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Analysis of Case Reports of Poison Cases that Underwent Plasmapheresis Using Plasma Separator-NIGALE XJC 2000 and NIGALE DigiPla 80

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Abstract

The word "apheresis" is derived from the Greek word "aphaeresis," which means to separate. This describes manual plasma exchange, the removal of units of whole blood anticoagulated with acid citrate dextrose followed by centrifugation to separate the blood into the cellular elements and plasma [1]. The cellular elements were then mixed with a replacement for the discarded plasma and reinfused [2]. Therapeutic Plasma Exchange (TPE), is an apheresis treatment in which the plasma component of blood is removed and replaced with supplemental fluids or processed before being returned to the patient. This is the most commonly used procedure. The volume removed is such that if it were not replaced, significant hypovolemia resulting in vasomotor collapse would occur. As a result, the removed plasma must be replaced with some form of replacement fluid [3]. Managing organophosphate poisoning can at times be difficult especially when there is no history about the type of poison ingested and when the compound presents with no odour. Plasmapheresis effectively helps in the management of such cases in the toxicology department and also replaces the circulating levels of pseudocholinesterase in blood [4]. Organophosphates (OP) are used in insecticides and as pest controls. They inhibit acetylcholinesterase present in the erythrocyte membrane, skeletal muscles and nerve tissues and results in cholinergic crisis. These OP can be absorbed through mucous membrane, skin, conjunctiva, GIT and Respiratory tracts in accidental exposures or intentionally in suicides and homicides [5]. OP poisoning is common amongst farmers in the developing countries [6]. The skin absorption of these compounds are usually slow and hence the symptoms occur slow, this delays the patient admittance time from the time of exposure resulting in more serious complications [7]. Compounds can be classified based on the atoms on the phosphate: Phosphates: when the four atoms contain oxygen, Phosphothioates: when Sulphur is present, Phosphoramides: when nitrogen is present, Phosphoramidothionates: when both nitrogen and sulphur are present, Phosphonates: when carbon is present, Phosphothionates- when carbon and sulphur are present; OP compounds are metabolized by hydrolysis in the liver, the elimination of phosphothioates are slower than phosphates due to their lipophilic nature [8]. The inhibition of the enzyme AChE by the OP causes accumulation of ACh in the synapses. Traditional treatment with atropine and oximes to treat OP poisoning is insufficient to reduce the morbidity and mortality and hence plasmapheresis is used which effectively separates the antibodies, immunocomplexes, exogenous and endogenous toxins from plasma and provides replacement with plasma proteins and coagulation factors [9]. This study focuses to study the effect of the plasmapheresis using the plasma separator Nigale XJC 2000 and DigiPla 80.

Keywords: Aphaeresis; Immunocomplexes; Hematological parameters; Plasma

Materials and Methods

Patients

We retrospectively reviewed all PE procedures for 60 patients during a period of 34 months from January 2016 to October 2018 in the emergency department and Intensive Care Unit of our tertiary care teaching hospital, Vinayaga Mission Hospital, Salem. The diagnosis and indication for plasmapheresis were established by proper clinical and laboratory evaluation. The patient's age, weight, height, gender, and clinical indication along with pre-procedure hematological parameters (platelet, prothrombin time, INR, aPTT, complete blood count, bleeding, clotting time), renal, liver function tests and serology for HIV, hepatitis B and C viruses were recorded. A baseline chest X-ray and electrocardiogram were also done before the procedure. All procedures were done by experienced dialysis personnel under the supervision of medical resident who reported to the treating nephrologist.

A repeat chest X-ray was done to confirm catheter position after insertion of an internal jugular catheter. The goal was to perform five exchanges with 30-50 ml/kg of plasma removal per session to achieve a total removal of 150–200 ml/plasma per kg body weight which was performed using the P 3001 or P 4018 disposable plasma apheresis set. Once the target plasma was obtained, the procedure was discontinued. As replacement, we used a standard institution-based protocol of 100 ml of 5% albumin diluted in 1 L of normal saline along with 2-3 units of FFP which were infused at the end of the procedure. All PE procedures were done in the neurological Intensive Care Units using the Plasma Separator DigiPla 80 XJC 2000 of NIGALE by the intermittent flow method. All results were expressed as mean ± standard deviation and statistical analysis was done using paired simple t-test was used to analyze differences (pre-plasmapheresis and post-plasmapheresis) in various hematology parameters.

Plasmapheresis method

Patients were treated using centrifuge plasmapheresis machine (Plasma Separator DigiPla 80 or Plasma Separator XJC 2000, PRC) as per availability which is easy operational complying with EU standards (Tables 1-3). The Nigale NGL XJC 2000, distributed by NIGALE Biomedical Co, Sichuan, PRC, is a new cellular separator exclusively dedicated to plasma separation by apheresis. This instrument, characterized by an intermittent blood flow with a single venous access, adopts the technology, namely the separation of blood components according to their density gradient by applying an appropriate centrifugal force. It permits to obtain plasma without any cellular contamination. In our hospital ICU, we evaluated, in terms of effectiveness and efficiency, the qualitative and quantitative performances of this equipment. Between 2-3 volumes were treated in each session every other day as per requirement. Vascular access was established with a double-lumen catheter from the central vein (Figure 1).

Results

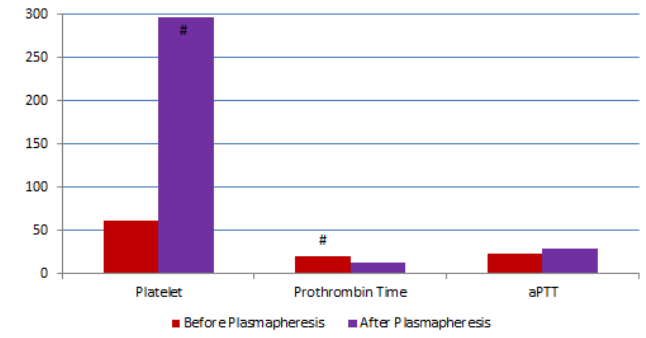

Figure 1: Change in Blood Parameters before and after Plasmapheresis.

Parameters	Before Plasmapheresis	After Plasmapheresis
Platelet (x109)	60.82 ± 72.12	297.12 ± 79.97#
Prothrombin Time (sec)	19.9 ± 5.7*	13.1 ± 4.1
aPTT (sec)	23.1 ± 2.11	28.8 ± 1.99

Table 1: Platelet count and prothrombin time after the plasmapheresis treatment. n= 60; values are mean ± SEM, #p<0.001, *p<0.01, There is a significant increase found in platelet count and prothrombin time after the plasmapheresis treatment. It was noted there an increase in aPTT time.

Parameters	Before Plasmapheresis	After Plasmapheresis
Pseudocholinesterase (IU/L)	220.82 ± 322.92	1557.12 ± 1379.37#

Table 2: Change in Pseudo cholinesterase levels before and after Plasmapheresis. n=60; values are mean ± SEM, #p<0.001, the mean level of serum PChE was increased after the PE procedure. A significant increase was observed statistically regarding PChE levels due to PE procedure (p<0.001).

Parameters	Before Plasmapheresis	After Plasmapheresis
INR	9.19 ± 8.92#	1.62 ± 2.64

Table 3: Change in INR levels before and after Plasmapheresis. n=60; values are mean ± SEM, #p<0.01, The INR level was increased after the PE procedure. A significant increase was observed statistically regarding INR levels due to PE procedure (p<0.01).

Discussion

Patients with immunologic disorders and toxicological exposures who respond poorly or are unresponsive to conventional therapy may recover after being treated with plasmapheresis. A variety of medical conditions have been treated with plasmapheresis. With respect to the removal of toxic substances from the blood, plasmapheresis may offer a rapid strategy for partial or complete removal of various poisonous agents. Organic phosphorus compounds can be absorbed quickly from skin, mucous membranes, gastrointestinal tract, eyes, and respiratory system. These compounds are distributed and accumulated in adipose tissue, liver, and kidney. Because they are stored in the adipose tissue, removal from the organ is slower.

Plasmapheresis is an apheresis procedure that separates and removes the plasma component from a patient. Plasma exchange is when plasmapheresis is followed by replacement with fresh frozen plasma infusion [10]. Plasmapheresis is performed by two different techniques: centrifugation or filtration. With centrifugation apheresis, whole blood is spun so that the four major blood components are separated out into layers by their different densities. With filtration plasmapheresis, whole blood passes through a filter to separate the plasma components from the larger cellular components of red blood cells, white blood cells, and platelets. Filtration plasmapheresis is commonly performed by nephrologists and intensivist mainly in the intensive care units [11].

The therapeutic benefit of plasmapheresis in acute poisoning and drug overdose is based on the rapid removal of drugs or toxins that cannot be eliminated adequately by usual therapeutic interventions. Plasmapheresis can remove rapidly toxins of all sizes, including protein- and lipid-bound toxins with a low volume of distribution [12]. As for any extracorporeal technique, plasmapheresis only removes substances located in the vascular compartment. As the volume of distribution increases, the usefulness of any Extracorporeal Treatments (ECTR) decreases substantially [13].

The tissue stores of a poison will remain unaffected except for re-equilibration with decreasing plasma concentrations. Other possible benefits of plasmapheresis in the treatment of poisoning and drug overdose are the effects on toxins induced complications such as hemolysis or thrombotic thrombocytopenic purpura. In addition, infusion of normal plasma may have beneficial effects, independent of removal of toxic circulating compounds [14].

Plasmapheresis involves withdrawal of venous blood, separation of plasma from blood cells, and reinfusion of cells with fresh frozen plasma or another replacement solution. Plasma and blood cells are separated by centrifugation or membrane filtration. Usually, the equivalent of 1 to 1.5 plasma volumes (or 2.5 to 4.0 L) is removed during a session [15]. To maintain plasma volume, the removed plasma

is replenished with an equal amount of replacement fluids. The typical replacement fluids are fresh-frozen plasma, 5% albumin or other plasma derivatives (e.g., cryosupernatant), and crystalloids (e.g., 0.9% saline, Ringer's lactate). The choice of fluid affects oncotic pressure, coagulation, efficacy of the procedure, and potential side effects.

Albumin usually is preferred to plasma because of the risk of hypersensitivity reactions and transmission of viral infections with the latter. For some indications for which infusion of normal plasma may be beneficial (e.g., organophosphate poisoning), fresh frozen plasma is the preferred replacement solution [16]. With poisons tightly bound to albumin, removal by plasmapheresis without replacement of albumin theoretically could increase its free fraction and may cause a transient resurgence of clinical toxicity. Similarly, in drugs that are highly bound to alpha-1-acid glycoprotein, such as quinidine, the combination of 5% albumin and fresh frozen plasma could be considered, although alpha-1-acid glycoprotein has a low binding capacity and there are no studies to confirm the clinical efficacy of this approach [17-19].

Conclusion

In this plasmapheresis study performed on 60 patients, it was found out that plasmapheresis showed a significant increase in the platelet count (60,000 to 2,97,000) and prothrombin time than the conventional treatment modalities (atropine, oxime treatment and gastric lavage). An increase in partial thromboplastin time was also observed. The pseudo cholinesterase levels also increased significantly after plasmapheresis. All these findings prove that plasmapheresis is an effective and promising treatment method for toxic cases. Literature also confirms plasmapheresis to be effective in amitriptyline, phalloid mushroom poisoning and in poisoning with drugs like propranalol, amlodipine, diltiazem, carbamazepine, verapamil, L- thyroxine, theophylline and mercury poisoning. Plasmapheresis and TPE are the terms used to describe different procedures and are often misused. Plasmapheresis is where less than 15% of total plasma is removed but not replaced whereas in TPE, the separated plasma is replaced with albumin, FFP or other crystalloids. The limitations of this study are its retrospective nature and the small study population. More studies must be staged explaining the provisional role of plasmapheresis and its rationale in measuring the substance elimination which is supported by high plasma protein binding (>80%) and low volume of distribution of the toxins (<02 L/kg bw). However, this study has proved an increase in plasma cholinesterase levels and improved oxygen saturation following plasmapheresis and patients showed good clinical improvement. The widespread use and availability of plasmapheresis machines in all toxicology departments and clinics should be made mandatory for effective handling of poison cases and reducing mortality.

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