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Dialyzers as a Cause of Hemolysis

Hemoliz Nedeni Olarak Diyalizörler

Gürkan YURTERİ [1*], Sibel ADA [2]

[1] Rentek Hemodialysis Center, İstanbul, Türkiye

[2] Department of Nephrology, Prof.Dr.Cemil Tascıoglu City Hospital, İstanbul, Türkiye

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Abstract

Objective: Hemolysis is a rare adverse effect of hemodialysis. ıt is induced by chemical pollution, heat, or mechanical harm to clogged hemodialysis lines. Lactate dehydrogenase transforms pyruvate to lactate in the absence of oxygen to make energy. LDH serum levels are raised due to tissue breakdown. A number of clinical illnesses, such as hemolytic disorders, are associated with high serum LDH.

Both the Rexeed and Leoceed dialyzers are made by AsahiKASEI. They had the same membrane architecture and permeability, but blood entry angle, chamber length, and hole count varied. The aim of this study is to examine if dialyzer design affects hemolysis.

Materials and Methods: A total of 142 patients who were chronically undergoing hemodialysis therapy at the Rentek Hemodialysis Center for a total of 12 hours per week were included. A retrospective examination of the patients was performed. The pre-HD and post-HD LDH levels of individuals who had undergone hemodialysis with both dialyzers during separate sessions of hemodialysis were compared.

Results: A hundred forty-two patients (63% female) on hemodialysis (HD) treatment were enrolled in the study. Twenty-eight patients (20%) had diabetes, 45 had hypertension (32%) and 16 had ischemic heart disease (11%) as a comorbid condition.

When LDH difference is compared between groups Leoceed dialyzer group) had statistically significantly higher LDH difference when compared with Rexeed dialyzer group (49.1 ± 20 U/l vs 229.8 ± 24.45 U/l; p=0.008).

Conclusion: It is possible that the design of the dialyzer contributes in some way to the cell damage that is caused by the larger serum LDH increase in the Leoceed dialyzer. In order to carry out corrective studies on dialyzer design, it would be helpful to analyze the impact of dialyzer design on cell damage using a larger series of patients.

Keywords: Hemodialysis, Dialyzer, Hemolysis

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Öz

Amaç: Hemoliz, hemodiyalizin nadir görülen bir komplikasyonudur. Kimyasal kirlilik, ısı veya tıkanan hemodiyaliz hatlarına mekanik zarar verilmesi sonucu oluşur. Laktat dehidrogenaz, piruvatı laktata dönüştüren ve serum seviyeleri, doku parçalanması nedeniyle yüksen bir enzimdir. Hemolitik bozukluklar gibi bir dizi klinik hastalık, yüksek serum LDH'si ile ilişkilidir. Hem Rexeed hem de Leoceed diyalizörler AsahiKASEI tarafından üretilen aynı zar yapısına ve geçirgenliğine sahip diyalizörlerdir ancak kan giriş açısı, hazne uzunluğu ve por sayısı farklıdır. Bu çalışmanın amacı, diyalizör tasarımının hemoliz üzerine etkisini incelemektir.

Gereç ve Yöntemler: Rentek Hemodiyaliz Merkezi'nde, haftada toplam 12 saat hemodiyaliz tedavisi gören 142 hasta retrospektif olarak değerlendirildi. Ayrı hemodiyaliz seanslarında her iki diyalizör ile hemodiyalize giren bireylerin HD öncesi ve HD sonrası LDH seviyeleri karşılaştırıldı.

Bulgular: Çalışmaya hemodiyaliz (HD) tedavisi gören 142 hasta (%63 kadın) dahil edildi. Komorbid durum olarak 28 (%20) hastada diyabet, 45 hastada (%32) hipertansiyon ve 16 hastada (%11) iskemik kalp hastalığı vardı.

LDH düzeyi, Leoceed diyalizer grubunda Rexeed diyalizer grubuna göre istatistiksel olarak anlamlı düzeyde yüksekti (49,1 ± 20 U/l vs 229,8 ± 24,45 U/l; p=0,008).

Sonuç: Diyalizörün tasarımı, hücre hasarını arttırarak Leoceed diyalizördeki LDH yüksekiğine neden oluyor olabilir. Diyalizör tasarımı konusunda düzeltici çalışmalar yapabilmek için daha geniş hasta serileri kullanılarak diyalizör tasarımının hücre hasarı üzerindeki etkisinin analiz edilmesi faydalı olacaktır.

Anahtar Kelimeler: Hemodiyaliz, Hemoliz, Diyalizör

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[*]**Sorumlu Yazar (Corresponding Author):** Gürkan Yurteri, **e-mail**: gyurteri@hotmail.com

Introduction

Hemolysis is a well-known yet uncommon complication of hemodialysis. Hemodialysis hemolysis is often triggered by chemical pollution, heat, or mechanical damage to erythrocytes from blocked hemodialysis lines (1-7).

Lactate dehydrogenase, often known as LDH, is an intracellular enzyme that converts pyruvate to lactate to provide energy in the absence of oxygen. The breakdown of tissue is the major cause of elevated blood LDH levels (8,9). Multiple clinical conditions, particularly hemolytic diseases (10-15), are associated with high LDH levels in the blood.

AsahiKASEI is the manufacturer of both the Rexeed (Japan) and the Leoceed (Japan) dialyzers. The construction and permeability of the membranes were same, but the angle at which blood entered the chamber, chamber length, and number of holes varied (Figure 1).

There have been cases of hemolysis resulting from improperly made or kinked blood lines. This study aims to determine whether or not the design of a dialyzer influences hemolysis.

Materials and Methods

This study comprised 142 patients who received chronic hemodialysis treatment at the Rentek Hemodialysis Center for a total of 12 hours per week. During separate hemodialysis sessions, the pre-HD and post-HD LDH levels of those who had hemodialysis with both dialyzers were compared. Every patient was assessed to be in a stable clinical condition, and they were all getting bicarbonate low-flux HD treatment on a regular basis. Ineligibility criteria included: 1) six months of HD; 2) three weeks of dialysis; 3) a current, unresolved acute illness of any etiology; 4) acute cardiovascular events and major surgery in the last three months; and 5) the presence of hepatic disease. The study was approved by Istanbul Prof. Dr. Cemil Tascioglu City Hospital Clinical Research Ethics Committee (approval number: 3.11.2022/E-486707-514.99 and the study was carried out in accordance with the Helsinki Declaration of Principles. All of the patients agreed to participate in the trial.

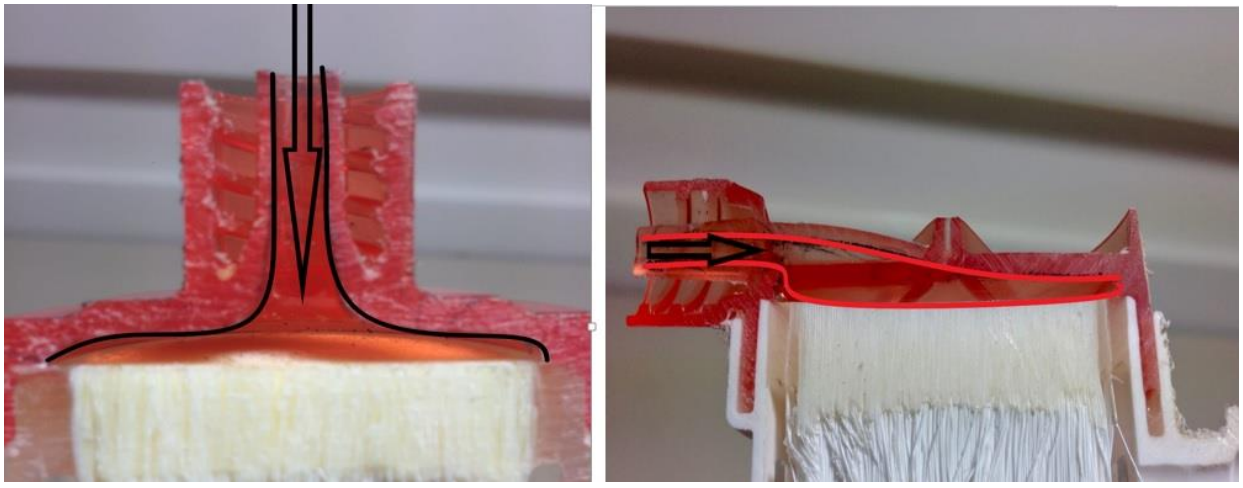

Figure 1. Dialyzers: Leoceed (left), Rexeed (right)

LDH Measurement

All of the blood samples for the laboratory tests were taken before and just after hemodialysis The samples were centrifuged at 3000 × g for 5 min, and then serum was used to analyze LDH level. LDH activity assay kit was used (sigma Aldrich) by colorimetric method. LDH difference was calculated by -post-dialysis LDH minus pre-dialysis LDH.

Statistical Analysis

SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. Normality distribution of the variables was analyzed using the Shapiro–Wilk test. The variables distributed normally are presented as mean± standard deviation. For normally distributed variables, comparisons between the two independent groups were performed using Student's t-test; Categorical variables were compared using the chi-square test. All of the reported P-values were 2-tailed, and those less than 0.05 were considered to be statistically significant.

Results

A hundred forty-two patients (63% female) on hemodialysis (HD) treatment were enrolled in the study. Twenty-eight patients (20%) had diabetes, 45 had hypertension (32%) and 16 had ischemic heart disease (11%) as a comorbid condition. Twenty-eight patients had diabetes (20%), 26 patients had hypertension (18%) and 18 (12%) patients had pyelonephritis as etiology of CKD. Eleven patients had polycystic kidney disease (8%), 35 of the patients had glomerulonephritis (25%) while in 24 patients (17%) etiology is unknown. (Table 1).

Table 1
Demographic Findings in Patient Group

Parameter	HD patients (n=142)
Age (years)	51.0±17.5
Gender (female, n, %)	89(63%)
Fistula (n, %)	117(82%)
Co-morbidities	
Diabetes (n, %)	28 (20%)
Hypertension (n, %)	45(32%)
Ischemic heart disease *(n, %)*	16 (11%)
Dialysis Vintage (months)	28.8±16.0
Cause of CKD (n, %)	
Diabetes	28 (20%)
Glomerulonephritis	35 (25%)
Hypertension	26 (18%)
Polycystic kidney disease	11(8%)
Chronic pyelonephritis	18 (12%)
Unknown	24 (17%)

When LDH difference is compared between groups Leoceed dialyzer group) had statistically significantly higher LDH difference when compared with Rexeed dialyzer group (49.1±20 U/l vs229.8±24.45 U/l; p=0.008) (Table 2).

Table 2
LDH Difference Between Two Dialyzers

Parameter	REXEED	LEOCEED	P
LDH(U/l)	29.8±24.45 U/l	49.1±20 U/l	0.008

When the patients are analyzed having diabetes or not: LDH tends to be higher in diabetic group but the difference was statistically insignificant (Table 3, Table 4).

Table 3
LDH Difference in Diabetic and Non-Diabetic Patients in REXEED Group

Parameter	DM (+)	DM (-)	P
LDH(U/l)	32.3±23.4 U/l	28.9±24.1	0.12

Table 4
LDH difference in diabetic and non-diabetic patients in LEOCEED group

Parameter	DM (+)	DM (-)	P
LDH(U/l)	52.4±24.4 U/l	48.3±23.1	0.1

Discussion

Hemolysis has been the subject of study in a variety of contexts. Hypoosmolality in the dialysate, the presence of hydrogen peroxide or formalin as a result of reuse, hypochlorite as a result of machine sterilization, copper as a result of pipe corrosion, and elevated temperatures are all possible causes of hemolysis. This situation may also be caused by a blocked pump, single-needle dialysis, catheter occlusion, or collapsed arterial line (1-7).

When the water supply has been contaminated, it is quite likely that the majority of patients receiving dialysis will display symptoms of hemolysis. Dialysate may include toxins in the form of bacteria, endotoxins, or disinfectants; nevertheless, it is uncommon for these toxins to cause hemolysis. The very unusual incidence of hemolysis in HD has been linked to the presence of kinks in HD blood lines.

When the Leocced dialyzer was used, the level of lactate dehydrogenase (LDH) in our patient group was dramatically and significantly elevated. Transporting the Leocced dialyzer has spurred the development of a novel packing solution. Moreover, they assert that less storage space is required. Instead of being exposed to nonphysiologically substantial pressures, the blood is harmed by the high shearing stresses caused as blood cells are driven through the limited flow channel of the tubing kink. This causes the blood to become compromised (16,17). Due to the angle at which the blood is linked to the dialyzer, shear stress equivalent to that which leads to tube kinking and hemolysis may be produced (figure 1). Because patients were treated with hemodialysis utilizing both dialyzers simultaneously, additional forms of hemolysis were inevitable.

A high LDH level in the blood is associated with a variety of clinical conditions, including inflammation, infection, and sepsis (18–23), hepatic diseases (24–26), and several oncologic pathologies (27–33). As a marker for cellular damage, LDH is sensitive but not specific for any particular kind of damage. Infected individuals, those with hepatic issues, and those with oncologic diseases were excluded from our analysis. As a result, we may infer that these various variables are not responsible for the varied LDH levels.

Despite the fact that this difference was not statistically significant, diabetes patients had considerably higher LDH levels than those without diabetes. Patients with diabetes, a well-known disease, have an increased chance of developing acute inflammation. LDH has been linked to various inflammatory markers

in the past, and prior research has shown that inflammatory cells may create LDH at serum-detectable quantities (20). LDH has also been linked to several inflammatory indicators (34-37). Diabetes may exacerbate inflammation, which may account for the increase.

Our patients exhibited a little amount of hemolysis. In addition, LDH levels may increase as a consequence of the dialysis operation. Due to the possibility of mechanical hemolysis in extracorporeal blood systems like dialysis, an increase in LDH may be seen and quantified (38, 39). (38, 39). In this regard, Vaziri et al. (41) observed that a single extracorporeal system transit increased overall serum LDH levels. It's probable that platelets contributed to this increase. In addition, Cheng et al. (41) found that patients with HD had higher LDH levels than those with ischemic heart disease and the healthy control group. This suggests that individuals with HD have a higher anaerobic metabolism and activity.

Conclusions

This is the first letter we are aware of reporting an increase in LDH and hemolysis due to a dialyzer. It is quite likely that the arrangement of the Leoceed dialyzer is one of the elements that contributes to the cell damage caused by the elevated serum LDH level. To do corrective research on dialyzer design, it would be advantageous to evaluate the effect of dialyzer design on cell damage using a larger patient sample size. This would provide a more precise evaluation of the influence of dialyzer design.

Ethics Committee Approval: The study was approved by Istanbul Prof. Dr. Cemil Tascioglu City Hospital Clinical Research Ethics Committee (approval number: 3.11.2022/E-486707-514.99 and the study was carried out in accordance with the Helsinki Declaration of Principles.

Informed Consent: Written consent was obtained from the participants or their legal guardians.

Conflict of Interest: Authors declared no conflict of interest.

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