Cold Agglutinins In On-Pump Cardiac Surgery: A Rare But Potentially Lethal Problem

N Madershahian, U Franke, H Jütte, J Wippermann, D Berz, T Wahlers

Citation

Abstract
Cold agglutinins (CA) represent IgM antibodies, which reversible interact with antigens on autologous erythrocytes at low temperatures. Most patients with CA remain asymptomatic, but in patients with high-titer and high-termal amplitude complications such as hemolysis, sludging of red blood cells with microvascular occlusion and decreased perfusion to various organ systems can cause unexpected morbidity and mortality.

Among 2294 consecutive patients the screening revealed a positive reaction in 37 patients (1.6%). Specific CA were found in only five patients (0.2%) showing anti-I blood group specificity.

The clinical significance of cold agglutininemia in patients requiring cardiac procedures using extracorporeal circulation is discussed controversially. The discussion is focused on the necessity of routine pre-operative screening for cold agglutinins [2,3]. The very low incidence contrasts to the severe and sometimes lethal complications.

INTRODUCTION
Cold agglutinins (CA) represent IgM antibodies, which reversible interact with antigens on autologous erythrocytes at low temperatures. Most patients with CA remain asymptomatic, but in patients with high-titer and high-termal amplitude complications such as hemolysis, sludging of red blood cells with microvascular occlusion and decreased perfusion to various organ systems can cause unexpected morbidity and mortality. Due to routine use of systemic or topical hypothermia in cardiac surgery, the incidence of clinical symptoms is increasing [1]. In response to a fatal experience with a patient’s death due to intracoronary precipitation of blood, we analyzed the incidence of CA in all patients undergoing on-pump cardiac surgery in our institution accompanied using a differentiated management.

MATERIAL AND METHODS
All patients undergoing on-pump cardiac surgery were screened for CA using the direct Coombs test, an unspecific reaction of serum against blood-group-0-RBC at both a temperature of 4°C and 37°C, respectively. In case of positive screening reaction at 4°C alone, additional specificity of CA as well as the titer of the antigens were tested. Patients were considered to be positive for CA in case of a titer of 1:70 or higher.

RESULTS
Among 2294 consecutive patients the screening revealed a positive reaction in 37 patients (1.6%). Specific CA were found in only five patients (0.2%) showing anti-I blood group specificity.

The first patient, a 77-year-old woman without pre-operative screening for cold agglutinins, was found to have unsuspected hemagglutination during moderate hypothermic extracorporeal circulation (31°C) using antegrade cold cristalloid cardioplegia (Buckberg-cardioplegia). On opening the coronaries, intracoronary clumping of red cells was noticed. Normothermic CPB and warm blood cardioplegia were immediately employed. Despite of extended warm reperfusion and intraoperative IABP insertion the patient developed severe myocardial ischemia and severe hemolysis. In the immediate postoperative period the patient died due to unmanageable VT. Postoperatively performed blood tests revealed the presence of CA, which caused blood coagulation at 30°C with a titer greater than 1:32.

Patient 2,3,4,5. In these patients (2 female, 2 male, mean age 73 1.5 years) preoperative tests showed specific CA. To avoid complications cardiac procedures were performed
using warm blood cardioplegia and normothermic cardiopulmonary bypass (36°C). Core body temperature was maintained at 36°C on cardiopulmonary bypass throughout the procedure. Operative and postoperative course of all patients was uneventful without any clinical or paraclinical evidence of microcirculatory impairment, hemodynamic events or hemolysis.

**DISCUSSION**

The clinical significance of cold agglutininemia in patients requiring cardiac procedures using extracorporeal circulation is discussed controversially. The discussion is focused on the necessity of routine pre-operative screening for cold agglutinins [2,3]. The very low incidence contrasts to the severe and sometimes lethal complications.

In the case of detection of significant specific cold agglutinins various patient management strategies have been described. Use of plasma exchange prior to surgery, total blood exchange transfusion, coronary arterial blood washout with normothermic crystalloid cardioplegia as well as normothermic, noncardioplegic, intermittent fibrillatory arrest have been performed with successful outcome [4,5].

Additionally, the use of warm blood cardioplegia in these patients combined with normothermic extracorporeal circulation leads to successful outcome after cardiac surgery as described by our data. The routine use of intermittent warm blood cardioplegia, which approves superior results in coronary surgery, would allow the abandonment of extensive presurgical screening for detection and characterization of CA [5]. For all patients undergoing cold cardioplegic arrest or hypothermic extracorporal circulation the screening for CA is mandatory.

**CORRESPONDENCE TO**

Navid Madershahian, M.D. Department of Cardiothoracic and Vascular Surgery Friedrich-Schiller University Jena Erlanger Allee 101 07740 Jena Germany Phone: +49 3641 9322989 Fax: +49 3641 9322902 E-mail: Navid.Madershahian@med.uni-jena.de

**References**

Author Information

Navid Madershahian
Department of Cardiothoracic and Vascular Surgery, Friedrich-Schiller University Jena

Ulrich F.W. Franke
Department of Cardiothoracic and Vascular Surgery, Friedrich-Schiller University Jena

Heike Jütte
Institute for Transfusion medicine, Friedrich-Schiller University Jena

Jens Wippermann
Department of Cardiothoracic and Vascular Surgery, Friedrich-Schiller University Jena

Dagmar Berz
Institute for Transfusion medicine, Friedrich-Schiller University Jena

Thorsten Wahlers
Department of Cardiothoracic and Vascular Surgery, Friedrich-Schiller University Jena