Registration study on the Application of intravenous lipid emulsion in patients with acute poisoning

2021-11-12

Study Protocol

1.Research background and purpose: research status at home and abroad, preliminary research basis

1.1 Research Background:

Poisoning refers to the occurrence of a series of reactions in the body tissues after exposure to chemical substances, resulting in permanent or temporary damage to the structure and function of human organs, or even serious threats to the patient's life, resulting in death.The severity of poisoning is determined by the type of chemical substances, which can be divided into subacute poisoning, chronic poisoning and acute poisoning. Among them, acute poisoning has the largest damage and rapid onset, and has a great impact on patients' health.Therefore, mastering the clinical characteristics of poisoning events can play a beneficial role in the further selection of emergency treatment plan.

Fat-soluble drugs is insoluble in water and soluble in fat and carbon tetrachloride, glycerin, grease and other organic solvents, drugs, it to each other with the phospholipid bilayer membrane fusion, easy to absorb, and compared with the water-soluble drugs are more likely to be through the liver metabolism, metabolic product by kidney, it has high utilization rate in clinic.However, in recent years, due to the improper use of fat-soluble drugs, patients

often suffer from fat-soluble benzodiazepines sedative hypnotics, fat-soluble calcium channel blockers and β -blockers, fat-soluble tricyclic antidepressants and other intoxication, which poses a serious threat to the safety of patients.In addition, organophosphorus pesticide (fat-soluble) in our country has a high utilization rate, severe organophosphate poisoning leads to multiple organs injury, treatment will cause death or disability, clinical treatment mainly gastric lavage, oxygen and other conventional treatment, and cooperate with medical drugs and blood dialysis, blood perfusion treatment, has obtained the certain effect, but the mortality rate is still high,Therefore, it is of great significance to explore more safe and effective treatment methods.

Lipid emulsion is the fat component used in total parenteral nutrition.Vein with fat emulsion (intravenous lipid emulsion, ILE) used in the treatment of cloth than the original because of local anesthetics, later also used to treat a variety of other lipotropy drug poisoning.The treatment of ILE is still in the preliminary stage and relatively limited.System evaluation to the treatment of acute poisoning of fat emulsion, found that support the overall quality in the research on the treatment of low or very low, but in the case report suggests that fat emulsion of verapamil, beta blockers, some tricyclic antidepressants, cloth than paid, chlorpromazine, and some

anti-arrhythmic drugs (such as, fluorine carney) poisoning patients have certain benefits].ILE may help treat hemodynamic instability in patients who have been poisoned by these drugs.

Possible adverse reactions of standard ILE treatment include hypertriglyceridemia, fat embolism, infection and hypersensitivity.Although these and other potential complications of ILE treatment have been reported, further studies are needed to determine the risk of complications from restricted ILE treatment in acute CCB overdose.

There are several speculations about the mechanism of ILE efficacy.The first mechanism is that fat emulsions act as a "lipid pool" that surrounds and disables lipophilic drug molecules.The second mechanism is that fatty acids in ILE provide a ready-made energy source for myocardium, thus improving cardiac function .In addition, ILE may act as a "lipidshuttle," wrapping toxins and transporting them to the liver and/or kidneys for metabolism.

In view of the fact that the research on the treatment of ILE still needs to be further improved and related adverse reactions need to be further discussed, we plan to launch a registered research program on the application of ILE.

1.2 research objectives :

(1) to study the therapeutic effect of ILE on acute poisoning of

fat-soluble substances.

(2) Further elucidate the related mechanisms of ILE in the treatment of fat-soluble drug poisoning.

(3) Standardize the relevant process of ILE detoxification treatment.

(4) Further explore the adverse reactions and coping strategies of ILE treatment.

2.1 Research subjects: According to the indications of ILE treatment poisoning in clinical toxicology, research subjects were divided into the following categories :

(1) calcium channel blocker poisoning

(2) β blocker drug poisoning

(3) tricyclic antidepressant poisoning

(4) the organophosphorus fat-soluble pesticide poisoning, such as bromine phosphorous, chlorpyrifos, and c, fenitrothion diazinon, methidathion, quetiapine phosphorus, butyl, thiazole phosphorus, oxygen pyrimidine phosphorus dimethoate, destroy the line p line, sulfur, phosphorus, and triazophos ethion, sulfoxide, phosphorus, sulfur, phosphorus, imines phosphorus worm, pyrazole fluorine sulphur phosphorous, isocarbophos, phorate, methyl parathion, parathion, dichlorvos, fenitrothion, etc.

(5) local anesthetic poisoning

(6) poisoning of other fat-soluble substances

2.1.1 Sample size At least 500 patients are planned to be included as observational subjects.

2.1.2 inclusion criteria :

(1) patients diagnosed with acute exposure to fat-soluble drugs and organophosphorus (fat-soluble) pesticides

(2) patients who failed conventional treatment, especially those with circulatory failure, such as ventricular arrhythmia, shock, and cardiac arrest, requiring intravenous fat milk treatment.

(3) non-allergic to lipid emulsion.

(4) signed informed consent.

2.1.3 exclusion criteria:

(1) patients with combined major organ dysfunction;

(2) patients complicated with malignant tumor;

(3) serious mental disorders affect the treatment;

(4) Incomplete clinical data.

2.2 Research design and methods:

When the fat emulsion infusion can cause serious adverse reactions, in combination with fat emulsion used for oral fat soluble drug poisoning guidelines [11], in accordance with the association of American medical toxicology 2016 recommended the latest plan for detoxification, fat emulsions as fat soluble drug poisoning causes hemodynamic instability, consider using to treat fat emulsion,

specific plan:① The first dose was given 1.5 mL /kg 20% fat milk for longer than 2-3min. If there was no reaction, it could be repeated.② then, the injection was continued at the rate of 0.25ml/(kg.min) and the efficacy was evaluated after 3min. If the efficacy was obvious, the dose was adjusted to 0.025ml/(kg.min) and the blood pressure, heart rate and other hemodynamic parameters were observed at least every 15min.③ If there is cyclic instability again when pushing at the speed of 0.025ml/(kg.min), the speed can be increased to 0.25ml/(kg.min), and in serious cases, the load can be pushed again

2.3 Statistical Methods

SPSS19.0 statistical software was used for data processing, and t test was used for measurement data.$P<0.05$ was considered statistically significant.The main efficacy indicators were provided with sample number, mean, standard difference and other statistics, and paired T-test (or the signed rank test of paired samples) was adopted.Descriptive statistics were used to summarize the data of secondary efficacy indicators, and sample number, mean and standard deviation were used for continuous variables.The classification variables were the number of cases and percentage.The paired T-test (or the signed rank test of paired

samples) was used to analyze continuous variables.The McNemar-bowkers test was used to analyze ordered variables.The efficacy analysis of this study was conducted using the full analysis set (FAS). Subjects who were unable to provide post-treatment efficacy data were excluded from the full analysis set, and the last data carry-over method (LOCF) was used to fill in the missing efficacy data.Safety analysis set (SS) was selected for safety analysis.

2.4 Announcement of quality control measures and research results

2.4.1 Research quality control Uniformly formulated data collection forms, and trained sample collectors before collecting original data.Data analysis will be performed by other study group members, and all staff involved in the collection, collation and analysis of data will sign confidentiality agreements.Subject selection in this study was determined by two investigators familiar with the intervention and reviewed by the project lead.Clinical data will be collected and analyzed by two other investigators.The project leader shall determine the content of objections during the research process.

2.4.2 End point

2.4.2.1 Primary end point

mortality within 24 hours

2.4.2.2 Secondary end point

(1) Time of circulation stabilization, including time of blood

pressure stabilization and time of malignant arrhythmia disappearance, etc.

(2) dosage of vasoactive drugs

(3) Mortality of patients at 1 week and 28 days

(4) occurrence of serious complications during ILE treatment

2.4.2.3 Criteria for Termination of the study If the study leader finds that the investigator seriously or persistently fails to comply with the protocol and other test procedures, which may interfere with the correct implementation of the study, the study leader has the right to suspend the study or abandon relevant study data.In case of termination of the experiment, the study leader shall provide relevant written reasons.The study termination criteria include but are not limited to:

(1) Unexpected, significant or unacceptable risks are found for the subject;

(2) Major errors were found during the execution of the test;

(3) The research drug/trial treatment is ineffective, or the continuation of the trial is pointless

2.5 Expenses of subjects This clinical trial was an observational study, aiming to observe the salvage treatment effect of intravenous fat milk on fat-soluble drugs and pesticides poisoning, and no corresponding intervention measures were taken in the treatment

process of patients.Fat milk is used as a life-saving measure only when the above-mentioned patients are still in critical condition such as circulatory failure after conventional treatment, so no financial compensation is given.