International Journal of Infectious Diseases 61 (2017) 62–66

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Changes in eosinophil count during bacterial infection: revisiting an old marker to assess the efficacy of antimicrobial therapy☆

B. Davido[a,*], S. Makhloufi[a,b], M. Matt[a], R. Calin[c], O. Senard[a,b], C. Perronne[a,b], A. Dinh[a], J. Salomon[a,b,d]

[a] Maladies Infectieuses, Hôpital Universitaire Raymond-Poincaré, AP-HP, 104 Bd Raymond Poincaré, 92380 Garches, France
[b] Université Versailles-Saint-Quentin en Yvelines, F78180, France
[c] Maladies Infectieuses et Tropicales, Hôpital Universitaire Pitié-Salpétrière, AP-HP, 47–83 Boulevard de l'Hôpital, 75013 Paris, France
[d] UMR 1181, Inserm, Institut Pasteur, Paris, France

ARTICLE INFO

Article history:
Received 1 January 2017
Received in revised form 30 May 2017
Accepted 4 June 2017
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Eosinopenia
Antimicrobial therapy
Sepsis
Bacterial
Marker

ABSTRACT

Introduction: Eosinopenia as a criterion of sepsis has been the subject of debate for decades. Different authors have proposed different cut-off values.
Methods: A prospective study was conducted from February to August 2016. Hospitalized adults suffering from a bacterial infection with eosinopenia, defined as an eosinophil count $<100/mm^3$, were included. Patients were divided into two groups according to the first day of effective antimicrobial therapy. They were observed for 5 days in order to evaluate whether recovery from eosinopenia was predictive of an appropriate antibiotic regimen.
Results: One hundred and twenty-two patients were screened and 96 were included. Group 1 patients ($n=70$) received effective antimicrobial therapy from day 0. Their eosinophil count increased significantly between day 0 and day 1 ($p<0.0001$). Group 2 patients ($n=26$) received delayed effective antimicrobial therapy, and there was no significant difference in eosinophil count between day 0 and day 1 ($p=0.55$). Moreover, eosinophil counts normalized on day 5 in both groups. The mean duration of antimicrobial therapy was comparable in the two groups (7.7 ± 1.16 days). The antibiotics most often prescribed in both groups were intravenous cephalosporins. During follow-up, all patients were considered to be cured after day 30.
Conclusions: The eosinophil count appears to normalize faster than C-reactive protein (CRP) and polymorphonuclear neutrophils in eosinopenic patients on appropriate antimicrobial therapy. This simple test is easy to perform as part of a regular complete blood count, with no additional costs as required for CRP or procalcitonin.

Introduction

Eosinopenia as a response to infection was first described in Zappert (1893). The pathophysiology of eosinopenia is related to the migration of eosinophils to the inflammatory site, presumably as a result of chemotactic substances secreted during the acute phase of inflammation (Bass et al., 1980).

C-reactive protein (CRP) was discovered in the 1960s and is considered a marker for the diagnosis of bacterial infection. Nevertheless, several studies performed during the last decades have shown that CRP, and more recently procalcitonin (PCT) (Le Bel et al., 2015), are not specific for sepsis but rather are markers of systemic inflammatory response syndrome (SIRS), as defined previously by the consensus conference for sepsis (American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference, 1992). Furthermore, PCT has been demonstrated to be useful in the intensive care unit (ICU) to shorten the duration of treatment (de Jong et al., 2016), particularly in pneumonia (Schuetz et al., 2012; Kook et al., 2012). However, adding a PCT-guided protocol does not reduce the use of antibiotics in febrile neutropenia (Lima et al., 2016).

Numerous studies have shown that PCT testing in the first days after admission to the ICU is associated with a significantly reduced length of stay, as well as reduced overall cost of care (Balk et al.,

☆ This work was presented in part at the ASM Microbe 2016 Conference, Boston, MA, USA, June 16, 2016.

* Corresponding author at: Infectious Diseases Department, Raymond Poincaré Teaching Hospital, Garches, France. Tel.: +33 1 47107740; fax: +33 1 47107790.
E-mail address: benjamin.davido@aphp.fr (B. Davido).

http://dx.doi.org/10.1016/j.ijid.2017.06.005

2016; Harrison and Collins, 2015). Nevertheless, the use of routine PCT testing is associated with additional costs. Biological markers to reduce antibiotic consumption are very much appreciated in the context of high costs due to antibiotic resistance (Chandy et al., 2014).

The eosinophil count has been revisited in recent decades, especially eosinopenia, which some authors consider a criterion of SIRS. There is no precise cut-off value in the literature to define eosinopenia, with different authors reporting values ranging from $<40/mm^3$ (Gil et al., 2003) to $<50/mm^3$ (Abidi et al., 2008). Meanwhile some authors argue that eosinopenia should be defined as an eosinophil count <1% of the total leukocytes (Rothenberg, 1998), implying that eosinopenia should be defined by a value $<100/mm^3$.

Recently, a study conducted in an ICU concluded that eosinopenia is a very sensitive but not specific marker of sepsis, and can be useful to guide physicians in their diagnosis (Shaaban et al., 2010). More recently, a study performed in an emergency department demonstrated that profound eosinopenia is very specific for sepsis, and it was suggested that it may become a helpful tool in daily practice (Lavoignet et al., 2016), as described previously by Simon (1922). Furthermore, eosinopenia has the advantage of not requiring further investigations, because it can be obtained easily from a simple complete blood count (CBC). Thus, it was hypothesized that recovery from eosinopenia during the treatment of bacterial infection may be a marker to evaluate whether a patient is receiving the appropriate antibiotic regimen.

Methods

Study design

Data were collected prospectively from adults hospitalized in the Infectious Diseases Department of Raymond Poincaré Teaching Hospital in Garches, France. This observational study was conducted between February and September 2016 during routine medical practice.

Data collection and definitions

Patients were included on the basis of a bacterial infection, defined either microbiologically (blood culture, urinary culture, microbiological specimen, urinary antigen test, or nasopharyngeal swab for RT-PCR), radiologically (typical illustration), or through clinical documentation (especially for skin and soft tissue infection). All patients were included on the basis of an uncomplicated infection without sepsis, as per the new 'SEPSIS-3' definitions (Singer et al., 2016), associated with the presence of eosinopenia on CBC. The absence of sepsis was assessed using the new bedside clinical score quickSOFA (qSOFA) (Singer et al., 2016); this was confirmed by the SOFA score if necessary.

Eosinopenia was defined as an eosinophil count $<100/mm^3$, in accordance with the literature (Rothenberg, 1998). The eosinophil count was obtained from the CBC, acquired using a Coulter LH780 Hematology Analyzer (Beckman Coulter Inc., Nyon, France).

Exclusion criteria were: (1) immunosuppression (HIV with CD4 $<200/mm^3$, corticosteroids >60 mg/day, chemotherapy, immunosuppressive therapy); (2) autoimmune disease; (3) haematological malignancy; (4) documented viral infection.

For each patient admitted, their age, sex, principal diagnosis, and biology were recorded. Day 0 was considered the first day of care admission, including emergency room.

As a first step, patients were divided into two groups according to the first day of effective antimicrobial therapy. Group 1 was composed of patients on effective antimicrobial therapy from day 0, i.e., started within 12 h of the initial CBC. Antibiotic regimens were provided at standard doses in accordance with guidelines and in respect to kidney function. Group 2 was composed of patients who received delayed effective antimicrobial therapy (after day 1), either because of delayed microbiological documentation or because of initial ineffective antimicrobial therapy.

As a second step, the course of antibiotics, CRP, leukocyte count (including polymorphonuclear neutrophil (PMN) and eosinophil counts), and temperature on days 1, 3, and 5 of hospitalization were analysed.

Finally, patients attended a follow-up consultation after 1 month as part of routine practice in the department.

Statistical analysis

The Student *t*-test was used to analyze continuous data in GraphPad Prism v.6.0d (GraphPad Software Inc., La Jolla, CA, USA). Statistical significance was defined as $p < 0.05$.

Ethical approval

All procedures in the study were performed as part as routine care and in accordance with the ethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki.

Results

One-hundred and twenty-two patients were screened during the study period (Figure 1). Six patients were excluded because they were not infected. Eleven further patients were excluded because they presented an infection with an eosinophil count $>100/mm^3$. In addition, nine patients were excluded because they had a viral syndrome.

A total of 96 infected patients were included. Seventy were assigned to group 1 with effective antimicrobial therapy from day 0, and 26 patients were assigned to group 2 because of delayed effective antimicrobial therapy (after day 1). Patient characteristics were comparable and are detailed in Table 1.

For all patients, the qSOFA score calculated was <2; therefore they were not investigated further with the SOFA score and were considered to have uncomplicated infections. Moreover, the qSOFA scores were comparable between groups (median 0, range 0–1).

The parameters studied (temperature, PMN and eosinophil counts) were also comparable on day 0 before monitoring and the

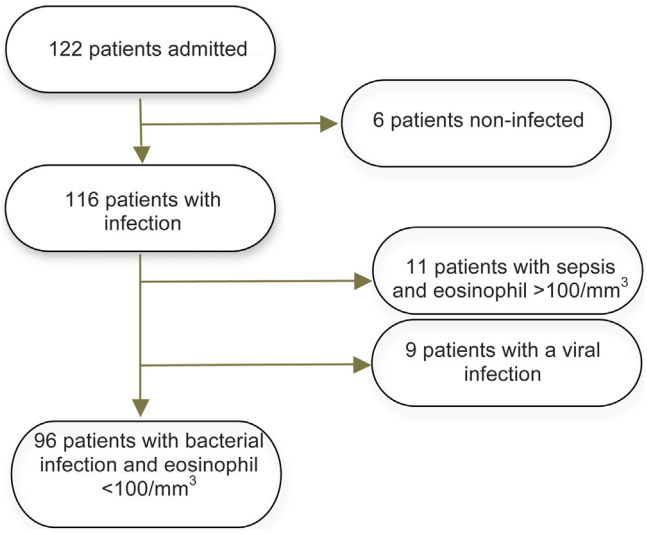

Figure 1. Flow chart of the study population at admission.