058
Infection 2015

Case study of 8 Patients with multiple organ failure treated additionally with Cytosorbents haemadsorption as adjunctive therapy in septic shock and severe SIRS in cardiac failure

Kogelmann K (1), Drüner M (1), Jarczak D (2)
(1) Department of Anesthesiology and Intensive Care Medicine, Klinikum Emden, Germany, (2) Department of Intensive Care Medicine, University Hospital Hamburg, Hamburg, Germany.

Introduction: In several studies and in in vitro data is demonstrated that the additional treatment with an extracorporal cytokine adsorption filter (CytoSorb®) may be helpful in patients with septic multiple organ failure due to increased blood cytokine levels by effective removal of toxic cytokine levels (1, 2, 5, 6, 9, 11, 12). CytoSorb® treatment can be used as adjunctive therapy not only in septic multiple organ failure but as well as e.g. in severe pancreatitis or other critical diseases due to an excess of cytokines (1). CytoSorb® therapy has meanwhile been used in over 200 hospitals worldwide in more than 5500 patients and is well tolerated and safe.
Objectives: We collected data from seven Patients with septic multiorgan failure treated additionally with cytokine-haemadsorption filter (CytoSorb®) as adjunctive therapy in septic shock and from one patient with severe SIRS and MOF in cardiac failure. The infectious focus was abdominal (four patients) and pneumonic (three patients), one patient was without any infection. The Indication for haemadsorption therapy has been: at least two-organ failure with APACHE-2 Score higher than 25, no decline in requirement of norepinephrine despite of adequate conventional therapy over a 24 h period as well as the need for renal replacement therapy. Aim of our case study was to show the effectiveness of CytoSorb® treatment used as adjunctive therapy in these cases.
Methods: The initial therapy of these patients followed the Surviving Sepsis guidelines (3, 7) focussed on adequate volume therapy, differentiated catecholamine therapy (administering norepinephrine to achieve a mean arterial pressure >60 mmHg), administering antibiotics not later than 1 h after detection of septic shock, lung-protective ventilation. If there was no decline of catecholamine demand even after an additional corticoid treatment for 24 h, CytoSorb® therapy was initiated. Sex, Age, APACHE-2 score, ventilator days, length of stay (ICU and in-hospital) and survival are shown in Table 1. Before treatment, during treatment and after treatment with CytoSorb® we calculated or collected SAPS II-Score, SOFA-Score, mean arterial pressure, requirement of norepinephrine, and blood lactate level. Furthermore we calculated the demand of norepinephrine (µg/h vs. mm Hg MAP) during therapy. The duration of therapy with CytoSorb® was predefined between 24 and 72 h, filter was changed every 24 h.
Results: 50 percent of the treated patients were female, overall survival was 62.5 percent. Currently two patients still are not discharged from hospital actually (1 at regular ward, 1 intermediate care). Five patients were treated over a 72-h period, three Patients over 48 h. Patient data are shown in Table 1. Mean age was 58.1 years (min 36, max 80, ±14.9), SAPS II-Score: 51.1 (min 36, max 73, ±11.7), SOFA Score: 11.1 (min 8, max 16, ±2.85). Mean APACHE-2 Score was 35.6 (min 27, max 52, ±9.9). Descriptives and data at the beginning of therapy are shown in Table 2.
During and after therapy we could only see marginal differences in SAPS II and SOFA-Score (mean at start/end of CytoSorb® therapy: SAPS II-Score at start 51.1 ± 11.74, at the end: 38.6 ± 9.7, SOFA-Score at start 11.1 ± 2.85; at the end 9.75 ± 2.2). After therapy, slightly decreased blood lactate could be seen (mg/dl, mean) at start: 29.2 ± 17.2, at the end: 13.9 ± 7.3. The effects on catecholamine demand we found were by far greater. To show these effects, we calculated the demand of norepinephrine in µg/h vs. the thereby achieved MAP (mm Hg). Start: 52.7 ± 26.9; End: 3.6 ± 4.7. Data during and after therapy are shown in Table 3 and in Figs. 1 to 4.

Table 1: Patient data

No	Sex	Age	SIRS source	Treatment (h)	Days ICU	Days hospital	Ventilator
1	Female	50	Peritonitis	72	34	Hospital woard	26
2	Male	60	Pneumonia	48	21	43	16
3	Female	36	Peritonitis	48	41	46	36
4	Male	65	Pneumonia	48	71	88	44
5	Female	80	Pneumonia	72	41	46	34
6	Male	42	Pancreatitis	72	3	36	27
7	Male	59	Peritonitis	72	50	51	50
8	Female	74	Cardiac failure	72	18	Intermediate care	16

Table 2: Descriptives (MAP = mean arterial pressure NOR = norepinephrine. LOS =length of stay

	Minimum	Maximum	Mean	SD
Age (years)	36	80	58.12	14.96
SAPS II-score	36	73	51.12	11.74
SOFA-score	8	46	11.12	2.85
MAP (mmHg)	35	70	59.62	10.87
NOR (µg/h)	2000	4000	2910	720
Lactat (mg/dl)	9.2	53.1	29.20	17.21
Ventilator (days)	16	50	31.12	11.48
LOS ICU (days)	18	71	39	15.62
LOS hospital (days)	43	88	51.17	17.06
APACJE-2 score	27	52	35.62	9.99

Table 3: Data at the beginning of (Start = 1) and after treatment (End = 2) with Cytosorb® (MAP = mean arterial pressure, NOR = norepinephrine, LOS = length of stay)

	Minimum	Maximum	Mean	SD
MAP (1) (mm Hg)	35	70	59.62	10.87
MAP (2) (mm Hg)	65	85	77.5	7.07
NOR (1) (µg/h)	2000	4000	2910	720
NOR (2) (µg/h)	0	1000	280	390
SOFA-score (1)	8	16	11.12	2.85
SOFA-score (2)	7	14	9.75	2/18
SAPS II-score (1)	36	73	51.12	11.74
SAPS II-score (2)	25	55	38.62	9.73
Lactat (1) (mg/dl)	9.2	53.1	29.2	17.21
Lactat (2) (mg/dl)	4.7	23.9	13.97	7.31
NOR µ/MAP (1) (µg/h * mmHg)	32.25	114.28	52.76	26.96
NOR µ/MAP (2) (µg/h * mmHg)	0	12.50	3.62	4.75

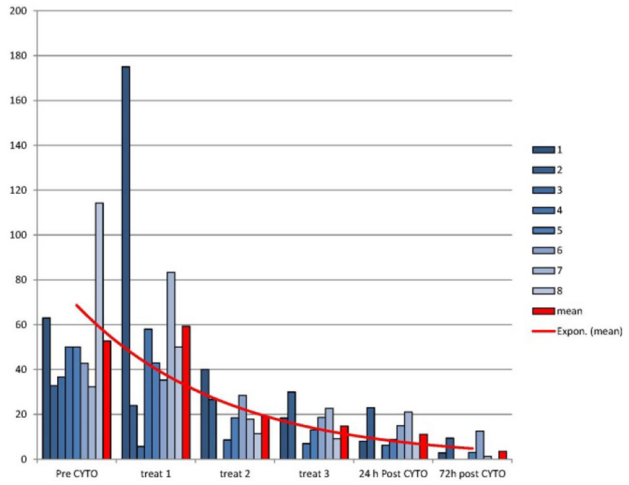

Fig. 1 µg Norepinephrine/mm Hg MAP

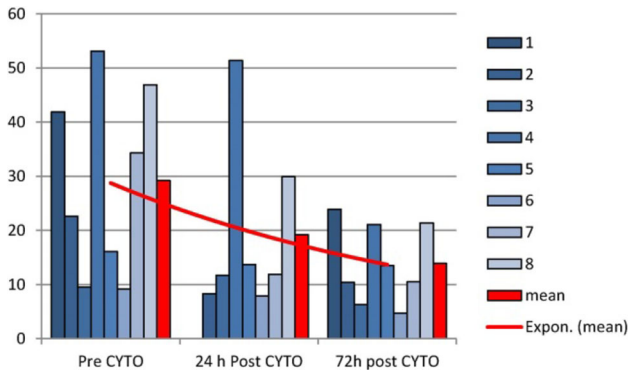

Fig. 2 Blood lactate level (mg/dl) pre/post Cytosorb® treatment

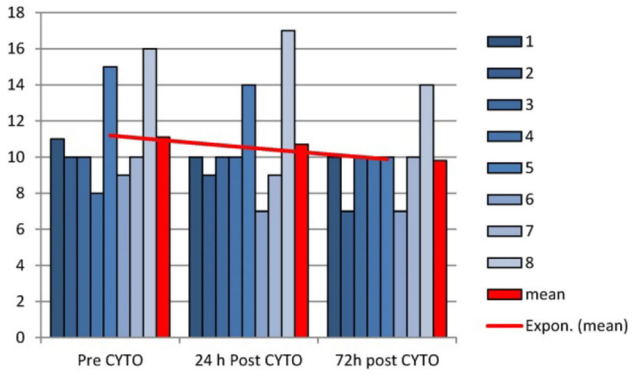

Fig. 3 SOFA Score pre/post Cytosorb® treatment

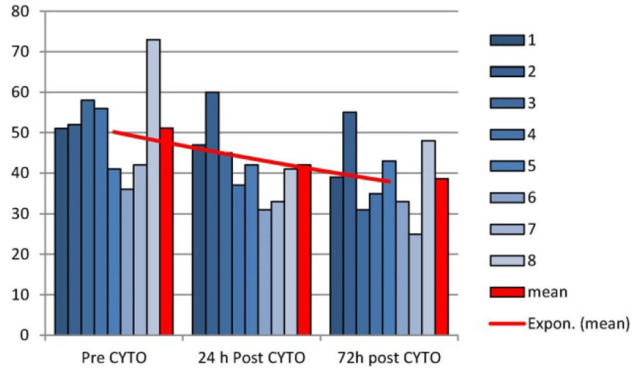

Fig. 4 SAPS II-Score pre/post Cytosorb® treatment

Conclusions: In this case-study with 7 septic patients and one patient with severe cardiac failure one effect we could determine was a pronounced decrease in catecholamine demand. Neither SOFA-Score nor SAPS II-Score decreased in treatment period and within 72 h after CytoSorb® therapy. Distinct tendency in decrease of blood lactate level could be seen in this period.

Generally compared with overall survival at about 45 % in severe sepsis including septic shock (4, 7, 8, 10) we could see survival in our patients of 62.5 %. Treatment with CytoSorb® adsorption filter in our patients has been safe and without any noticed side effects.

Our indication for CytoSorb® therapy is comparable to former indication for activated, recombinant human Protein C (drotegocin alfa activated): at least 2-organ failure with APACHE-2 Score higher than 25, no decline in requirement of norepinephrine despite of adequate conventional therapy over a 24 h period. Whether other patients could profit by this adjunctive treatment is uncertain and should be investigated.

References: [1] Born F, Pichlmaier M, Peterss S, Khaladj N, Hagl C. Systemic inflammatory response syndrome in der herzchirurgie: Neue Therapiemöglichkeiten durch den Einsatz eines Cytokin-Adsorbers während EKZ 2014;23:41–6. [2] Bracht H, Schneider EM, Weiss M, Hohmann H, Georgieff M, Barth E. Pattern of cytokine removal using an adsorption column CytoSorb during severe candida albicans induced septic shock. Infection 2013;41:1–90. [3] Dellinger RP, Carlet JM, Masur H, et al. Surviving sepsis campaign guidelines for management of severe sepsis and septic shock. Intensive Care Med (2004) 30:536–55. [4] Engel C, Brunkhorst FM, Bone HG, et al. Epidemiology of sepsis in Germany: results from a national prospective multicenter study Intensive Care Med (2007)33:606. [5] Hetz H, Berger R, Recknagel P, Steltzer H. Septic shock secondary to ß-hemolytic streptococcus-induced necrotizing fasciitis treated with a novel cytokine adsorption therapy. Int J Artif Organs 2014;37:422–6. [6] Kellum JA, Song M, Venkataraman R. Hemoadsorption removes tumor necrosis factor, interleukin-6, and interleukin-10, reduces nuclear factor-kappaB DNA binding, and improves short-term survival in lethal endotoxemia. Crit Care Med 2004;32:801–5.9. [7] Kortgen A, Niederprum P, Bauer M. Implementation of an evidence-based "standard operating procedure" and outcome in septic shock. Crit Care Med 2006; 34 (4): 943–49. [8] Martin, G.S., et al., The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med, 2003. 348(16): p. 1546–54. [9] Mitzner SR, Gloger M, Henschel J, Koball S. Improvement of hemodynamic and

inflammatory parameters by combined hemoadsorption and hemodiafiltration in septic shock: A case report. Blood Purif 2013;35:314–5.8. [10] Reinhart K, Brunkhorst F M, Bloos F. Fortschritte in der Therapie der Sepsis. Dtsch Arztebl 2003; 100: A 2080–2086 (Heft 31–32). [11] Schädler D, Porzelius C, Jörres A, Marx G, Meier-Hellmann A, Putensen C, et al. A multicenter randomized controlled study of an extracorporeal cytokine hemoadsorption device in septic patients. Crit Care 2013;17:62.4. [12] Taniguchi T, Kurita A, Mukawa C, Yamamoto K, Inaba H. Dose-related effects of direct hemoperfusion using a cytokine adsorbent column for the treatment of experimental endotoxemia. Intensive Care Med 2007;33:529–33.5.

063
Infection 2015

Frequency of Necrotizing fasciitis during last 7 years

Avdoshin IV (1), Chernyshev OB (2), Shatil MA (2),
Akinchits LG (2), Demin VN (2), Sulima VV (2), Protasova MV (2), Bubnova NA (1)
(1) Saint-Petersburg State university, medical faculty, Saint-Petersburg, Russia, (2) City Hospital of St. George, Department of Surgical Infections and Sepsis, Saint-Petersburg, Russia.

Introduction: Necrotizing fasciitis (NF) is one of the most severe disease among surgical infections characterized as rapid necrosis of fascia, soft tissue, severe sepsis, septic shock and still high mortality rate. During last years NF is increasing inspite of modern treatment methods.
Objectives: To investigate frequency and features of NF.
Methods: A 7 years retrospective analysis of 20,580 admitted patients to the department of surgical infections and sepsis from 2007 till 2014 years was performed.
Results: There were 170 patients with NF in 2007–2014 years. All patients had severe sepsis or septic shock with multiple organ dysfunction proved by lab tests and were treated in ICU. There were six patients in 2007 with NF, in 2008—13 patients, in 2009—18 patients, in 2010—16 patients, in 2011—33 patients, in 2012 29 patients, in 2013—20 patients, in 2014 35 patients correspondingly. The most important result is that NF became the first cause in case-structure of severe sepsis and shock. The most frequent accompanying immunodeficient disorder is diabetes. The amount of patients with NF increased in 5.5 times by 2014 compared to 2007. The mortality rates are still high, about 50–60 %.
During microbiological monitoring from 2007 till 2014 we mentioned that mixed cultures had been more dominated: enterococcus spp. (16.5 %), staphylococcus aureus (16 %), MRSA (12.5 %), Klebsiella pneumonia (15 %), streptococcus (12.5 %), *E. Coli* (12 %), Pseudomonas aeruginosa (11 %), *Acinetobacter* spp. (10.2 %) anaerobic cultures (4 %). If we saw that gram-positive bacteria group had been more frequent in obtained cultures in 2012 compared to previous years. In 2014 gram-negative bacteria group became more frequent. All admitted patients had been treated immediately with high doses of intravenous antibiotics and extensive surgical treatment of the infection lesions. We pay a very serious attention to the immunotherapy with NF that makes therapy more effective and improves results. We usually use (pentaglobin, recombinant Il-2, human immunoglobulins).
Conclusions:
1. NF became the first cause of severe sepsis and shock.
2. Both MRSA and gram-negative bacteria group became more frequent in NF.
3. Regular microbiological monitoring of wound infection should be performed.
4. We consider immunotherapy as important part of treatment in NF.

072
Infection 2015

Intermittent use of cytokine adsorption in combination with CRRT in a patient with necrotising pancreatitis, septic shock and MOF

Emmerich M (1), Zietlow S (1), Emmerich M (2), Tiesmeier J (1)
(1) Institute for Anesthesiology and Intensive Care Medicine, Muehlenkreiskliniken, Krankenhaus Bad Oeynhausen, Germany, (2) St. John's College, University of Oxford, United Kingdom.

Introduction: Re-establishing the balance between pro- and anti-inflammatory cytokines using cytokine-haemoadsorption with specific polymer adsorptives (Cytosorb®) is a novel therapeutic approach in intensive care. Early data from experimental and clinical studies have yielded encouraging results with regard to haemodynamic stabilisation and improvement of organ function.
Objectives: A 60-year-old female patient suffered septic shock and MOF post-cholecystectomy. This was complicated by massive aspiration during emergency gastroscopy and necrotising pancreatitis requiring necrostomy. On admission to ITU, the patient was in respiratory failure and required an FiO_2 of 100 % and an inverse inspiration to expiration ratio. There was a high need for vasopressors and fluids, and acute renal failure. Following initial stabilisation, colonic perforation and renewed septic shock occurred on day 13 post-operation, necessitating colectomy and further necrostomy on day 14.
Methods: Lung-protective ventilation and haemodynamic stabilisation using nuanced fluid and norepinephrine therapy with advanced haemodynamic monitoring were commenced. Antibiotic therapy was with meropenem and linezolid. CRRT (CiCa-CVVHD) was started on day 2 post-operation and combined with 48 h of haemoadsorption using Cytosorb. A second 96 h course of haemoadsorption was given from day 13 post-operation.
Results: During the first 48 h of haemoadsorption, norepinephrine requirements decreased from 0.13 to 0.00 mcg/kg/min. During the second use of haemoadsorption the initial norepinephrine need was 0.13 mcg/kg/min. This rose to a maximum of 0.43 mcg/kg/min 12 h post-operatively, but the infusion could be stopped after 40 h. The general condition of the patient improved dramatically despite multiple further operations for intra-abdominal bleeds, necrosis and wound healing impairment. CRRT could be stopped 11 days after the second course of haemoadsorption. Two days after this, the patient was successfully weaned from ventilation.
Conclusions: We successfully used intermittent cytokine haemoadsorption to manage a patient with recurrent septic shock, necrotising pancreatitis and MOF. Supplementing the standard treatment for sepsis with two courses of haemoadsorption facilitated rapid haemodynamic stabilisation. Cytosorb® was easy to use and no adverse effects were observed.