

Experience with IgM-Enriched Immunoglobulins as Adjuvant Therapy in Septic Patient after Redo Cardiac Surgery

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Abstract

Infective endocarditis after combined mitral valve repair and coronary artery bypass surgery, multi-organ failure and sepsis, were treated with mitral valve replacement, antibiotics and adjunctive therapy. Sepsis caused by Gram-negative bacteria, was identified based on the grave clinical status, hemodynamic findings and high levels of pro-inflammatory cytokines. On the day of the redo surgery, the APACHE II and SOFA scores were 26 and 14, respectively. The IgM-enriched immunoglobulin Pentaglobin[®] was administered on the first postoperative day after redo procedure. The cardiac index improved from 1.9 L/m² to 3.7 L/m² on the 1st postoperative day, accompanied with increasing values of mixed venous oxygen saturation from 59.3% to 77%, while systemic vascular resistance 887 dyn·s/cm⁵ was maintained by vasopressor agent. On the 4th postoperative day the inotropes and pressors ceased. The acute physiology and chronic health evaluation (APACHE II) score and sequential organ failure assessment (SOFA) score decreased to 10 and 2, respectively. The prompt improvement in patient's general clinical condition, stabilised hemodynamic parameters, balanced perfusion and oxygen pattern, accompanied by notable reduction of pro-inflammatory cytokine expression, were the outcome of the presented therapeutic approach.

Keywords: APACHE II; Hemodynamic parameters; Laboratory data; Pentaglobin[®]; Redo cardiac surgery; Severe sepsis; SOFA score

Introduction

Severe sepsis and septic shock in cardiac surgery are associated with substantial mortality, particularly in elderly and critically ill patients [1]. Eradication of infection with appropriate antibiotics and source control, aggressive supportive care and adequate central venous oxygen saturation are early goal-directed therapy [2]. Attempts to modulate the inflammatory response in sepsis are often required [3], but they are generally unsuccessful and currently under broad debates [4,5]. Therapies that improve host immunity showed promising findings in sepsis [5], but they are still on the level of preclinical investigations and clinical trials [4]. The aim of this case report was to present the efficacy of the early-goal directed therapy along with immunoadjuvant therapy (IgM-enriched immunoglobulins, Pentaglobin[®]) in gram-negative bacterial sepsis. The treated patient underwent mitral valve replacement (MVR) after prior mitral valve repair (MVP) and coronary artery bypass grafting (CABG) surgery in the same hospitalization.

Case report

A 63-year-old male patient was admitted to the tertiary care institution for elective CABG and MVP surgery. Preoperative assessment and transesophageal echocardiography (TEE) showed mitral valve insufficiency (MVI) grade III with low left ventricular ejection fraction (LVEF<15%). The MVP and coronary artery triple bypass grafting were performed without any complication in high risk patient.

Ten days later, the patient was readmitted to the intensive care unit (ICU) due to cardiorespiratory failure and de novo MVI grade III confirmed by TEE. However, the presence of mitral valve vegetation has not been detected. The redo procedure, mitral valve replacement (MVR), has been performed two weeks after the first operation.

Hemodynamic parameters	0-POD redo surgery		1-POD	2-POD	3-POD	4-POD
	before	after	Th start	Th administration	Th stop	
CI (L/min/m ²)	1.9	3.6	3.7	3.6	3	3.1
MAP (mmHg)	58	81	62	72	75	82
PCWP (mmHg)	17	12	14	12	16	20
CVP (mmHg)	8	10	9	10	10	12
SVR (dyn·s/cm ⁵)	887	684	570	680	704	844
PVR (dyn·s/cm ⁵)	85	102	65	102	69	89
SvO ₂ (%)	59.3	72	77	74.8	71.5	70
Epinephrine [*] (µg/kg/min)	na	6.4	4	1.6	0.8	na
Norepinephrine ^{**} (µg/kg/min)	na	12.8	8	3.2	na	na
Hemodynamic drugs	*1 mg in 20 ml solution 0.9% NaCl			**2 mg in 20 ml solution 0.9% NaCl		
	na-not administered					

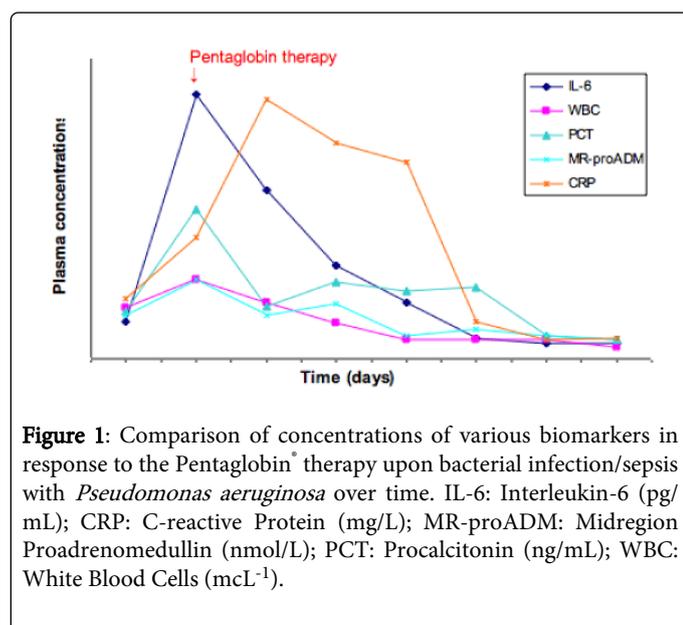
Table 1: Improvement of hemodynamic parameters during the Pentaglobin[®] therapy. Legend: CI: Cardiac Index; CVP: Central

Venous Pressure; MAP: Mean Arterial Pressure; PCWP: Pulmonary Capillary Wedge Pressure; PVR: Pulmonary Vascular Resistance; SvO₂: Mixed Venous Oxygen Saturation; SVR: Systemic Vascular Resistance; POD: Postoperative Day; Th: Therapy.

The bacterial sepsis has been confirmed by isolated *Pseudomonas aeruginosa* from the mitral valve ring and blood culture. The severe sepsis was evaluated by clinical conditions [1,3], laboratory and hemodynamic data. The daily sequential organ failure assessment (SOFA) score and acute physiology and chronic health evaluation (APACHE II) score were calculated to estimate illness severity during patient's stay in the ICU [6].

The progression of acute renal failure was confirmed both prior to and after the redo surgery. The high values of urea 15.7 mmol/L and creatinine 179 µmol/L, associated with anuria, were treated with continuous infusion of furosemide, and the renal function was restored in two weeks.

Preoperatively and during the redo procedure, the considerable hemodynamic fluctuations were treated by infusion of inotropes (epinephrine) and vasopressor (norepinephrine). The Cardiac index (CI) improved from 1.9 L/m² to 3.7 L/m² on the 1st postoperative day (POD), accompanied with increasing values of mixed venous oxygen saturation (SvO₂) from 59.3% to 77% and maintained above 70% during the rest of the patients stay in the ICU (Table 1), while systemic vascular resistance (SVR) 887 dyn·s/cm⁵ was maintained by norepinephrine. On the day of the redo surgery APACHE II score was 26 and SOFA score was 14. One day after the redo surgery (1st POD), based on the grave clinical status, hemodynamic findings and high levels of proinflammatory cytokines, the severe sepsis was identified and Pentaglobin[®] was administered. Besides the clinical scores and hemodynamic parameters, the biohumoral modulation was also evaluated (Figure 1).



The IgM-enriched immunoglobulin Pentaglobin[®], with relative composition of 76% IgG, 12% IgA and 12% IgM was used in this case. In the first two and a half hours the continuous infusion of 40 ml (0.4 ml/kg body weight/hour) was administered, followed by 20 ml/h (0.2 ml/kg body weight/hour) until the total dose of 1500 ml (15 ml/kg

body weight) in 72 hours has been infused [7]. After the therapy administration (4th POD), the hemodynamic parameters improved (Table 1) and the inotropes and pressors ceased. The APACHE II score decreased to 10 and SOFA to 2 on the 7th POD. Finally, on the last day of the patient's stay in the ICU (38th POD), the APACHE II was 5 and SOFA was 1, owing to adequate antibiotic and adjunctive therapy. Six months later, the preformed patient's check-up showed normal findings.

Discussion

In the case of infective endocarditis a surgical approach is essential. If the severe sepsis is present, the adequate antibiotics supported by inotropes and vasopressors are necessary to adjust cardiac preload (central venous pressure and pulmonary capillary wedge pressure), afterload (systemic and pulmonary vascular resistance) as well as a pattern of tissue perfusion.

Early recognition of sepsis is crucial as well as an early therapeutic approach. No single biomarker of sepsis may be ideal, but many are helpful in terms of identifying critically ill patients [8]. The procalcitonin (PCT) is the reliable biomarker for identifying systemic bacterial infection and sepsis diagnosis [9]. In this case, it has been used along with interleukin (IL)-6, midregion proadrenomedullin (MR-proADM), leukocyte count (WBC) and C-reactive protein (CRP) as an example of multimarker strategy useful for monitoring antibiotic's efficacy [7], and for supervising the trends of infections [9]. As presented in Figure 1, on the day of Pentaglobin[®] administration, there was a prompt decrease in values of: PCT, IL-6, MR-proADM and WBC whereas CRP values continued to increase considerably for several days and returned to normal levels two weeks later.

Early goal-directed therapy in sepsis, which includes the optimization of hemodynamic parameters, is applied to improve end points of resuscitation, to limit organ dysfunction and to enhance resource management. The advance in sepsis therapy [10] targets an immune system and a host individual response to microbial agents. Commercial available intravenous immunoglobulins (IVIG) preparations are in use since 1950s [10,11]. Pentaglobin[®] has polyvalent capabilities for modulating host immune response, and it has been developed and introduced into clinical practice during 1990s [7]. IgM antibodies play a key role in clearing pathogens and enhance primary immune response [12]. There have been numerous recent advances in understanding of the mechanisms of action of IVIG [13], but the optimal timing of administration, adequate dose of IgM preparations as well as target group still remain unsettled [14]. According to Molnar et al., the early administration of IgM preparation has beneficial effects in treatment of critically ill patients [7]. On contrary, the research of Alejandria et al., which included the data from the Cochrane Database, showed insufficient evidence to support the IgM adjunctive therapy on adults thus consider it as experimental [15]. In this case, the continued Pentaglobin[®] therapy applied within 24 hours after sepsis appearance contributed to significant improvement of the patient's hemodynamic and clinical status. The decrease in values of APACHE II and SOFA scores after the adjunctive therapy was evident.

Conclusion

In our opinion, Pentaglobin[®] had a substantial impact on the patient's clinical status regarding severity of the illness. Early postoperative infective endocarditis and the onset of sepsis

accompanied by heart failure, acute renal insufficiency and prolonged stay in the ICU, were considered as a reasonable indication for Pentaglobin® administration. The therapeutic approach in this septic patient was successful, but it should be regarded that the benefits of the IgM adjuvant therapy are still under debate. The presented experience and results in treatment of sepsis with Pentaglobin® therapy need to be estimated through future multicentre and randomized clinical trials and research, despite limits in its administration due to high costs.

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