisoning is one of the most common threats against public health. According to reports from the World Health Organization, acute poisonings rank fourth among the causes of morbidity and mortality of children.[20] Therefore, it is imperative to pay more attention to acute poisoning in children.

Some types of poisoning display marked geographic differences in incidence. In China, the most common substances for acute poisoning in children include pesticides, pharmaceuticals drugs, food poisoning, and envenomation by snakes and wasps,[21–23] while in developed countries, the pattern is different, with the top 3 most common poisonings in children age 5 years or less are due to cosmetics/personal care products,

Table 5

The adverse events occurred during ECTR sessions.

	HD (n = 21)	HP (n = 757)	TPE (n = 507)	CRRT (n = 65)
Adverse events	1 (4.76%)	66 (8.72%)	38 (7.50%)	2 (3.08%)
Oral cavity bleeding	0	12 (1.59%)	2 (0.39%)	0
Allergy	0	11(1.45%)	19 (3.75%)	0
Hypothermia	0	0	12 (2.37%)	0
Hypotension	1 (4.76%)	20 (2.64%)	5 (0.99%)	0
Blood coagulation	0	23 (3.04%)	0	2 (3.08%)

CRRT = continue renal replacement treatment, ECTR = extracorporeal treatment, HD = hemodialysis, HP = hemoperfusion, TPE = therapeutic plasma exchange.

household cleaning substances, and analgesics.[24] In the present study, the most common type of poisoning was pesticide poisoning, due to their wide usage in agriculture and hence ready availability, the lower health education of the population in the rural areas (keeping the pesticides in inappropriate places, taking them out of their original containers or administrating a toxic substance to a child by mistake), and lack of supervision for unattended children.

ECTR is life-saving under certain conditions. To determine the indications of ECTR for a specific poisoning, clinical decisions should be made on a case-by-case basis by considering whether poisoning can be managed by supportive measures, what benefits would be derived from ECTR, and whether the advantages of ECTR would outweigh disadvantages.[20,25] Once a decision is made to prescribe ECTR, the next is to decide which modality of ECTR best suits a given patient.

The United States toxic exposure surveillance system suggested that HD might have partially replaced HP in many clinical cases because of HD's superior efficacy, HP cartridges' high cost, and clinicians' lower rate of experience in HP procedures.[26] In the present study, HP was used more frequently compared with HD. HD was performed on a total of 7 patients (2.07%), including 3 cases of valproic acid poisoning, and 4 cases of different kinds of poisoning with kidney failure. HP was performed on a total of 174 patients, of which 62.07% had been poisoned with pesticides poisoning, 15.52% with biotoxins, and 20.11% with pharmaceuticals. Any of several reasons may account for the high use of HP. First, the most common toxic substances are pesticides and biotoxins, the majority of which are protein-bound and have large molecules, more suitable for removal by HP than HD. Second, pesticides are the most common causes of poisoning in China,[27] as observed in the present study. Many clinicians and nurses are experienced in HP procedures. Third, the HP technique is no more complicated than HD, and it does not require a purified water system. Finally, high-flux membranes and advanced HD technologies have not been popularly applied in children in China. It may be that, along with improved HD techniques in developing countries, there will be an increase in the use of HD in the treatment of poisoning.

CRRT is often recommended for hemodynamically unstable patients and in cases of toxins with rapid redistribution.[10,11] In our study period, because there was no specific small-volume tubing (HD dialyzer or HP cartridge) available for very young infants, CRRT, as an alternative, was applied in 6 infant patients. Another 8 patients with MODS and 2 hemodynamically unstable patients were also treated with CRRT. The high cost, long duration of therapy, and physicians' lack of expertise may limit its use in poisoned children.

The most common toxic substance and the leading cause of death in our study was paraquat, which is well-known to be highly toxic to humans.[28–30] A total of 22 patients with paraquat poisoning died. Paraquat poisoning is characterized by acute lung injury, pulmonary fibrosis, respiratory failure, and multiorgan failure, with high mortality and morbidity rates.[30] Wang et al reported that CRRT was effective in reducing patient fatality rates, particularly when combined with HP.[31] In the present study, HP, PE, and CRRT were performed in 54, 60, and 3 patients with paraquat poisoning, respectively. The combination of HD + HP was used in 2 patients. No matter which modality of ETCR was used, the sooner the blood purification was performed, the better the outcome. For patients for whom the Jones equation predicted a high risk of mortality,[32] appropriate combinations of extracorporeal therapies might be more effective than a single modality alone.

Biotoxins were the second cause of death, as supported by previous studies from developing countries.[21–23] Wasp stings are not uncommon in rural areas. MODS can occur as a consequence to a massive wasp attack, with high risk of mortality.[33] In the present study, HP, TPE, or CRRT was performed on 30 patients with wasp venom toxicity, of whom 19 experienced MODS and 4 died. No definitive treatment for MODS secondary to wasp envenomation has yet been established. Previous studies suggested that PE + CVVHDF or high-volume hemofiltration + HD approaches could be used for the successful management of patients suffering from wasp-venom-induced MODS.[33,34] Mushroom poisoning may be life-threatening. The best known and the most toxic type of mushroom is *Amanita phalloides*, with the greatest number of fatalities caused by late-onset hepatorenal failure.[11,35] HD has been reported to be ineffective when used as the sole treatment for the management of amatoxin syndrome, but it should be applied if renal failure occurs.[17] Previous studies reported that plasmapheresis, HP, fractionated plasma separation and adsorption, and molecular adsorbent recirculating system were effective in reducing mortality of *A phalloides* poisoning.[11,17,35–37] In our study, based on patients' clinical condition, a single- (HD, HP, or TPE) or combined-modality (TPE + CRRT, HD + HP) was used in 12 patients exposed to poisonous mushrooms, 10 of whom recovered, and 2 of whom died from hepatic failure. Snake venom may cause disseminated intravascular coagulation, thrombocytopenia, and even tissue necrosis.[33] Without proper treatment, patients may risk amputation or death. In our study, there were a total of 17 snakebite patients, all of whom recovered without limb loss. Fifteen patients were treated with TPE, highlighting the effectiveness of TPE in victims of snakebite.

Complications associated with ECTR are usually minimal.[5] In the present study, adverse reactions associated with ECTR were mostly mild and manageable, indicating that ECTR was well tolerated by children. Successful extracorporeal therapies are dependent on appropriate vascular access for adequate blood

flow, suitable anticoagulation to prevent clotting of the circuit, and adequate treatment time to account for rebounding of toxic substance levels.[8]

It is noteworthy that, in our study, the mortality rate (10%) was much higher than that reported in other studies. A study from France showed the mortality of 2998 poisoning children admitted to the pediatric emergency care unit to be 0.33/1000.[38] Patel reported that the mortality of 12,021 children with acute intoxications admitted to pediatric intensive care units was 0.63%.[39] The high mortality in our study can be explained by any of the following facts. First, all patients were severely poisoned and did not respond well to conventional treatments. Second, the majority of deaths (24/34, 70.59%) were intentional. Individuals attempting suicide patients deliberately swallow hypertoxic and high doses of poison, which decreases the probability of successful treatment, highlighting the need to improve education on primary prevention of poisoning and pay more attention to psychological health of teenagers. Third, paraquat poisoning was the leading cause of death. The treatment of paraquat poisoning is very difficult because no specific antidotes exist and ingestion of even a small amount (≥40 mg/kg) can cause death.[28,40,41] A meta-analysis showed that mortality from paraquat poisoning was 78% overall, 70.7% for those who underwent HP combined with conventional treatments and 90.3% for those who underwent conventional treatments alone.[29] Finally, the initiation of ECTR in fatal poisoning is critically time-sensitive. Earlier initiation of ECTR may result in better outcomes. Delayed treatment initiation in patients with severe poisoning is associated with significant permanent morbidity and mortality, regardless of the treatment.[19] The decision processes around the use of ECTR in poisoning are complex. ECTR is justified if clinical conditions are progressively deteriorating, especially when the natural removal mechanism is impaired. Each case should be individualized according to the poison's characteristics, the patient's clinical status, and the available resources. It is essential to ascertain whether the benefits of ECTR exceed its risks, when the best time for ECTR treatment is, and which modality of ECTR is optimal.

This study has some limitations. This is a retrospective descriptive analysis, and there was no control group treated by traditional or other treatments to assess the effects of ECTR, mainly because of the ethical difficulties of including control groups in studies of severe poisoning. In addition, there was no quantitative index to estimate the efficacy of poison removal by ECTR, as it was difficult to take account in toxic substances' enterohepatic circulation, hepatic metabolism, or urinary excretion. Finally, there was no consistency in the application of ECTR modality to any particular poisoning, mainly because even for poisoning with the same substances, the clinical presentations may vary according to the doses of poison and age, height, weight, and general baseline health (congenital diseases, comorbidities, nutrition status) of the children.

5. Conclusion

This study may have important clinical implications. HP and TPE were found to be safe, clinically effective approaches to the treatment of poisoning by pesticides, biotoxins, and pharmaceuticals, indicating they are important modalities in toxicology and treatment and well-tolerated by children. With the availability of HP devices coated with drug-specific antibodies or the antidote of the toxin instead of activated charcoal, ECTR will become more specifically useful.

Author contributions

Conceptualization: Xiaomei Sun, Liqun Dong.
Data curation: Xiaomei Sun, Xiuying Chen, Jing Lu, Lijuan Zhang.
Funding acquisition: Liqun Dong.
Writing – original draft: Xiaomei Sun.
Writing – review and editing: Yuhong Tao, Liqun Dong.

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