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RESEARCH ARTICLE

NOW HELPFUL IS PLASMAPHERESIS IN THE MANAGEMENT OF ACUTE LIVER FAILURE IN ADULTS

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Abstract

Objective: To compare the efficacy of plasmapheresis against other modalities of management in patients of acute liver failure
Study Type: Cross-sectional Study
Place and Duration of Study: Department of Gastroenterology, Pak Emirates Military Hospital Rawalpindi, from **June 2023 to July 2024**
Methodology: Patients of either sex between 18 years to 75 years of age meeting the acute liver failure criteria were enrolled into the study. Patients with liver failure due to pre-exiting liver disease, septicaemia, and heart failure were excluded from the study. The detailed history and clinical information were taken from all individuals after enrolment. The blood sample for serum alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, prothrombin time, international normalised ratio, bilirubin, and creatinine were taken pre- and post- plasmapheresis sessions. The plasmapheresis was done until clinical improvement was achieved. The data was analysed using the Statistical Package for Social Sciences (SPSS) Version 25.0.
Results:A total of one hundred and seventy-six (n=176) were included in this study with median age of 47.00 (36.00-57.00) years. There were 53 (30.11%) females and 123 (69.89%) males. The median pre-plasmapheresis serum ALT was 602.00 (455.00-764.00) while post-plasmapheresis it was 324.00 (192.00-463.00). The median pre-plasmapheresis serum bilirubin was 34.00 (25.00-43.00) while post-plasmapheresis it was29.00 (21.00-39.00). The international normalised ratio was 24.00 (21.00-26.00) and 19.00 (15.00-20.00) pre and post plasmapheresis session. The improvement in liver markers was statistically significant ($p<0.001$) post plasmapheresis.
Conclusion: The plasmapheresis sessions were very effective in improving the outcome in patients of acute liver failure.

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Introduction:-

Liver is the metabolic powerhouse of body with a very diverse role from biosynthesis of important proteins and enzymes to their catabolism, excretion and detoxification of the body.[1] Many factors contribute to its dysfunction

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including viruses, bacteria and genetic disorders like hemochromatosis and Wilsons disease. This dysfunction cane be acute, slowly progressive (chronic) and acute on chronic. Many organizations and societies including Asian Pacific Association for the Study of the Liver (APASL) and the European Association for the Study of the Liver (EASL) have defined the liver failure with some variations in their definitions and parameters. Acute liver failure has been defined as a rapid deterioration in liver functions which is characterized by jaundice, coagulation impairment, and hepatic encephalopathy in those individuals who have no previous hepatic impairment.[2]

The liver dysfunction is not only limited to alteration in its diverse biosynthetic roles or detoxification but it also threatens the function of other organs starting from itching of a skin to cardiac and neuronal impairment like hepatorenal syndrome, cerebral oedema, hepatic encephalopathy, multi organ dysfunction syndrome (MODS) and death.[3-5] Since the identification of catastrophic complications of hepatic failure, the medical professionals have been long trying to find a viable and patients friendly cure with better mortality and morbidity indices, and better outcomes. Initially, it was medically conservative management but later more proactive time validated procedures and methods include plasmapheresis (PLEX), exchange transfusions (ET), molecular adsorbent recirculating system (MARS), extracorporeal albumin dialysis systems (ECADS), single pass albumin dialysis (SPAD), and fractionated plasma separation and adsorption (FPSA) have been developed and used.[6-8] Despite all these developments, the mortality and morbidity with ALF persists.[9,10] Among these measures, he Liver Transplant (LT) remains the gold standard and treatment of choice. And the conservative medical treatment being the least effective. The only and foremost problem with the liver transplants is finding a suitable donor and somebody at least willing to donate.[11,12] Keeping this in view, the liver dysfunction support systems (LDSS) are next in line, they act as bridge for liver transplant in some.Among these LDSS, PLEX has shown promising results though the data is very limited in our community and still needs validation in our medical setups.

Keeping above in view, this prospective study was planned to see effect of PLEX in acute liver failure patients and its impact on mortality and morbidity indices. Moreover, this study will also look into changes in hepatic markers, pre- and post- PLEX sessions. This study will help our clinicians in this resource constraint community to offer better treatment option in the absence or non- availability of liver transplant.

Methodology:-

This observational cross-sectional study was conducted at Department of Gastroenterology, Pak Emirates Military Hospital Rawalpindi **from June 2023 to July 2024 for a period of 12 months**. The study was started after approval of study protocol form institutional Ethics Committee Approval A/28/ERC/46/24**.**Due to rare nature of the complication (ALF), the formal sample size calculation was not done. Consecutive sampling technique was used to enrol patients. The informed consent was taken for patients and from guardians/ family members in case patient was not in condition to give consent.

Inclusion Criteria:

Patients of either sex between 18 years to 75 years of age meeting the ALF criteria of EASL were enrolled into the study.[2]

Exclusion Criteria:

Patients with liver failure due to pre-exiting liver disease, septicaemia, and heart failure were excluded from the study.

The detailed history and clinical information was taken from all individualsafter enrolment. The blood sample for serum alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), prothrombin time (PT), international normalised ratio (INR), bilirubin (BR), and creatinine were taken pre- and post- PLEX sessions. For PLEX, double lumen 11-Fr dialysis catheter was inserted in either right femoral vein or right internal jugular vein depending upon the patient condition and vascular status. After explaining the procedure, PLEX sessions were started on Machine.The replacement fluid was 100% fresh frozen plasma (FFP). The requirement of FFP was calculated using Kaplan formula (PV = [0.065 X wt(kg)] X [1-Hct]). The Plex was done by trained medical staff and continuous monitoring was done during PLEX sessions. The sessions were done daily until a satisfactory clinical improvement was achieved. Any complication during the procedure was noted. Patient were also kept in supportive medical therapy like parenteral nutritional supplements and vitamins, prophylactic antibiotics and renal replacement therapies like haemodialysis in case of renal compromise.

The data was analysed using the Statistical Package for Social Sciences (SPSS) Version 25.0. The Shapiro-Wilk Test was used to check the normality of data. The quantitative variables were presented using mean ± standard deviation (SD) or median and inter-quartile range (IQR) depending on the results of data normality test. The qualitative variables were presented using frequencies and percentages (%). The Chi-square test was used for categorical variables, student T-test was used to compare means of normally distributed variables while the Mann-Whitney U test was used to compare means of skewed variables. The p-value less than 0.05 was taken as significant.

Results:-

A total of one hundred and seventy-six (n=176) were included in this study with median age of 47.00 (36.00-57.00) years. There were 53 (30.11%) females and 123 (69.89%) males. The hypertension and diabetes were seen in 56 (31.82%) individuals. The median pre-PLEX serum ALT was 602.00 (455.00-764.00) while post-PLEX it was 324.00 (192.00-463.00). The median pre-PLEX serum bilirubin was 34.00 (25.00-43.00) while post-PLEX it was29.00 (21.00-39.00).Rest of the details are given in Table-I.

Table I:- Characteristics of sample population with ALF (n=176).

Characteristics	Values
Age (years)	47.00 (36.00-57.00)
Gender	
Male	123 (69.89%)
Female	53 (30.11%)
Hypertensionn(%)	56 (31.82%)
Diabetesn(%)	56 (31.82%)
Pre-Plex Liver Makers	
ALT	602.00 (455.00-764.00)
AST	506.00 (298.50-617.50)
Total Bilirubin	34.00 (25.00-43.00)
PT	24.00 (21.00-26.00)
INR	1.71 (1.50-1.86)
Serum Creatinine	91.00 (75.00-114.75)
PLEX Sessions	
1-3	29 (16.48%)
4-6	84 (47.73%)
>7	63 (35.80%)
Survival	
Died	13 (7.39%)
Alive	163 (92.61%)

The strong statistical association was found between pre- and post- PLEX sessions. Almost every marker showed a statistically significant reduction in levels pre and post dialysis sessions. The details of results are given in Table-II.

Table II:- Statistical analysis of Pre and Post PLEX liver marker levels (n=176).

Variables	Pre-Plex Markers	Post-PLEX markers	p-value
Pre-Plex Liver Makers			
ALT	602.00 (455.00-764.00)	324.00 (192.00-463.00)	<0.001
AST	506.00 (298.50-617.50)	263.00 (167.00-396.00)	<0.001
Total Bilirubin	34.00 (25.00-43.00)	29.00 (21.00-39.00)	<0.001
PT	24.00 (21.00-26.00)	19.00 (15.00-20.00)	<0.001
INR	1.71 (1.50-1.86)	1.5 (1.35-1.78)	<0.001
Serum Creatinine	91.00 (75.00-114.75)	80.00 (69.00-96.75)	<0.001

Discussion:-

Liver has very important role in maintaining the homeostasis of the body. Its dysfunction leads to very drastic outcomes including haemorrhage, accumulation of cytotoxic substances, skin bruises, neuronal complications and even death.[3-5]This study was done to evaluate the response of liver enzymes to plasmapheresis therapy. In this study, a total of one hundred and seventy-six (n=176) patients were included with median age of 47.00 (36.00-57.00) years. The median serum alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, prothrombin

time, international normalised ratio, bilirubin, and creatinine showed marked improvement in levels post plasmapheresis sessions. The PLEX did not only improve the liver markers but also brought clinically recovery in these patients. Our of one hundred and seventy-six individuals included in the study only 13 (7.39%) percent people died in 30 days.

The EASL and American Society of Apheresis (ASFA) have recommended as grade-I and first line treatment option for acute liver failure and also for Wilsons disease associated liver dysfunction.[2,13] There are no as such consolidated guidelines for the frequency and duration of plasmapheresis session but it has been observed that biochemical liver markers and other survival indices improve even with a one session of plasmapheresis.[14]In this study too, we found a significant improvement in a clinical status of of patients after second session of plasmapheresis though none of our patients showed clinical improvement after one session of PLEX. This might be explained by duration of disease and removal of toxic metabolites from the body thus improving the not only the biochemical profile but also the clinical status. In different investigations, patients received treatments on an alternate day or the same schedule until their clinical condition improved, they passed away, or they had a liver transplant.[15,16]

One of its kind randomised clinical trial was conducted to compare PLEX with standard supportive medical therapy which was later followed by a systemic review comparing different PLEX regimens.[17,18] Both the trial and systemic review showed a significant benefit of PLEX. The PLEX not only improved the liver markers but also a brought a significantly promising clinical recovery in patients. It also showed better mortality and morbidity indices in the patients undergoing PLEX. In this study, the PLEX was done on daily basis until clinical recovery was achieved. This research also found a significant reduction in hepatic transaminases, INR and PT which was also statistically proved ($P<0.001$).

In another meta-analysis conducted by Kanjo et al comparing different liver support systems, showed PLEX had a marked improvement in mortality indices when compared against standard medical therapy.[19] In this research too, only 13 (7.39%) died during the treatment regimen or within one month of ALF despite PLEX while 163 (92.61%) survived the first month post-PLEX. This improved survival in ALF patients might be due to removal toxic substances from the blood and injury inciting agents.

In a randomised clinical trial, the PLEX is reliable and efficient in ALF patients and may increase survival.[20] Similar to the findings of our research, in which we also a found a improvement in laboratory markers and clinical condition of the patient. This might be due to removal of cytokines, ammonia and toxic metabolic agents. In another study, the researchers found the PLEX to be effective therapy for ALF.[21]

Limitations

This study has few limitations as well. First, it is a single centre study with limited sample size. Moreover, this study has inherited bias of being cross-sectional, so a long-term and randomised clinical trial needs to be done so true outcomes can be ascertained. We also suggest hybrid treatment regimens with MARS, ECAD and CRRT should also be evaluated for better management of patients who are waiting for LT and do not have the donors.

Conclusion:-

In this study, we have identified the PLEX as one of the efficient and reliable treatment modality for patients waiting for liver transplant, cannot afford LT or are not suitable for it. The PLEX has better safety and mortality profile.

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Conflict of Interest:

None.

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