Effect of intravenous administration of freeze-dried sulfonated human normal immunoglobulin for septic patients

Conclusions The gentamicin Vd cannot be predicted by age, the presence of renal failure or any studied comorbidities. Therefore, in order to obtain adequate therapeutic levels as soon as possible, a high first gentamicin dose (that is, at least 7 mg/kg) should be given to all patients. In women, even higher doses may be needed.

Reference

1. Sawchuk R, Zaske D: **Pharmacokinetics of dosing regimens which utilize multiple intravenous infusions.** *J Pharmacokinet Biopharm* 1976, **4:**183-195.

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Does early appropriate antibiotic therapy improve the outcome of severe sepsis or septic shock?

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Critical Care 2009, **13(Suppl 1):**P320 (doi: 10.1186/cc7484)

Introduction The Surviving Sepsis Campaign Guideline 2008 [1] recommends starting appropriate antibiotic therapy within 1 hour after making the diagnosis of septic shock. In the ICU of our emergency center, we perform empiric antibiotic therapy for septic shock patients within 6 hours after admission.

Methods Cases of severe sepsis or septic shock diagnosed and treated in the ICU of our emergency center for more than 48 hours between January 2005 and September 2008 were retrospectively analyzed. The cases were divided into a survival group and a nonsurvival group, and were compared in relation to primary diagnosis, clinical findings, and type of pathogen. The chi-square test and paired *t* test were used to perform the statistical analysis.

Results There were 107 cases, 24 cases of severe sepsis and 83 cases of septic shock, and 73 of them were in males. The mean and standard deviation of the patients' age was 66.4 ± 15 years. The severity of their illness according to the APACHE II score was 22.3 ± 8, and their Sequential Organ Failure Assessment score was 9.1 ± 4. The causes of the sepsis were pneumonia (51.4%), peritonitis (13.1%), and soft tissue infection (13.1%). Mortality was 26.2%. There were 79 cases in the survival group and 28 in the nonsurvival group. The two groups are presented in Table 1. We performed a multivariate regression analysis to identify prognostic factors, and the only independent prognostic factors were age (OR = 0.955 (P = 0.022; 95% CI = 0.91 to 0.99)), acute respiratory disease syndrome (ARDS) (OR = 5.789 (P = 0.002; 95% CI = 1.91 to 17.4)) and base deficit (OR = 1.113 (P = 0.008; 95% CI = 1.02 to 1.2)). Early appropriate antibiotic therapy (EAAT) was not correlated with survival.

Table 1 (abstract P320)

	Survival	Nonsurvival	*P* value
Early appropriate antibiotic therapy (%)	67	60.7	0.645
Gram-positive coccus (%)	39.2	53.5	0.297
Gram-negative rod (%)	29.1	39.2	0.351

Conclusions EAAT did not affect the outcome. The prognostic factors for severe sepsis and septic shock identified in this study were age, base deficit and ARDS.

References

1. Dellinger RP, Levy MM, Carlet JM, *et al.*: **Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock.** *Crit Care Med* 2008, **36:**296-327.
2. Kumar A, Roberts D, Wood KE, *et al.*: **Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock.** *Crit Care Med* 2006, **34:**1589-1596.

P321

Strategy to reduce antibiotic prescription in cases of airway aspiration

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Critical Care 2009, **13(Suppl 1):**P321 (doi: 10.1186/cc7485)

Introduction Airway aspiration (AWA) of gastric content is a very frequent complication in patients presenting to emergency rooms after incidents linked to a depressed level of consciousness. The routine use of antibiotics in this situation determines a high-pressure selection for multiresistant microorganisms. However, how often AWA is the causative situation for early ventilator-associated pneumonia is not known. Also a gold standard for a diagnostic workup is needed. Our aim was to know how frequent AWA determines infectious aspiration pneumonia confirmed by evolution and microbiological samples, and to propose a methodological approach to rule out antibiotic usage.

Methods Over a 2-year period, in 82 patients admitted to our ICU, AWA was confirmed by the direct observation of gastric content when orotracheal intubation was performed by a trained physician due to a Glasgow coma scale below 12. Usual diagnosis: acute brain injury, 52 patients (73%); Simplified Acute Physiology Score II 37 ± 11; age, 44 ± 15 years; all were mechanically ventilated, average 6 ± 2 days; ICU stay ± 10 days; mortality 21%. Rectal fever, leukocytosis, thoracic radiology and PaO_2/FiO_2 were recorded on a daily basis. The Clinical Pulmonary Infection Score (CPIS) and semiquantitative tracheal aspirates (SQTA) were performed twice: in the first 48 hours and between the third and fifth days.

Results Out of 82 patients, 23 (28%) developed clinically and microbiologically confirmed pneumonia. Fever and leukocytosis showed no significant differences in patients with or without pneumonia during the first 5 days. Also the PaO_2/FiO_2 index was not different. As for radiology, when unilateral focal condensation was present, pneumonia was confirmed later (relative risk = 3.3, 95% CI = 1.7 to 6.4). CPIS in the first 48 hours showed a negative predictive value for pneumonia of 89%, and SQTA with no microorganism growth a negative predictive value of 96%. In our patient group, 42 (51%) had CPIS <6 and SQTA growth; in them no antibiotic usage is recommended. On the contrary, out of 20 patients who had CPIS ≥6 and positive SQTA, 16 (75%) developed pneumonia within the first 5 days of the ICU stay; this group deserves antibiotics. CPIS ≥6 without pneumonia, probably due to lung inflammation, was observed in 10 out of 28 patients (36%).

Conclusions (1) In our ICU population, pneumonia develops in only 28% of those presenting with AWA. (2) Through CPIS <6 and negative SQTA performed in the first 48 hours we could identify that in more than one-half of AWA patients antibiotics are not needed. (3) CPIS is not a reliable early indicator of pneumonia in patients with AWA.

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Effect of intravenous administration of freeze-dried sulfonated human normal immunoglobulin for septic patients

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Critical Care 2009, **13(Suppl 1):**P322 (doi: 10.1186/cc7486)

Introduction The proinflammatory cytokine TNF plays a critical role in the formation of severe sepsis when it is excessively released.

Recently, it was revealed through our animal models that intravenous administration of freeze-dried sulfonated human normal immunoglobulin (IVIG) makes anti-inflammatory effects by enhancing insulin-like growth factor 1 (IGF-1) production through stimulation of sensory nerves, which inhibits the production of TNF. In this study, we examined whether IVIG for septic patients enhances IGF-1 production.

Methods Fourteen septic patients indicating a high level of soluble E-selectin were surveyed, who were transported to our hospital from April to November 2007. They were divided into two groups, IVIG group (G-group, 5 g/day x 3 days, nine cases, 67.2 ± 8.64 years old) and nonadministered group (control group, C-group, five cases, 69 ± 12.9 years old).

Results In the G-group, the values of IGF-1 on the fifth day (162.22 ± 52.91 ng/ml) and seventh day (150.44 ± 29.06 ng/ml) were significantly higher than that on day 0 (88.59 ± 29.79 ng/ml, $P<0.05$). Furthermore, The value of IGF-1 of the G-group (162.22 ± 52.91 ng/ml) was significantly higher than that of the C-group (68.80 ± 24.04 ng/ml) on the fifth day ($P<0.05$).

Conclusions We revealed that IVIG for septic patients enhances IGF-1 production. Furthermore we will enhance the effect of sulfanated immunoglobulin compared with that of intact immunoglobulin in the difference of the anti-inflammatory effect and the mechanism.

References

1. Okajima K, Harada N, Suga H,Nakagawa T: **Rapid assay for plasma soluble E-selectin predicts the development of acute respiratory distress syndrome in patients with systemic inflammatory response syndrome.** *Transl Res* 2006, **148:**295-300.
2. Harada N, Okajima K, Kurihara H, Nakagata N: **Antithrombin prevents reperfusion-induced hepatic apoptosis by enhancing insulin-like growth factor-I production in mice.** *Crit Care Med* 2008, **36:**971-974.

P323

Levels of soluble fibrin in severe septic patients given intravenous immunoglobulin

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Critical Care 2009, **13(Suppl 1):**P323 (doi: 10.1186/cc7487)

Introduction It is known that severe sepsis causes multiple organ failure and high mortality. Intravenous immunoglobulin (IVIG) is used for severe sepsis patients. The mechanism of IVIG is clearly unknown. Suggested, however, is the possibility that IVIG prevents organic injury by suppressing the inflammation. Soluble fibrin (SF) is intermediate between fibrinogen and fibrionoligomer. It is better than fibrinogen as the material for thrombin. IVIG is used as one of the effective factors for repair of the damaged vascular endothelium. In this study we used SF as a marker of severity of illness in patients with or without IVIG and compared the levels of SF in two groups.

Methods Nineteen severe septic patients were divided into two groups. The control group ($n = 9$) was not given and the other group ($n = 10$) was given IVIG (5 g/day for 3 days). SF of serum from patients was measured on 0 days, 1 day, 3 days, 5 days and 7 days, and the results were analyzed.

Results The levels of SF were: control group: 4.77 ± 9.44 (0 days), 3.13 ± 2.53 (1 day), 3.33 ± 2.75 (3 days), 2.53 ± 2.58 (5 days), 2.58 ± 3.75 (7 days); other group: 7.71 ± 8.28 (0 days), 12.26 ± 16.75 (1 day), 14.34 ± 25.56 (3 days), 8.06 ± 9.08 (5 days), 11.95 ± 12.71 (7 days). There was a significant difference in the levels of SF between groups with and without IVIG at 1 day, 5 days and 7 days.

Conclusions Monocyte has the Fcγ receptor. It is thought that stimulating Fcγ of monocyte with IgG plays a role in increasing SF. Without severe DIC, increasing fibrin is used in the repair of the damaged vascular endothelium as a matrix and it prevents the invasion of germs. It is thought that increasing fibrin is the appropriate stimulation for coagulation and one of the reactions of biomechanical defense. We think SF is one of the important factors for the damaged cell and a useful marker of severity for severe sepsis. We also think IVIG is effective for severe sepsis.

Reference

1. Echtenacher B, *et al.*: *Infect Immun* 2001, **69:**3550-3555.

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Efficacy of corticosteroids on survival in patients with sepsis and septic shock: meta-analysis

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Critical Care 2009, **13(Suppl 1):**P324 (doi: 10.1186/cc7488)

Introduction Previous studies have recommended the use of low-dose corticosteroids in patients with septic shock. Specifically, response to corticotropin tests has been recognized as a prognostic factor in critically ill patients, especially in patients with no response to the corticotropin test. A recent large randomized controlled trial evaluating the efficacy of low-dose corticosteroids revealed no benefit on overall survival or in patients with no response to corticotropin in patients with severe sepsis and septic shock. Recently, recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients were published as consensus statements from an international task force by the American College of Critical Care Medicine [1]. However, some studies were not included in these statements.

Methods We conducted a systematic search of EMBASE and MEDLINE (through August 2008) for double-blind randomized clinical trials that evaluated the effect of corticosteroids on mortality in patients with severe sepsis and septic shock. Study selection criteria were all trials before August 2008 in which participants were randomized to corticosteroids or placebo and in which mortality was reported.

Results Data from 17 randomized, controlled trials with a total of 3,638 participants were analyzed. Corticosteroid use was not associated with a risk reduction in overall mortality (pooled risk ratio = 0.99 (95% CI = 0.90 to 1.09), $P = 0.823$). Low-dose corticosteroids (150 to 300 mg/day) did not show benefit on all-cause mortality in patients with severe sepsis and septic shock (risk ratio = 0.92 (95% CI = 0.79 to 1.06)). Furthermore, low-dose corticosteroids in patients with severe sepsis and septic shock who did not respond to the corticotropin test showed no benefit on 28-day mortality (risk ratio = 0.91 (95% CI = 0.76 to 1.09)). Corticosteroids use was not associated with increased complications, such as gastrointestinal bleeding or increased infections.

Conclusions This meta-analysis indicated that administration of low-dose corticosteroids was not beneficial on overall mortality in patients with severe sepsis or septic shock.

Reference

1. Marik PE, *et al.*: **Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: consensus statements from an international task force by the American College of Critical Care Medicine.** *Crit Care Med* 2008, **36:**1937-1949.