CASE REPORT

Cholesterol in the ICU: a cheap and reliable marker for illness severity?

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Several markers as C-reactive protein and procalcitonin are used in the ICU to monitor the success of the treatment. Recently, studies about the prognostic value of cholesterol have been reported. In this case series we discuss cholesterol as a cheap and reliable marker for daily follow up, to monitor improvement or deterioration of patients in the ICU.

Introduction

An intensive care unit frequently deals with acute-phase responses of patients to several noxae, whether infectious or not. Clinicians gather circumstantial evidence about improvement or deterioration of their patients every day. There is, however, no single parameter which informs the physician whether the initiated treatment is right or complications are developing.

Evidence for infectious complications is important because the potentially evolving sepsis is associated with morbidity and mortality [1]. Fever has been seen as an early marker for infectious complications, although its positive predictive value for having an infectious complication has been questioned [2]. Also the combination of fever with other systemic inflammatory response syndrome criteria (tachycardia, tachypnoea and leucocytosis) is not very specific for infection and can occur in non-infectious conditions [3]. As an addition to clinical signs, daily inflammatory laboratory parameters as C-reactive protein (CRP) and procalcitonin can help to identify infectious complications. One can argue that if there is a definite improvement in the patient, routine measurements are not cost-effective. However, when the patient is not responding or responding slowly to treatment, infectious complications have to be considered. Measurements of CRP, procalcitonin and leucocytes have been linked to infectious complications. It was shown that a CRP ≥ 50 mg/L in combination with systemic inflammatory response syndrome (SIRS) in the first week of admission was a good predictor of infectious complications [4]. Another paper stated that patients with an increase of 8.7 mg/L in consecutive daily

CRP measurements had an 88% risk of infection [5]. The much more expensive procalcitonin is also an excellent parameter for early detection of infectious complications. Several overview articles explain the value of procalcitonin in the identification of infectious clinical problems [6].

For several years, research in this field has also focussed on the interaction between the acute-phase response and cholesterol [7]. The serum lipid profile undergoes several changes during septic shock. It has been shown that cholesterol levels decrease during the acute phase whereas different subclasses as high-density lipoprotein (HDL) also undergo an additional change in constitution [8, 9]. Recently, even prognostic implications from low levels of HDL have been reported [10-12].

This raises the question if cholesterol can be of help to guide decisions about acute-phase responses when it is determined routinely every day. If so, cholesterol could be an adequate and cheap tool for monitoring treatment and could indicate improvement or deterioration of patients.

Methods

During the routine rounds of laboratory evaluation on the mixed surgical and medical intensive care unit in the Catharina Hospital Eindhoven, we measured procalcitonin, CRP and total cholesterol. We evaluated these levels in correlation to the clinical course of the disease. Five of these cases with laboratory values are shown in the graphs below.

Cases:

Case 1

The patient was admitted postoperatively after aortic valve replacement for decompensated aortic stenosis. The patient had a paravalvular leakage which required re-operation. During the stay in the ICU the patient developed pneumonia on day 2,

which was treated with flucloxacillin. Sputum cultures showed Staphylococcus aureus (Fig1a).

1a. CRP - PCT - Cholesterol
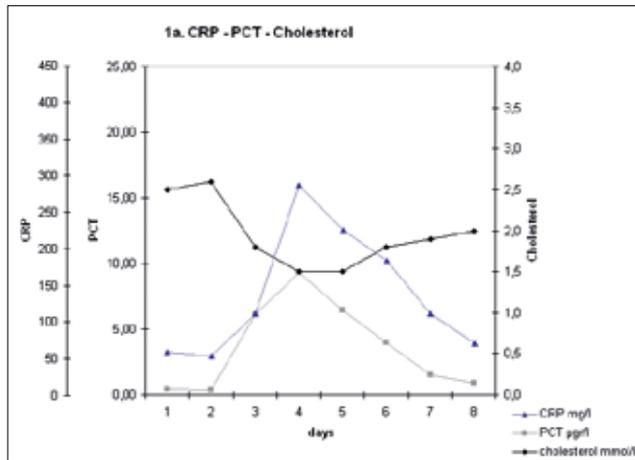
Graph evaluation: When the pneumonia developed, the cholesterol and procalcitonin levels responded at about the same time. When the patient recuperated, the cholesterol levels increased about one day after the decrease of procalcitonin, and at the same time as the decrease in CRP.

Case 2

The patient was admitted after aortic valve replacement for a decompensated aortic stenosis with severe left ventricular hypertrophy and a decreased right ventricular function. After surgery the patient showed an initial improvement. A few days later, however, the patient developed septic shock from either mesenteric ischaemia or a central venous catheter infection (Fig1b).

1b. CRP - PCT - Cholesterol
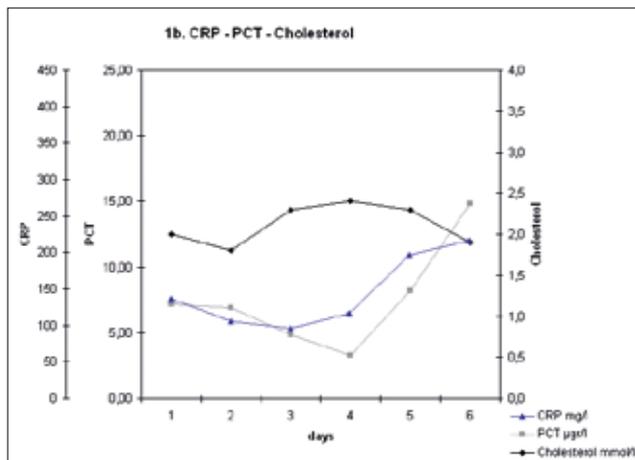
Graph evaluation: Initially, the postoperative cholesterol increased and procalcitonin decreased. When the infectious complications developed, the cholesterol levels started decreasing. Along with this decrease in cholesterol, a rise in procalcitonin was observed. Initially, the CRP remained at about the same level (100-120 mg/L but started increasing along with the above-mentioned parameters.

Case 3

A 56-year-old patient was admitted postoperatively after correction of internal intestinal herniation due to adhesions. The patient suffered from adult respiratory distress syndrome (ARDS). This improved slowly (Fig1c).

1c. CRP - PCT - Cholesterol
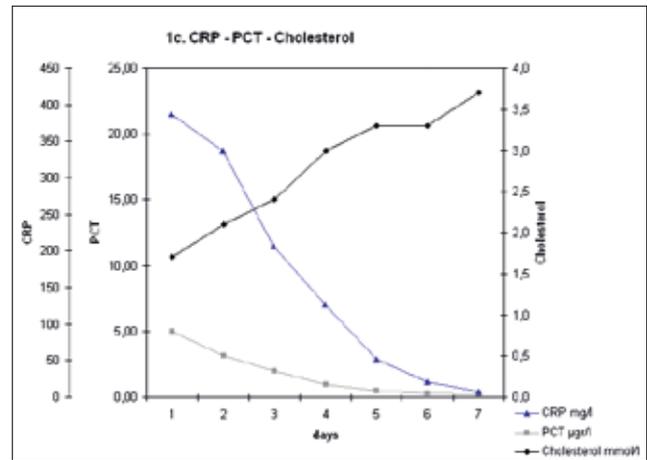
Graph evaluation: The levels of procalcitonin and CRP decreased and the cholesterol levels increased with the improving condition of the patient.

Case 4

An 83-year-old patient was admitted to the ICU because of intestinal ischaemia which developed after total hip replacement. Due to his poor pre-existent performance and comorbidity the patient was treated with antibiotics without undergoing surgery. With this treatment, the condition of the patient improved over the next few days (Fig1d).


1d. CRP - PCT - Cholesterol
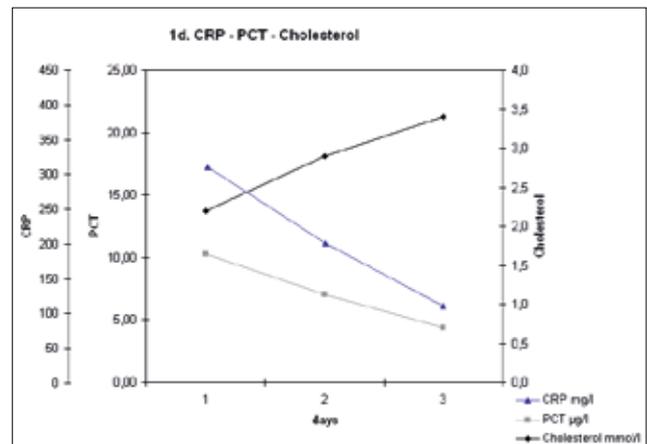
Graph evaluation: With the improving condition, the procalcitonin and CRP decreased and the cholesterol levels increased.

Case 5

Postoperatively after an aortic bi-femoral bypass, ischaemia of the right lower extremity developed. With the start of antibiotics

on day 4 the patient underwent a femoral-popliteal bypass and fasciectomy. After this intervention the clinical condition of the patient improved (Fig1e).
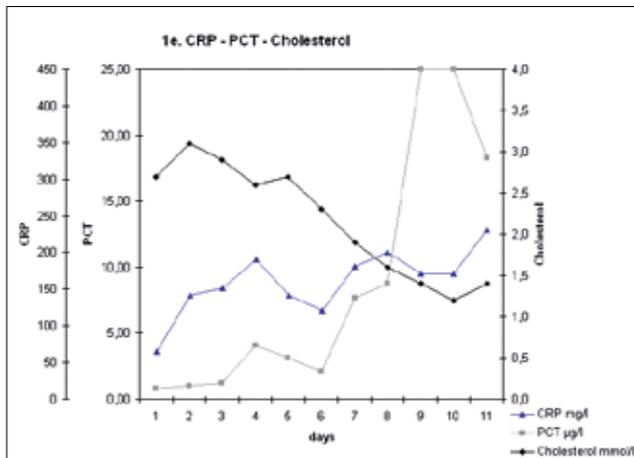
Graph evaluation: Limb ischaemia developed immediately after surgery. This non-infectious event is shown in the graphs by the decreasing cholesterol levels, and a normal procalcitonin. After 4-6 days, however, infectious complications developed. A femoral-popliteal bypass with fasciectomy was performed on day 6. This is shown as a sudden rise in procalcitonin and a further decrease in cholesterol. When the procalcitonin levels stabilised, the cholesterol starts to increase (day 10).

Discussion

When looking into our own database and comparing cholesterol, CRP and procalcitonin to the clinical courses of our patients, we have the impression that, as shown above, there is a correlation between cholesterol and the other inflammatory parameters. Moreover, there seems to be an association between cholesterol and the clinical course. Cholesterol has been known to be associated with the severity of disease. Research is focussing on the explanation of the decrease in the separate subclasses of cholesterol and its meaning in view of severe sepsis [7, 9-12]. Total cholesterol, which we measured in our study, can be divided into low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides which are mainly transported through the blood by very low-density lipoprotein (VLDL) cholesterol. During severe sepsis, LDL cholesterol reaches its minimum early in the course of the disease [9]. This decrease is thought to be due to a diminished synthesis and efflux of cholesterol from the liver [13, 14].

As far as HDL cholesterol is concerned, it keeps decreasing during the most fulminant phase of sepsis and increases again with the improvement of the clinical condition [9]. The mechanisms behind this process are complex and only partially elucidated. In healthy persons, the core of the HDL particle consists of apolipoprotein (Apo) A-1 or Apo A-2. During severe sepsis this core is replaced by another protein called serum amyloid A (SAA).

SAA has chemoattractant properties promoting migration adhesion and tissue infiltration [15]. This can be advantageous during sepsis. The acute-phase response upregulates enzymes which facilitate conversion of the HDL particles and probably facilitate receptor binding [16-18]. These complex processes are responsible for the low HDL levels in the circulation. The SAA protein, in particular, has been investigated as a possible inflammatory marker during pancreatitis and turned out to be a good predictor of severity and complications [19].

The research on triglycerides shows somewhat more conflicting results. Earlier ex vivo studies (animal models) showed a rise of triglyceride levels in sepsis models [20], whereas, more recently in vivo research also showed decreasing triglyceride levels during sepsis [9]. Lipid-rich sedation regimes and intravenous nutrition may play a role in these results. Combining these three components explains the decrease of total cholesterol during severe sepsis or septic shock.

In-depth statistical analysis of our database proved difficult because when we correlated cholesterol directly to CRP and procalcitonin, we encountered individual baseline differences for the three parameters (CRP, procalcitonin and cholesterol). Although, in general, a decreasing cholesterol was accompanied by an increasing CRP and procalcitonin, it did not always do this in the same timeframe or with the same tenacity.

In the presented graphs cholesterol seems to be a parameter to monitor the overall clinical condition of the patient, i.e. it seems to be a marker for overall deterioration or improvement. Compared with CRP, cholesterol levels seem to change a bit earlier in the clinical course than CRP levels do. Like CRP, cholesterol is not a specific marker for infection. However, when cost awareness is pivotal: determining cholesterol involves about 3 cents reagent costs and is 10 times cheaper than C-reactive protein and about 500 to 600 times cheaper than procalcitonin. We, therefore, think that cholesterol may be a promising cheap and early marker for daily follow-up of patients with SIRS or sepsis. In our view it can be a valuable addition to other parameters in determining the course of these patients, although further studies are needed.

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