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Case Report
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Clinical Results of Lipopolysaccharide Filter Use in Sepsis Developed After Liver Transplantation: Report of Two Cases

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Abstract

Background and Case Presentation: Sepsis remains as a preventable cause of mortality in ICU inpatients. Lipopolysaccharide (LPS) is the endotoxin, a structural component of the cell wall of gram-negative bacteria. Its release in systemic circulation results in the release of a group of inflammatory mediators, leading to initialization and/or exacerbation of sepsis. We report two cases with a history of Liver Transplantation (LT) cases that underwent LPS filter treatment with a diagnosis of Gram-negative related septic episode and discuss the related literature.

Conclusions: Our cases demonstrate that LPS filters have significant and accountable effect on prognosis in treatment of sepsis. Further studies would be promising to clarify mechanisms and effectivity profiles of these techniques to provide better treatment algorhytms.

Keywords: Sepsis; Lipopolysaccharide; Lipopolysaccharide filter

Background

The incidence of sepsis, one of the leading causes of mortality and morbidity in intensive care unit (ICU) patients, shows a continuous increase despite all developments in the diagnosis and treatment of intensive care infections [1]. Sepsis remains as a preventable cause of mortality in ICU inpatients. Despite advances in antimicrobial therapy, multidrug resistance in microbiological agents causing intensive care infections has led to the search for adjuvant or aftercare treatment methods in addition to antibiotic therapy in researchers working in this area [2]. Treatment methods based on extracorporeal circulation are the result of the search in this field. These treatment methods, which were initially designed to indiscriminatingly remove inflammatory and pro-inflammatory cytokines involved in sepsis, have changed over time to become more selective in terms of the molecules they target. Lipopolysaccharide (LPS) is the endotoxin, a structural component of the cell wall of gram-negative bacteria. Its release in systemic circulation results in the release of a group of inflammatory mediators of the host by activation of the coagulation cascade with macrophages, neutrophils, and endothelial cells [1-3].

While patients undergoing liver transplantation due to chronic liver failure are prone to early and late infections due to both immunosuppressive treatment regimens and complex surgical procedures, the sepsis response of the transplanted liver is insufficient to limit the inflammatory process compared to healthy liver tissue [4].

In our study, it is aimed to present the results of cases where endotoxins removed from the circulation through extracorporeal circulation on the patients in our institute with a history of liver transplantation and being treated in the ICU due to sepsis-related multiple organ failure and discuss the literature on the subject.

Case Presentations

Case1

A 26-year-old male patient who had a history of liver transplantation with live donor 3 months ago was admitted to the ICU with the diagnosis of secondary abdominal sepsis to the infectious biloma. Mean arterial blood pressure (MAP) at the time of admission was 61.6 mmHg, consciousness was blurred, and he was tachypneic. There was a Klebsiella pneumoniae growth in the blood culture taken from the patient. Due to developing adult respiratory distress syndrome (ARDS), elective

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Table 1: Hemodynamic findings before and after the procedure as well as laboratory and physiological scoring results of the cases.

	CRP	PCT	WBC	PLT	FIBRINOGEN	INR	NLO	CRE	LACTATE Mmol/L	PaO_2/FiO_2	URINE ml/day	SOFA	SAPS II
Case 1day 0	2.53	82.35	3.8	16	188	1.3	3.72	1.56	3.2	287	2410	12	34
Case 1 Day 5	3.1	3.65	5.9	56	375	1.24	24.6	0.83	1	547	4705	5	26
Case 2 Day 0	1.31	38.81	1.6	43	195	1.32	4.03	0.49	2.3	210	2850		
Case 2 Day 5	5.9	5.85	10.5	114	334	1.3	18.2	0.5	1.4	246	2710	13	33
P-value	***0.001***	0.142	0.096	0.406	0.229	0.85	0.0003	0.002	0.176	0.00004	0.05	11	20

endotracheal intubation (ETI) and subsequent mechanical ventilation (MV) were performed. The patient was applied LPS filter (Alteco® LPS Adsorber, Sweden) for 1 session (6 hours) with a continuous veno-venous hemodiafiltration (CVVHDF) device. At follow-up, the patient's clinical condition improved significantly 2 days after the procedure and the patient was extubated.

Case 2

A 25-year-old female patient with a history of liver transplantation 25 months ago was admitted to the ICU due to ARDS. The patient who had severe hypoxemia symptoms was started to receive MV after ETI. The patient with a MAP value of 60 mmHg was provided with the vasopressor support (noradrenaline 0.1 mcg/kg/min). Proteus vulgaris and *E. coli* growth in the blood culture and Proteus mirabilis growth in the sputum culture were detected. The patient was applied LPS filter (Alteco® LPS Adsorber, Sweden) for 1 session (6 hours) with a hem adsorption device. At follow-up, the patient showed a significant improvement in clinical condition on day 3 after the procedure, thus, MV was terminated.

Hemodynamic findings, as well as laboratory and physiological scoring results of the cases before and after the procedure, are summarized in (Table 1).

Statistical analysis was carried out with PASW Statistics 18.0, Chicago, IL. Data are presented as the mean ±standard Deviation (SD). The comparison of continuous variables between group was made with t-Test and Mann Whitney U test for independent samples. Also, the Fisher exact chi-square test was used to compare categorical variables.

Discussion

Although the contribution of extracorporeal filter systems in the treatment of sepsis is not well known, studies on the positive results of different filters have been published [5,6]. Many filters have been developed to treat sepsis-induced multiple organ failure statuses by removing cytokines from the circulation through extracorporeal circulation [7]. The fact that the graft survival is negatively affected in the secondary sepsis in infections caused by gram-negative microorganisms in patients after liver transplantation was revealed in Yokoyama S et al. [8]. However, currently, there is no English study in the literature evaluating the effectiveness of any of the various filter systems in this group of patients.

The recognition of LPSs, one of the cell wall components released by pathogens during sepsis, by antigen presenting cells (APC) stimulates other cells from the inflammatory process and inflammatory mediator release. There is damage to both the cell and tissue levels in direct proportion to their volume. The 'immunoparalized' condition that develops as much as these cytotoxic effects also pave the way for secondary nosocomial infections [2,3]. Microorganisms responsible for multiple organ failure in the cases we presented are the results of such processes. In recent studies, it has been shown that the increase in LPS and other endotoxin levels in gram (-) negative sepsis is in direct proportion to the severity of sepsis [9,10].

After the application of LPS filter in our cases, significant changes in CRP and neutrophil/lymphocyte ratio (NLR) levels, known to be correlated with the severity of sepsis, are found [11,12].

Physiological scoring systems with clinical and laboratory parameters directed at multiple organ systems are used in the diagnosis and treatment of sepsis patients [6,10]. However, there is no consensus on how often these scoring systems should be applied in the follow-up of patients. In the literature review, no study with such content in their methodology was found. Similarly, in our cases, no significant change was observed in physiological scoring systems after LPS filter application, but there was a significant improvement in PaO_2/FiO_2 ratio that showed the severity of ARDS clinic which is the main cause of both cases being followed up with mechanical ventilation that paved the way for them to be taken in ICU. This is consistent with the clinical improvement in patients.

Conclusion

There are studies that compile the effectiveness of different filter systems in the follow-up of sepsis patients and reveal different results [2-4,10,12]. We believe that the studies according to the methodological and clinical results of these methods such as timing and technique of administration will contribute positively to the future consensus of the filter systems for treatment of sepsis.

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