PROGNOSTIC ROLE OF PROCALCITONIN IN THE EARLY DETECTION OF PATIENTS AT RISK OF POST-OPERATIVE INFECTION

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[Ruolo prognostico della procalcitonina nell'individuazione precoce di pazienti a rischio d'infezione nel post-operatorio]

ABSTRACT

The authors evaluate the risk of postoperative infection in 20 patients undergoing major abdominal surgery through the measurement of procalcitonin, white blood cells and body temperature. They examine the results in charts and confirm the use of PCT as a prognostic index, useful in case of surgical patients at risk of infection.

Key words: Monitoring, marker, specificity, surgery, prognosis.

Received *April 12, 2012;* ***Accepted*** *April 19, 2012*

Introduction

Most of the parameters currently used as indicators of the inflammatory reaction - i.e. body temperature, white blood count, erythrocyte sedimentation rate, C-reactive protein - are sensitive and reliable, but non-specific[1].

Even the direct microbiological diagnostics, though essential, provide results that are often delayed and with low percentages of positive blood cultures (20%).

Since 1996, with the appearance of procalcitonin (PCT), a glycoprotein precursor of calcitonin[2], a highly specific and sensitive diagnostic parameter became available, able to detect serious bacterial infections and to indicate complications of systemic inflammation with a high degree of reliability[3].

Experimental studies and clinical observations have identified the main stimulus for the induction of PCT in the systemic effect of bacterial endotoxins[4].

The PCT can be induced by other stimuli of lesser extent, but it is ascertained that it cannot be induced only by surgical trauma[5].

The aim of our work was to assess through seriated blood samples, perioperatively, the trend of procalcitonin, the movement of white blood cells with the three populations of lymphocytes, monocytes and granulocytes, and the trend of the body temperature in patients undergoing major abdominal surgery that came to our attention.

Materials and methods

For our prospective observational study, we enrolled 20 patients aged between 40 and 80 years (60 years on average) including 16 males and 4 females. These patients were subjected to different types of surgery: 8 were operated of sigmoid colon tumour, 3 of rectum tumour, 1 of cæcum tumour, 1 of cephaloduodenopancreatectomy, 1 of VBP tumour, 3 of kidney tumour, 2 of diverticular disease. For each patient we evaluated the ASA index,

associated diseases, antibiotic therapy and any type of anaesthesia performed. Of all the patients examined, 15 were ASAIII, 5 were ASAII;

10 suffered from hypertension (3 associated with diabetes and 1 associated with epilepsy), 4 of ischemic heart disease, 2 of diabetes, 1 of liver disease associated with hypertension and ischemic heart disease, 1 of COPD, the other 2 did not have associated pathologies.

Almost all were subjected to antibiotic therapy before and after surgery.

A general anaesthesia +IOT was performed on 18 of them and on 2 a general + epidural.

In addition to standard clinical, instrumental and biohumoral evaluation, the enrolled patients were monitored using seriated blood samples taken from a peripheral vein of the forearm or hand. We then analyzed the following data from an EDTA tube: the counts of white blood cells (lymphocytes, monocytes and granulocytes) and, after centrifugation, we analyzed the concentration of procalcitonin (PCT) on plasma.

These data were recorded preoperatively (T0), 30 min after induction of anaesthesia (T1), at the end of surgery (T2), 24 hours after the end of surgery (T3).

At T3 was also measured the body temperature.

We also evaluated the criteria of SIRS and sepsis in all patients, in accordance with the ACCP \ SCCM.

Some patients, who then presented complications during surgery - such as respiratory or cardiac insufficiency, intraoperative bleeding or who were re-operated - were excluded from our study, while others - who presented a normal perioperative course - were examined in the study.

For the dosage of procalcitonin we used an immunochromatographic PCT-Q test (Brahms), semiquantitative, with an incubation time of 30 min (picture 1).

The data obtained are closely correlated to those obtained with the methods in luminescence.

This test uses a mouse monoclonal anti-calcitonin antibody, conjugated to colloidal gold (tracer) and a goat polyclonal anti-calcitonin antibody (solid phase).

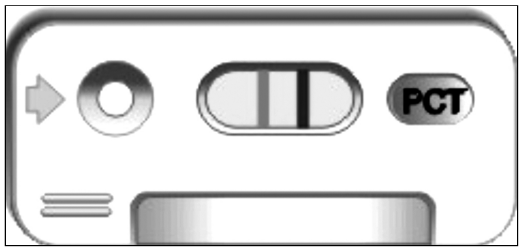
After adding the patient's plasma to the test strip, the tracer binds to the PCT of the sample, forming a definite antigen-antibody complex.

This complex moves by capillarity through the system, passing through the area containing the test band.

Here the antigen-antibody complex binds to the fixed anti-calcitonin antibodies, forming a "sandwich" complex.

At a concentration of PCT ≥ 0.5 ng\ml, this sandwich complex can be viewed as a red-coloured band. The colour intensity of the band is directly proportional to the concentration of the sample and PCT and, with the aid of a reference board, it is related to the following concentration ranges of PCT:

- <0,5 ng\ml
- ≥0,5 ng\ml
- ≥2 ng\ml
- ≥10 ng\ml



Picture1: Immunochromatographic PCT-Q test (Brahms).

The unbound tracer spreads over the area of the control band, where it is fixed by producing a control band of intense red colour, which allows to check the functionality of the test.

For the count of white blood cells and of leukocyte subpopulations, we used a cell counter "coulter microdiff 18" of the Instrumentation Laboratory.

Results

From the data obtained we can say that in all the cases we observed, the progress of the PCT, WBC and body temperature reflected the clinical course.

In all 20 patients studied, the concentration of PCT at time T0 and T1 was maintained below 0.5 ng/ml, confirming the data of literature. At time T2, in 16 patients, it was always below 0.5 ng/ml, only 4 exceeded this value. At T3 in nearly all patients (80%) the concentration of PCT recorded a significant increase, but remaining always within the 2 ng/ml. Only in few cases it has exceeded this value (chart 1).

From our sampling it was ascertained that the trend of the leukocytes, starting from different baseline values (T0), records a slight decrease in almost

all patients at T1. At T2 almost all have reported a significant increase of leukocytes confirming the well known post-intervention leucocytosis. Only a few did not show this peak. At T3, the trend was irregular as some patients have experienced a decrease that brought the leukocyte values almost to baseline (T0), while others at T3 have maintained values similar to T2. Patients who did not had a leukocyte peak at T2 showed a rise of these values at T3 (chart 2).

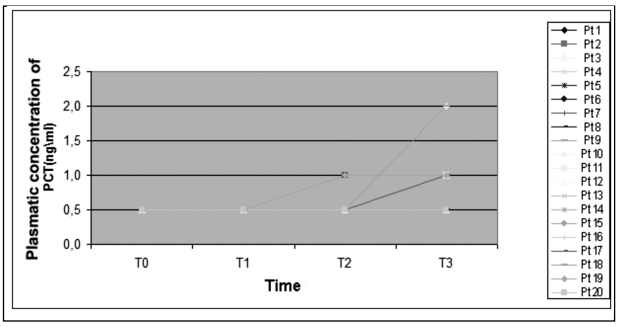


Chart 1: Trend of procalcitonin during the four sampling times

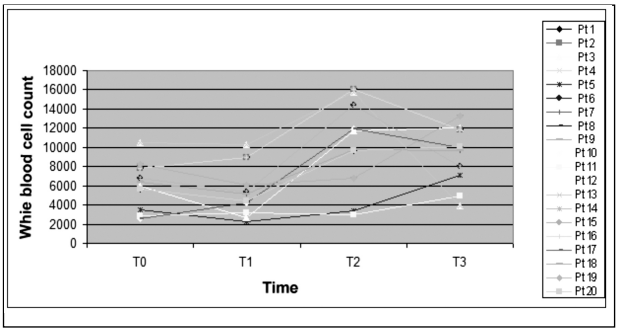


Chart 2: Trend of leukocytes during the four sampling times.

Considering specifically the three leukocyte populations, we can confirm that the trend of lymphocytes, starting from different values at T0, had in almost all patients a decrease at T1. These values remain constant in almost all at T2 and T3. Only a few reported at T2 a slight increase of these values, a few others have shown a significant increase at T3.

The trend of monocytes was fairly linear in the four times of sampling, recording for all patients only a slight increase in T1. Only some have deviated from this trend, showing a peak at T2 instead of T1, while others have reported an increase in values at T3.

The granulocytes, starting from different values at T0, show a decrease in T1 in almost all the patients with the exception of only one, which shows an increase at T1. At T2, almost all the patients show more or less significant peak values. At T3 there was a decrease in almost all the patients, one of which recorded a decreased value compared to baseline (chart 3).

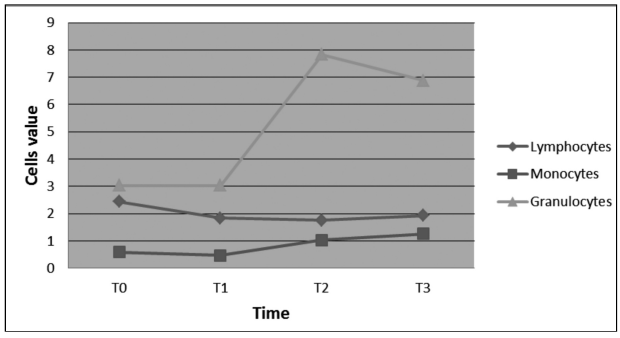


Chart 3: Trend of the mean values of lymphocytes, monocytes and granulocytes during the four sampling times

As regards the trend in body temperature, we found that almost all patients were afebrile before surgery. Some had an increase in temperature at T3, others remained afebrile (chart 4).

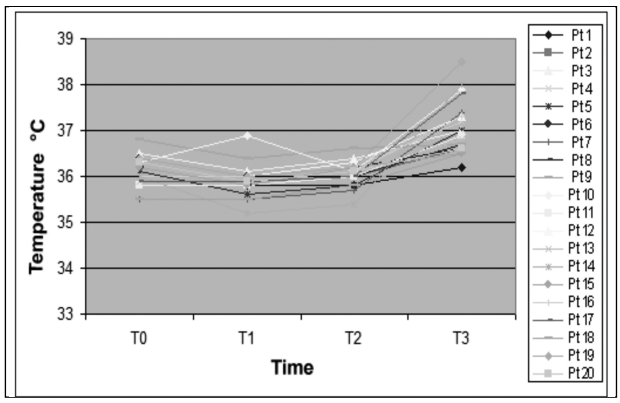


Chart 4: Trend of body temperature during the four sampling times.

Discussion

From the analysis of the results we can conclude that the increase of PCT in almost all patients studied, only 24 hours after surgery, confirms the importance of this marker in the early identification of any infectious condition. In particular, we have observed that the values of PCT appear to increase after 24 hours in major abdominal surgery[6].

We have never observed values above 10ng\ml - This confirms that, however, the concentrations of PCT over 10ng\ml are unusual in patients with uncomplicated postoperative course.

In summary, the postoperative increase of PCT can be observed in some patients with normal postoperative course, although there are signs of bacterial infection or other inflammatory processes.

On the contrary, in 2 patients, we found no high values of PCT in the immediate postoperative period, or at 24 hours after surgery, although such patients presented the clinical signs of inflammation and infection.

This result can still be useful if interpreted as a sign of an effective antibiotic therapy initiated promptly in an empirical way.

In the postoperative period, the mechanisms of induction of the increase of PCT in patients with normal postoperative course, have not been fully elucidated to date. The PCT could be induced by a transient bacterial contamination during operations, or preparations of intestinal anastomosis, or by the release and translocation of bacterial endotoxin during the period of intestinal malperfusion.

The PCT can not be correlated with the plasma levels of endotoxin when endotoxin concentrations are low. However, plasma concentrations of PCT are still high when the endotoxin levels are above 10 ng\ml.

Also the leukocyte movement, that we found in the majority of patients, is in line with literature data.

It is commonly known that an inflammatory condition promotes the activation of some leukocyte populations such as monocytes, granulocytes and lymphocytes.

However, the trend of leukocytes, although important, unfortunately causes problems with regard to the specificity.

Also the body temperature turned out to be a highly aspecific data.

The PCT, however, in patients at risk, increases promptly within 24 hours, allowing us to make an early diagnosis and timely treat our patients with an effective antibiotic therapy.

Conclusions

On the basis of these results, we can confirm that PCT is greatly helpful to distinguish an infection from an inflammation. Moreover, it plays a very important prognostic role in the early detection of patients at risk of infection in the post-operative period.

In conclusion, we believe that the preliminary data we obtained to date from our studies are encouraging, although further studies are needed with larger case records in order to draw definitive conclusions about the reliability of PCT, particularly in some clinical situations.

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