

Effectiveness of Endotoxin Scattering Photometry for Determining the Efficacy of Polymyxin B-immobilized Fiber Treatment in Septic Shock: Report of a Case

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Abstract

The limulus test, which has been established as a test for endotoxin measurement, is associated with problems, including that posed by the presence of a response inhibitor factor and the longer time needed for the measurement of low concentrations. On the other hand, the technique of direct hemoperfusion with a polymyxin B immobilized fiber column (DHP-PMX) was developed in Japan in 1994 and has been used for the control of endotoxemia in septic shock. The limulus test, which is a common endotoxin measurement test, has several problems with regard to sensitivity. Therefore, this test is no longer used to determine the effectiveness of DHP-PMX. Here, we describe a patient presenting with colonic perforation who recovered from septic shock with DHP-PMX. This treatment effect was reflected by a decrease in plasma endotoxin levels as demonstrated more readily with endotoxin scattering photometry assay than with the standard limulus test. We conclude that endotoxin measurement with endotoxin scattering photometry is superior to nephelometry in patients with endotoxemia. (J Nippon Med Sch 2010; 77: 119–122)

Key words: polymyxin B-immobilized fiber (PMX), septic shock, endotoxin scattering photometry

Introduction

Sepsis was defined in 1992 as a systemic inflammatory response syndrome associated with infection¹. Because sepsis is associated with diffuse coagulopathy and multiple organ failure despite advances in intensive care, the mortality rate of severe sepsis remains greater than 30%².

On the other hand, the technique of direct hemoperfusion (DHP) with a polymyxin B

immobilized fiber (PMX) column (DHP-PMX; Toray Industries Inc., Tokyo, Japan) was developed in Japan in 1994 and has been used for the control of endotoxemia in septic shock. The use of PMX has been shown to be associated with a reduction in serum endotoxin levels³. Reductions in the levels of inflammatory cytokines and other mediators have also been reported with the use of a PMX column⁴⁻⁷. A previous multicenter prospective randomized controlled trial of DHP-PMX treatment has suggested that it improves cardiac and renal

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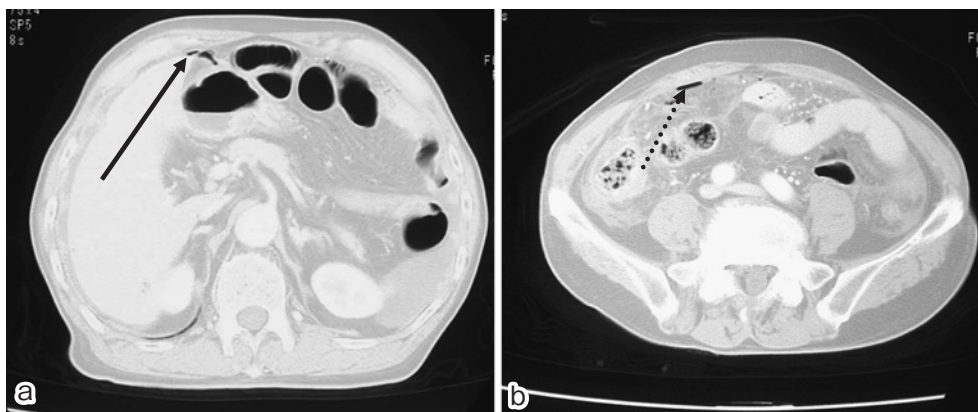


Fig. 1 Axial contrast-enhanced computed tomographic scan of the abdomen.

a: The black arrow shows free air.

b: The black dashed arrow shows free air.

functions impaired by sepsis or septic shock⁸. A systemic review study has suggested that DHP-PMX effectively reduces endotoxin levels and has effects on blood pressure elevation when used with vasoactive agents, improves gas exchange, and decreases mortality rates⁹. However, a chief mechanism of treating septic shock with this column may be endotoxin reduction.

A recent study has demonstrated the potential usefulness of a new method of detecting endotoxin with laser scattering photometry¹⁰.

Case Report

A 71 year-old man was admitted to our hospital with abdominal pain. Abdominal examination revealed significant muscular guarding of the abdomen. He was, therefore, suspected to have peritonitis. Because the cause of peritonitis was still in doubt, abdominal computed tomography was performed. Contrast-enhanced computed tomography of the abdomen revealed free air in the peritoneal cavity (**Fig. 1a, b**).

The patient was taken to the operating room for surgical treatment of bowel perforation. Intraoperatively, a large tumor of the ascending colon was detected with oral side perforation. On the basis of these findings, a diagnosis of ascending colon perforation was confirmed. We performed resection from the ileocecal lesion to the ascending colon. Because intraoperative management was difficult owing to unstable hemodynamics, we performed a

Table 1 Changes in SOFA score and serum endotoxin level associated with DHP-PMX

	before DHP-PMX	after DHP-PMX
Endotoxin (pg/mL)	7.3	5.2
Endotoxin: ESP methods (pg/mL)	52.8	1.8
Systolic Blood Pressure (mmHg)	88	144
PaO ₂ /FiO ₂ ratio	176.7	225.0
SOFA score	13	13

staged operation. After the first operation, rapid fluid resuscitation was immediately started; however, the systolic blood pressure continued to decrease. Because the postoperative hemodynamics was unstable, the patient was treated with rapid fluid resuscitation and intensive care including DHP-PMX. After the hemodynamics became stable, the patients underwent a second operation.

We performed only ileocecal resection in the first operation because of the poor circulatory condition. After circulation became stable during the second operation, we performed end-to-end ileocolostomy.

This treatment resulted in a marked decrease in the serum endotoxin level as measured with endotoxin scattering photometry (ESP) assay. On the other hand, the standard method showed no marked change (**Table 1**). The required dose of catecholamines decreased, and systolic blood pressure increased (**Fig. 2**). The histologic diagnosis was moderately differentiated adenocarcinoma of the ascending colon without lymph node metastasis.

Effectiveness of ESP in Septic Shock

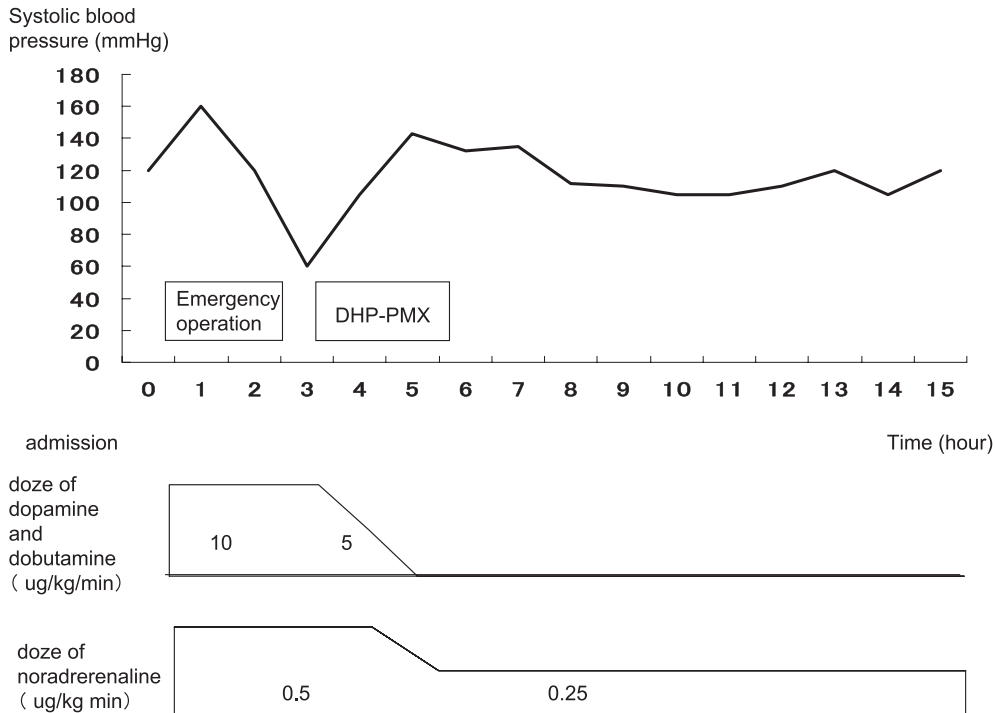


Fig. 2 Clinical course: serum endotoxin level, systolic blood pressure, and required dose of catecholamines are shown.

The patient was discharged on postoperative day 55.

The Acute Physiology and Chronic Health Evaluation (APACHE) II score¹¹ on the first day in the intensive care unit and the Sepsis-Related Organ Failure Assessment (SOFA) score¹² before the start of DHP-PMX were 35 and 13, respectively.

ESP Assay

Plasma was disposed and mixed with Limulus amoebocyte lysate (LAL) lyophilized powder in a test tube (to start the LAL reaction) with a flash mixer for 30 seconds, and a 300- μ L aliquot was dispensed to a photometric cuvette for laser scattering photometry. The reaction mixture was observed with laser scattering photometry at 37°C. The assay was stopped when small particles were detected¹⁰.

Discussion

The PMX-DHP Clinical Study Group in Japan has reported that the adsorption of plasma endotoxins with a PMX column may have beneficial effects on the symptoms and prognosis of patients with severe sepsis, including those with septic shock³. Because

the PMX column had been developed to eliminate endotoxin from the peripheral circulation¹³, reductions in many sepsis-related factors have also been reported with the use of the PMX column⁴⁻⁷, but adsorption of endotoxin is thought to be the main effect with a development process.

The limulus test, which has been established as a test for endotoxin measurement, has several problems, including those posed by the presence of a response inhibitor factor and the longer time needed for the measurement of low concentrations. LAL reacts with bacterial endotoxin to form gel clots¹⁴. The gelation time for the entire LAL solution depends on the concentration of endotoxin in the sample. The LAL cascade reaction is extremely slow, and gelation does not proceed when the level of endotoxin is extremely low¹⁵.

The ESP assay has recently been reported. The principal difference between the ESP assay and other LAL test assays is that during gelation the LAL reaction mixture is agitated and mixed to homogeneity with a spin bar. Incidentally, the ESP assay is the only method that can detect the appearance of small particles in a solution.

Many studies have shown that endotoxin can induce hypotension, lung injury, and shock¹⁶⁻²⁰. In

reference to these studies, we found in the present study that a decrease in the endotoxin level results in an improvement of the clinical condition.

On the other hand, no standard criteria for the use of DHP-PMX have been established. Various poor prognostic indicators have been reported as criteria for the use of DHP-PMX, such as an APACHE II score of 30 or greater³. In our case, the APACHE II score was 35; therefore, we judged this case as a suitable candidate for DHP-PMX treatment.

We have reported on a patient presenting with severe septic shock and increased serum endotoxin levels in whom DHP-PMX treatment was successful. In this case, because the endotoxin level estimated with the ESP assay was consistent with the clinical course, treatment effect was reflected by a decrease in the plasma level of endotoxin more readily with the ESP assay than with the standard limulus test. We, therefore, propose that endotoxin measurement with the ESP assay is superior to nephelometry for the clinical measurement of endotoxemia.

This report suggests that the ESP assay might become the standard criterion for assessing the effective use of DHP-PMX and for assessing the effect of this treatment in patients with septic shock.

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