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Original Article

Impact of Regular Hemodialysis on Short- and Long-Term Liver Function Evaluated by the Galactose Single Point Test

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ABSTRACT

Background: Liver illness significantly exacerbates the advancement of end-stage renal disease [ESRD]. Patients on long-term maintenance hemodialysis may experience enhanced liver function. The galactose single point [GSP] test is a novel technique for evaluating residual liver function.

Aim of the study: The study aims to assess the influence of regular hemodialysis on liver function, as measured by the galactose single-point test.

Patients and Methods: This prospective cohort study involved recruiting 80 patients on regular dialysis from the hemodialysis unit of the Internal Medicine department at Al-Azhar University Hospital, New Damietta, who met our selection criteria for six months.

Results: We found a powerful negative correlation between GSP and months of dialysis; significant negative correlations are observed between hemodialysis duration and both post-dialysis GSP and predialysis GSP, indicating that longer hemodialysis duration is associated with lower levels of GSP before and after dialysis.

Conclusion: Patients undergoing long-term hemodialysis maintenance observe a positive enhancement in liver functionality. Galactose metabolism relies on both liver blood flow and hepatic functional mass. It is possible that after hemodialysis [HD], there is a modest increase in blood flow to the liver, potentially leading to enhanced liver function, as observed in the GSP test

Keywords: Galactose Single Point test; End-Stage Renal Disease, Hemodialysis; Liver Function.

INTRODUCTION

Chronic kidney disease [CKD] is a widespread global health issue affecting nearly all age groups from children to elderly population [1]. Chronic kidney disease [CKD] is an escalating global public health issue characterized by elevated morbidity, death, and significant healthcare expenditures [2].

Liver disease significantly contributes to the occurrence of end-stage renal disease [ESRD]. This is due to constriction and narrowing of renal blood vessels due to substances liberated in the circulation of patients with advanced liver disease [3].

Patients on long-term maintenance hemodialysis may have an enhancement in liver function. However, a single high-definition [HD] session has a minimal impact on liver function, as evaluated by the galactose single point [GSP] test [4].

The galactose elimination capacity [GEC] test was developed years ago to assess liver function in people quantitatively. However, the necessity for numerous blood samples to evaluate the reduction in galactose levels rendered the test challenging in clinical settings. Consequently, researchers shifted their focus to the feasibility of utilizing galactose single point [GSP] techniques for evaluating liver function [5].

The United States Department of Health and Human Services and the Food and Drug Administration have recently approved the GSP test. This evaluation quantifies the hepatic clearance of drugs, irrespective of their metabolic condition. GSP levels are associated with the severity of cirrhosis and hepatocellular cancer [4].

The study's objective was to assess the influence of regular hemodialysis [HD] on liver function, as measured by the galactose single point [GSP] test.

PATIENTS AND METHODS

In this prospective cohort study, we recruited 80 patients on regular dialysis from the hemodialysis unit of the Internal Medicine department, Al-Azhar University Hospital, New Damietta, who fulfilled our selection criteria for six months.

Adults on regular dialysis three times weekly for four hours per session were included. In contrast, patients with decompensated liver disease, HCC, or Hepatitis were excluded.

The recruited patients had a comprehensive assessment, including a detailed medical history, thorough general and local clinical examinations, and Laboratory assessments, including a complete blood count [CBC], liver function test, coagulation profile, and renal function test.

Procedures:

An intravenous infusion of a galactose solution with a 0.4 g/mL concentration was supplied at 0.5 g/kg body weight. The infusion was restricted to a length of three to five minutes. The blood collection lasted for 60 minutes after the injection.

Galactose Measurement:

Blood samples for each galactose assay were obtained 60 minutes post-infusion of galactose. The blood samples were obtained by puncturing a vein with a needle 60 minutes post-injection. Pre-dialysis Pre-hemodialysis GSP testing was conducted. Glycated serum protein [GSP] testing was conducted six months after dialysis.

The galactose levels were determined using a modified neonatal screening test employing a colorimetric galactose dehydrogenase technique. We used Galactose and Lactose Colorimetric/Fluorometric Assay Kit [Catalouge number MAK011] Produced by Sigma Aldrich [Sigma-Aldrich Co. LLC, USA], on SPECORD® 40/50, single or double beam spectrophotometer [Analytik Jena Inc., USA]. The calibration curve's concentration range typically falls between 50 and 1000 mg/mL.

Statistical Analysis:

The gathered data was processed, encoded, and organized using the Statistical Program for Social Science [IBM Corp. Released 2017]. The software employed is IBM SPSS Statistics for Windows, Version 25.0. It was created by IBM Corporation and is based in Armonk, New York. The data were appropriately presented and evaluated based on the type of information obtained for each parameter. For example, the continuous data were summarized by their arithimatic mean, median [interquartile range] and standard deviations. In addition, the categorical data were summarized by frequency and percentages. Values before and after dialysis was compared by paired samples "t" test or Wilcoxon signed rank. The correlation between two variables was measured by the calculation of Spearman's correlation coefficient and p value < 0.05 was considered significant.

RESULTS

Table 1 presents the study subjects' baseline demographic and clinical characteristics, with a sample size n=80. In Table 2, the biochemistry parameters for the study subjects are provided.

Table 3 compares pre-dialysis and post-dialysis levels of the Galactose Single Point [GSP] among the study subjects. The pre-dialysis GSP level has a mean of 518.27 g/mL with a standard deviation of 201.50. The GSP level decreases to a mean of 431.65 g/mL post-dialysis, indicating that the decrease in GSP levels from pre-dialysis to post-dialysis is statistically significant [p=0.008].

In Table 4, examining correlations between the Galactose Single Point [GSP] and various parameters, only two show statistical significance: a powerful negative correlation between GSP and months of dialysis with a p-value of less than 0.001, suggesting that GSP levels decrease significantly with the increase in dialysis duration; and a powerful positive correlation with predialysis GSP, with the p-value is less than 0.001, indicating high consistency in GSP measurements under similar conditions.

In Table 5, significant negative correlations are observed between hemodialysis duration and both post-dialysis GSP [g/mL] [$rs = -0.980$, $p < 0.001$] and pre-dialysis GSP [g/mL] [$rs = -0.970$, $p < 0.001$], indicating that longer hemodialysis duration is associated with lower levels of GSP before and after dialysis.

Table [1]: Baseline demographic data in the studied subjects

Study subjects n=80		
Age (years)	Mean ± SD	60.26 ± 6.29
	Median (Min-Max)	60.50 (48.00-72.00)
Female (%)	Female	27(33.8%)
	Male	53(66.2%)
Predialysis body weight (kg)	Mean ± SD	63.02 ± 9.67
	Median (Min-Max)	61.00 (53.00-91.00)
Duration of Dialysis (months)	Mean ± SD	72.58 ± 34.26
	Median (Min-Max)	66.50 (37.00-152.00)

Table [2]: Biochemistry parameters among studied subjects

Study subjects n=80		
Random Glucose (mg/dL)	Mean ± SD	145.34 ± 53.75
	Median (Min-Max)	133.50 (91.00-285.00)
AST (U/L)	Mean ± SD	27.32 ± 13.39
	Median (Min-Max)	24.50 (14.00-64.00)
ALT (U/L)	Mean ± SD	24.10 ± 12.07
	Median (Min-Max)	23.50 (11.00-58.00)
Alk-p (U/L)	Mean ± SD	82.28 ± 39.32
	Median (Min-Max)	68.50 (50.00-238.00)
Albumin (g/dL)	Mean ± SD	2.94 ± 0.58
	Median (Min-Max)	2.9 (2.0-4.0)
Uric acid (mg/dL)	Mean ± SD	7.26 ± 0.86
	Median (Min-Max)	6.90 (6.60-10.20)

Table [3]: Comparison of predialysis and post-dialysis GSP among studied subjects

		Predialysis	Post-dialysis	Test Result
GSP (g/mL)	Mean ± SD	518.27 ± 201.50	431.65 ± 121.94	Z: 2.662, p=0.008*
	Median (Min-Max)	492.00 (309.00-1130.00)	420.06 (278.00-718.46)	

Table [4]: Correlation between GSP and studied parameters

	r_s	p
Age (years)	0.212	0.059
Body weight (kg)	-0.085	0.453
Glucose (mg/dL)	0.073	0.520
AST (U/L)	0.084	0.457
ALT (U/L)	0.01	0.932
Alk-p (U/L)	0.15	0.185
Albumin (g/dL)	0.069	0.544
Uric acid (mg/dL)	-0.149	0.187
Predialysis Cr (mg/dL)	0.135	0.234
Post-dialysis Cr (mg/dL)	-0.116	0.306
Pre-dialysis BUN (mg/dL)	-0.038	0.739
Post-dialysis BUN (mg/dL)	-0.091	0.424
Predialysis Hematocrit (%)	-0.056	0.623
Post-dialysis Hematocrit (%)	-0.093	0.410
Duration of Dialysis (months)	-0.980	<0.001*
Predialysis GSP (g/mL)	0.990	<0.001*

r_s: Spearman correlation coefficient, * for significant p-value (<0.05)

Table [5]: Correlation between hemodialysis duration and studied parameters

	r_s	p
Post-dialysis GSP (g/mL)	-0.980	<0.001*
Predialysis GSP (g/mL)	-0.970	<0.001*
Age (years)	-0.191	0.089
Predialysis body weight (kg)	0.069	0.546
Glucose (mg/dL)	-0.091	0.424
AST (U/L)	-0.070	0.535
ALT (U/L)	-0.033	0.769
Alk-p (U/L)	-0.136	0.229
Albumin (g/dL)	-0.073	0.517
Uric acid (mg/dL)	0.125	0.270
Predialysis Cr (mg/dL)	-0.135	0.232
Postdialysis Cr (mg/dL)	0.096	0.396
Predialysis BUN (mg/dL)	0.053	0.640
Postdialysis BUN (mg/dL)	0.090	0.430
Predialysis Hematocrit (%)	0.072	0.526
Post-dialysis Hematocrit (%)	0.087	0.442

r_s: Spearman correlation coefficient, * for significant p-value (<0.05)

DISCUSSION

Chronic kidney disease (CKD) is an escalating global public health issue characterized by significant morbidity, mortality, and excessive healthcare expenditures [2]. Liver illness significantly contributes to the onset of end-stage renal failure. Patients receiving long-term hemodialysis may observe enhancements in liver function [4]. The galactose single-point test is innovative in evaluating residual liver function [5].

The study seeks to assess the effect of conventional hemodialysis on hepatic function, as measured by the galactose single point (GSP) test. The participants' average age is recorded as 60.26 years. The gender distribution exhibits a more significant percentage of males (66.2%) than females (33.8%). This age difference was previously noticed in ESKD from the same study demographic area [6]. The duration of dialysis has a mean of 72.58 months. In the study of **Hou *et al.*,** the mean dialysis duration was 60.77 months; they noticed that the duration of hemodialysis may influence the GSP level [4].

Evidence demonstrates that individuals with chronic kidney disease (CKD) display diminished serum levels of ALT relative to those with normal kidney function. This raises the question of whether the reduced levels are attributable to chronic kidney disease-related factors or the hemodialysis treatment [7]. Indeed, **Fabrizi *et al.*** [8] found that individuals undergoing hemodialysis (HD) had lower levels of alanine aminotransferase (ALT) compared to patients with chronic kidney disease (CKD) who were receiving conservative treatment (predialysis). This indicates that ALT serum levels decrease as renal dysfunction worsens.

In this study, the liver function biochemistry parameters are within normal levels; the AST level has a mean of 27.32 U/L, while the ALT level shows a mean of 24.10 U/L. The alkaline phosphatase presents a mean of 82.28 U/L. Albumin levels have a mean of 2.94 g/dL. The findings of **de Oliveira Liberato *et al.*** seven support our data and suggest that hemodilution may contribute to reducing ALT levels.

Our liver function biochemistry findings were slightly higher than those of Hou et al.[4]. Transaminase enzyme levels (AST and ALT) were significantly decreased in patients with renal insufficiency receiving hemodialysis. Moreover, a substantial decrease in these enzyme levels was seen when comparing predialysis with post-dialysis readings [9].

Curiously, the patients undergoing hemodialysis experienced fluid accumulation before the dialysis session, yet this decreased once the session conducted. Indeed, one study has shown that ALT levels are reduced before hemodialysis and elevated post-dialysis, exhibiting an inverse relationship with the reduction in body water weight [10]. The liver is essential for the regulation of glucose levels. The liver does gluconeogenesis during low plasma glucose levels and glycogenolysis during high plasma glucose levels [11].

The relationship between galactose metabolism and hepatic blood flow in hemodialysis patients is intricate. Studies on rats with glycerol-induced acute renal failure demonstrated an initial decrease in cardiac output and hepatic blood flow within the first 12 hours following induction. Nevertheless, a further elevation in these values was observed between 24 and 48 hours, as evaluated using radioactive microspheres [11].

We compare predialysis and after-6-month post-dialysis levels of the Galactose Single Point among the study subjects. Post-dialysis GSP level decreases to a mean of 431.65 g/mL, indicating that the decrease in GSP levels from predialysis to post-dialysis is statistically significant (p=0.008).

The metabolism of galactose is similarly influenced by hepatic blood flow. In rats, a fall in blood flow below a specific threshold resulted in a reversible reduction in both galactose elimination and oxygen uptake, which co-occurred with the decrease in blood flow [12]. **Van Der Hoven *et al.*** In individuals with chronic hemodialysis, the hepatic clearance of sorbitol exhibited no significant alterations before and after the procedure. The hepatic extraction of sorbitol is inversely related to hepatic blood flow and is reduced compared to healthy individuals [13].

In our current study, we discovered that HD treatment enhanced hepatic blood flow and increased galactose metabolism, aligning with the findings of **Hou *et al***.[4]. Unlike our results, **Rootjes *et al.***

discovered that hemodialysis patients exhibited reduced splanchnic blood flow, cardiac output, and stroke volume, as evidenced by stable clinical parameters such as blood pressure [14].

Post-dialysis, blood flow is reinstated to baseline levels autonomously. This suggests renal replacement therapy temporarily diminished splanchnic perfusion in critically ill individuals with stable hemodynamics [15].

The current investigation could not identify any significant link among GSP, AST, or ALT. Unlike our study, Tang and Hu found positive correlations between GSP, AST, and ALT [16]. This could be due to different study samples that conduct their work on regular volunteers and cirrhotic patients. Also, **Hou *et al.*** [4] find no significant correlation between GSP and liver function parameters.

We found a significant negative correlation between hemodialysis duration and both post-dialysis GSP ($p < 0.001$) and predialysis GSP ($p < 0.001$), indicating that longer hemodialysis duration is associated with lower levels of GSP before and after dialysis. Also, **Hou *et al.*** [4] discovered an inverse correlation between the level of galactose and the number of years a person has been undergoing maintenance hemodialysis (HD).

Ultimately, the patients in this study who have been doing maintenance hemodialysis for multiple years have observed an enhancement in their liver function. They were considering that galactose metabolism depends on hepatic blood flow and the liver's functional mass, examining whether there is a slight increase in liver blood flow after hemodialysis is crucial. The GSP test suggests that this augmentation in blood flow may improve liver function.

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