

## **Reference list**

 Adamik B, Zielinski S, Śmiechowicz J, Kübler A Endotoxin Elimination in Patients with Septic Shock: An Observational Study. Arch Immunol Ther Exp 2015 Jun 21. <u>https://pubmed.ncbi.nlm.nih.gov/26093653/</u> Topic: septic shock
 Results: Endotoxin elimination was performed using hemoperfusion with the Alteco LPS Adsorber. Effective endotoxin elimination resulted in a significant improvement in hemodynamic parameters and of organ function. The application of the EA assay was useful for the bedside monitoring of endotoxemia in critically ill ICU patients.

 Ala-Kokko T.I, Laurila J, Koskenkari J *A New Endotoxin Adsorber in Septic Shock: Observational Case Series.* Blood Purif. 2011 Sept 2:32:303-309 <u>https://pubmed.ncbi.nlm.nih.gov/21893976/</u> **Topic:** septic shock

**Results:** Two-hour hemoperfusion with Alteco LPS Adsorber was initiated in patients with septic shock and endotoxemia. Controls were matched for age, focus and severity of illness. Alteco LPS Adsorber treatment was associated with a decrease in noradrenaline dose, decrease in SOFA scores and LPS concentrations.

 Blomquist S, Gustafsson V, Manolopoulos T, Pierre L *Clinical experience with a novel endotoxin adsorption device in patients undergoing cardiac surgery.* Perfusion 2009 Jan;24(1):13-7. <u>https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.1033.3778&rep=rep1&type=pd</u> <u>f</u>

**Topic:** cardiac surgery

**Results:** No adverse events were encountered when the Alteco LPS Adsorber was used in the circuit. Blood flow through the device was easily monitored and kept at the desired level. The Alteco LPS Adsorber can be used safely and is easy to handle in the bypass circuit. No complications related to the use of the device were noted.

 De Silva R.J, Armstrong J, Bottrill F, Goldsmith K, Colah S, Vuylsteke A *A lipopolysaccharide adsorber in adult cardiopulmonary bypass: a single center randomized controlled pilot trial.* Interact Cardiovasc Thorac Surg. 2010 Jul;11(1):86-92 <u>https://academic.oup.com/icvts/article/11/1/86/725054</u>

Topic: cardiopulmonary bypass

**Results:** This study demonstrated Alteco LPS Adsorber to be safe in a complex cardiac surgery setting.



- Duszyńska W, Śmiechowicz J, Adamik B, Zieliński S, Kübler A Advanced therapeutic methods for the treatment of meningococcal septic shock. Case report. Anaesthesiol Intensive Ther. 2012 Oct-Dec;44(4):212-6. https://pubmed.ncbi.nlm.nih.gov/23348489/
  - **Topic:** septic shock

**Results:** Hemoperfusion with Alteco LPS Adsorber was performed to eliminate endotoxin from the bloodstream. Rapid pathogen identification, adequate antimicrobial therapy and endotoxin elimination from the bloodstream improved the hemodynamic and respiratory parameters of the patient. The application of routine plus non-standard methods of treatment of septic shock prevented the progression of the biological cascade in sepsis and improved the patient's clinical condition.

• Gromova E, Kisselevskiy M, Anisimova N, Kuznetsova L

*Clinical experience with lipopolysaccharide adsorber in cancer patients with severe sepsis and septic shock.* Crit Care. 2010; 14(Suppl 1): P409. Published online 2010 Mar 1. doi: 10.1186/cc8641

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2934292/

**Topic:** cancer, severe sepsis, septic shock

**Results**: After LPS adsorption with Alteco LPS Adsorber, the LPS level in patient serum was significantly reduced. Simultaneously, concentrations of some cytokines (IL-6, TNF $\beta$ , IL-8) were reliably decreased. But the Alteco LPS Adsorber probably does not eliminate soluble receptors like sCD14 and RIL-1 from blood. So the LPS adsorption may represent a significant improvement in the treatment of cancer patients with severe gram-negative sepsis and septic shock.

• Hadade Adina N, Breazu Caius M., Ilie Iulian V, Mitre Calin I

The Use of Endotoxin Adsorption in Extracorporeal Blood Purification Techniques. A Case Report, The Journal of Critical Care Medicine, 2017;3(2):73-78 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5769914/

**Topic:** septic shock, purulent peritonitis

**Results:** A case of a 64-year-old man with severe gram-negative sepsis was presented. To reduce the amplitude of the general effects of endotoxin the Alteco LPS Adsorber was used.

The efficacy markers were the overall hemodynamic profile, translated into decreased vasopressor requirements, the normalization of the cardiac index, and the systemic vascular resistance index combined with the lactate level and the reduction in procalcitonin levels. A decrease in the sequential organ failure assessment (SOFA) score at twenty-four hours was demonstrated.

The clinical course following treatment was favorable for the days immediately following the treatment. This was attributed to the removal of endotoxin from the systemic circulation.



 Khubutiia SM Sh, Abakumov M M, Aleksandrova I V, Reĭ S I, Il'inskiĭ M E, Khvatov V B, Borovkova N V, Pertsev A S, Zinkin V lu Selective adsorption of endotoxin in the complex treatment of patients with severe sepsis. Anesteziol Reanimatol Sep-Oct 2010;(5):65-9. PMID: 21395145 <u>https://pubmed.ncbi.nlm.nih.gov/21395145/</u> Topic: postoperative gram-negative sepsis Results: A session with Alteco LPS Adsorber caused a significant drop in the blood level of and the second toward better.

of endotoxin and procalcitonin and it was accompanied by a trend toward better hemodynamics and lung gas exchange and alleviated organ dysfunction.

• Kulabukhov V.

*Use of an endotoxin adsorber in the treatment of severe abdominal sepsis.* Acta Anaesthesiol Scand 2008; 52:1024-1025.

https://pubmed.ncbi.nlm.nih.gov/18494849/

Topic: abdominal sepsis

**Results:** After LPS adsorption with the Alteco LPS Adsorber, the level of LPS in the patient's bloodstream was almost eliminated: from 1.44 EU/ml before treatment to 0.03 EU/ml post treatment. The procalcitonin level and inflammatory cytokines were concurrently reduced. Also, an obvious improvement in the status of the patient's hemodynamics was seen. Forty-five days after treatment the patient is still alive. LPS adsorption may represent a significant improvement in the treatment of gram-negative sepsis and further studies are planned.

• Kulabukhov V, Chizhov A

*The use of a novel technique for adsorption of lipopolysaccharide in patients with severe gram negative sepsis.* Poster. International Sepsis Symposium, Granada, Spain 2008 **Topic:** gram-negative sepsis

**Results:** The use of Alteco LPS Adsorber for LPS adsorption in patients with severe sepsis leads to significant improvement of systemic hemodynamics and oxygenation. The clinical course following the treatment was favorable and may in part be attributed to the removal of endotoxin from the systemic circulation. Negative effects are negligible.

• Kulabukhov V, Chizhov A, Kleuzovich A, Kudryavtsev A

*Clinical effects of adsorption of lipopolysaccharide in the treatment of Gram-negative severe sepsis.* Crit Care. 2010; 14 (Suppl 2): P28. Published online 2010 Sep 1. doi: <u>10.1186/cc9131</u> PMCID: PMC3254946 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3254946/

**Topic:** gram-negative sepsis

**Results:** A statistically significant improvement in hemodynamics, oxygenation, and reduced markers of endotoxemia in group therapy with Alteco LPS Adsorber compared with traditional therapy. These effects were attributed with the removal of endotoxin from the systemic circulation. Only in one case using hemofiltration for acute renal failure in the study group (in the reference group in all patients), 28-day mortality was 16.7% and



66.7% respectively. Negative effects were negligible.

 Lipcsey M, Tenhunen J, Pischke SE, Kuitunen A, Flaatten H, De Geer L, Sjölin J, Frithiof R, Chew MS, Bendel S, Kawati R, Larsson A, Mollnes TE, Tønnessen TI, Rubertsson S. Endotoxin Removal in Septic Shock with the Alteco<sup>®</sup> LPS Adsorber was Safe But Showed No Benefit Compared to Placebo in the Double-Blind Randomized Controlled Trial - the Asset Study. Shock. 2019 Dec 26. doi: 10.1097 https://pubmed.ncbi.nlm.nih.gov/31880758/

## **Topic:** septic shock

**Results:** The investigation was terminated after 527 days with eight patients included in the LPS Adsorber group and seven in the Sham group. The termination was made due to difficulties in recruiting subjects, despite modifying the inclusion criteria. The intended number of subjects was 32-44, but the included number of subjects according to protocol was only eight. Because of the low number of subjects recruited according to protocol, any observed differences between the Alteco LPS Adsorber and placebo device groups may be due to random variation. It is therefore not possible to draw any conclusions with respect to performance based on the data collected in this clinical investigation. Adverse event data, safety laboratory, vital sign and Richmond Agitation-Sedation Scale data provide no evidence of any risks associated with Alteco LPS Adsorber treatment. Twenty-one adverse effects, judged not to be related to the device. Two patients in the Sham group and no patients in the LPS Adsorber group died within 28 days.

 Tenga N, Giordano R.S, Iodice F, Belloni L, Panetta V, Allegretto F, Pinto G, Piazza L Type A Aortic Dissection treated in Emergency conditions with Alteco<sup>®</sup> LPS Adsorber during extracorporeal circulation. MedTASS-CARACT 2017, 6th - 8th April 2017, PALERMO

## Topic: type A Aortic Dissection

**Results:** Early use of Alteco LPS Adsorber during CPB is safe, without lower platelet count or bleeding. Alteco LPS Adsorber reduces the levels of endotoxin resulting in peripheral lactate levels reduction and improvement of tissue perfusion.

 Yaroustovsky M, Abramyan M, Krotenko N, Popov D, Plyushch M, Rogalskaya E, Nazarova H

*Combined extracorporeal therapy for severe sepsis in patients after cardiac surgery* Bakoulev Scientific Centre for Cardiovascular Surgery, Moscow, Russia **Topic:** Severe sepsis, endotoxin, LPS adsorption, haemodialysis, high cut-off haemofilters

**Results:** Combined use of LPS adsorption and haemodialysis with high cut-off haemofilters in conjunction with standard therapy is a safe, effective method for treating patients who have severe sepsis. After the completion of the two combined procedures of LPS adsorption and high cut-off HD, the initial MAP increased from 76 (65–81) to 90 (85–102) mm Hg (18% increase, p < 0.01). In the process of treatment there was an increase in the oxygenation index in all patients, and, by the end of the extracorporeal therapy



sessions, this difference was 29%. Analysis of the obtained results revealed a statistically significant decrease in the EAA (19%) and the endotoxin concentration (75%; LAL test). The 28-day survival rate among patients in the study group was significantly higher compared with the control group.

 Yaroustovsky M, Abramyan M, Popok Z, Nazarova E, Stupchenko O, Popov D, Plushch M, Samsonova N

Preliminary Report regarding the Use of Selective Sorbents in Complex Cardiac Surgery Patients with Extensive Sepsis and Prolonged Intensive Care Stay. Blood Purif. 2009 Aug 14;28(3):227-233.

https://pubmed.ncbi.nlm.nih.gov/19684388/

Topic: complex cardiac surgery

**Results:** Thirteen patients with gram-negative sepsis underwent the procedure of selective lipopolysaccharide adsorption using Alteco LPS Adsorber (group I) or Toraymyxin columns (group II). This therapy positively influenced the course of sepsis. After the second procedure, levels of serum endotoxin and procalcitonin markedly decreased in both groups. We also discovered a positive effect on leukocytosis levels and a trend towards normalization of body temperature, improvement of hemodynamic indices and increase of the lung's oxygenating function. Blood cultures taken several days after the procedure were negative.

• Yaroustovsky M, Gelfand B, Popok Z, Abramyan M, Nazarova E, Yakovleva I, Popov D, Plyushch M

*Lipopolysaccharide adsorption in combined therapy of patients with severe sepsis.* Critical Care200812(Suppl 2):P455

https://doi.org/10.1186/cc6676

**Topic:** severe sepsis - nine cardiac surgery with cardiopulmonary bypass and three patients with severe pancreatitis

**Results:** Decreasing LPS and PCT concentrations after LPS adsorption were observed. Our experience of LPS adsorption shows evidence of potential efficacy of this method in combined therapy for severe Gram-negative sepsis. Further investigations are required.