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Blood Procalcitonin Dosage in the Diagnosis of Infectious and Inflammatory Diseases in Bamako

Valeur du dosage de la procalcitonine sérique dans le diagnostic des maladies infectieuses et inflammatoires à Bamako

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ABSTRACT

Objective. To report the prescription of procalcitonin in the diagnosis and monitoring of infectious and inflammatory diseases in Bamako, Mali. **Methodology.** This was a descriptive prospective study of patients registered between January [1,] 2017 and June 30, 2017. We included 253 records of patients in whom Procalcitonin (PCT) was dosed. **Results**. PCT was prescribed for subjects aged 3 days to 90 years with a mean age of 41.68 ± 22.66 years in men and 40.99 ± 19.14 years in women. The most frequently reported clinical information was renal and infectious tests respectively 33.20% and 23.71%, the least frequent were lung infections and shock. Depending on the degree of severity of the infection in relation to the PCT rate we have: absence of bacterial infection (≤0,25 ng/ml) in 33.99%; localized bacterial infection (0.25 - 0.5 ng/ml) in 5.53%; systemic bacterial infection (0.5 - 2 ng/ml) in 14.23%; severe sepsis (2 - 10 ng/ml) in 18.97%; and septic shock (>10 ng/ml) in 27.27%. **Conclusion.** PCT was prescribed as part of the renal workup, and in the majority of cases in febrile states. PCT values were predictive of infection. And allows a differential diagnosis between infection and systemic diseases.

RÉSUMÉ

Objectif. Présenter les résultats de la prescription du dosage de la procalcitonine dans le diagnostic et le suivi des maladies infectieuses et inflammatoires à Bamako, Mali. **Méthodologie.** Il s'agit d'une étude transversale descriptive et prospective réalisée entre le 1er janvier et le 30 juin 2017. Nous avons inclus les données de 253 patients chez qui la procalcitonine (PCT) a été dosée dans le sang. **Résultats**. Le dosage de PCT a été prescrit à des sujets d'âge compris entre 3 jours et 90 ans (moyenne: 41.68 ± 22.66 ans chez les hommes et 40.99 ± 19.14 ans chez les femmes). Les renseignements cliniques les plus fréquemment reportés était le bilan rénal (33.20%) et le bilan infectieux (23.71%). Les indications moins fréquentes étaient l'infection pulmonaire et le choc septique. En fonction de la sévérité de l'infection mesurée par le taux de PCT, les résultats étaient les suivants: absence d'infection bactérienne (≤0,25 ng/ml) dans 33.99% des cas; infection bactérienne localisée (0.25 - 0.5 ng/ml) dans 5.53% des cas; infection bactérienne systémique (0.5 - 2 ng/ml) dans 14.23% des cas; sepsis sévère (2 - 10 ng/ml) dans 18.97% des cas et choc septique (>10 ng/ml) dans 27.27% des cas. **Conclusion.** Le dosage de la PCT a été prescrit essentiellement dans le cadre d'un bilan rénal et souvent aussi pour évaluer un état fébrile. Les valeurs de PCT étaient en règle prédictives de la présence d'une infection et permettaient de différencier entre infection localisée et affections systémiques.

INTRODUCTION

The management of patients with suspected bacterial infection is complex. There is a need for a biomarker that is sufficiently sensitive and specific to allow the diagnosis or ruling out of a bacterial infection to be made safely and rapidly [1]. Procalcitonin (PCT) is a precursor of calcitonin, usually secreted by the C-cells or parafollicular cells of the thyroid gland in very small amounts. Under the influence of endotoxins or cytokines more frequently associated with bacterial infections, such as IL-1, TNF-α and IL-6, it is secreted by thyroid parenchymal cells and thus appears to be an interesting marker for bacterial infection[1, 2]. Calcitonin is synthesized as a pro-hormone, procalcitonin or PCT. It's a biochemical marker of infection rather than inflammation [3]. In Mali; PCT dosage is increasingly prescribed in hospital settings. This is why we initiated this study, which aims to study the prescription of procalcitonin in the diagnosis and

monitoring of infectious and inflammatory diseases in Bamako, Mali.

PATIENTS AND METHODS

It was a descriptive prospective study of patients registered between January [1,] 2017 and June 30, 2017. Patient data collection was carried out at the PA and KA laboratory in Bamako. Data from patients registered in computerized medical records during the study period who received serum or plasma PCT were included.

The data collected were, epidemiological information (age, sex, service, and prescribing health structure), clinical information (fever, renal failure, renal test, diarrhea, infectious test, pain...) and biological information (PCT values). The analytical assay technique used was chemiluminescence immunoassay (CLIA). PCT values were expressed in ng/ml and interpreted as follows : a PCT level of less than 0.25 ng/ml was considered normal (absence of bacterial infection); a PCT level between 0.25 and 0.5 ng/ml was considered localized infection; a PCT level between 0.5 and 2 ng/ml was considered systemic infection; a level between 2 and 10 ng/ml was considered severe sepsis; and a level greater than or equal to 10 ng/ml was considered septic shock.

A check during and after the entry allowed to clean up inconsistencies in the Excel database. The Excel data were processed and analysed on Epi Info® Version 7.2.2.6. The Chi-square test was applied to the cross-tabulated variables, and was considered significant at a probability less than or equal to 0.05.

RESULTS

During the study period, we included 253 patient records of which 48.2% were female versus 51.8% male. The mean age of the female population was 40.99 ± 19.14; the mean for males was 41.65 ± 22.66. The minimum age was one day and the maximum 93 years of age for both sexes. Children under the age of 15 accounted for 9%. The 30 - 45 age group was the most represented with 72%. This age-class difference was statistically significant (*p=0*.00) (see *Table II*).

The majority of PCT prescribing health services and facilities were privately owned and the specialities most in demand were nephrology and internal medicine, this information is compiled in *Table I*.

The distribution of the mean PCT rate and the predictive rates of bacterial infections by severity according to sex, age and clinical information are compiled in *Table II*.

Analysis of mean serum PCT levels by sex showed a statically significant difference, with mean PCT values higher in women (19.08 ng/ml) than in men (13.07 ng/ml) with extremes ranging from 0.01 to 110 ng/ml (Chi-square, P-value = 0.00478).

Depending on the degree of severity of the infection in relation to the PCT rate we have : absence of bacterial infection (≤0,25 ng/ml) in 33.99%; localized bacterial infection
(0.25 - 0.5 ng/ml) in 5.53%; systemic bacterial infection (0.5 - 2 ng/ml) in 14.23%; severe sepsis (2 - 10 ng/ml) in 18.97%; and septic shock (>10 ng/ml) in 27.27%. According to the clinical information on the PCT prescription sheet, patients with renal failure came first with 32.20%, followed by infection status with 23.71% (see *Table II*).

Table I : Distribution by health facilities and PCT prescribing services

Health services and Facilities	Number	pcent
Clinics and private practices	134	57,26
Nephrology	69	29,49
Internal Medicine	13	5,56
Rheumatology	9	3,85
Cardiology	4	1,71
Internal Medicine	3	1,28
Sickle Cell Disease Research and Control Centre	1	0,43
Pneumology	1	0,43
Subtotal	234	100,00
No information	19	7,51
Total	253	

Table II: Distribution of PCT by gender, age, clinical information and interpretation of PCT

Variables	Staff	Mean PCT value (ng/ml)	P-value	Absence of BI: n ≤0,25 ng/ml	Localized BI: n 0,25 – 0,5 ng/ml	Systemic BI: n 0.5 - 2 ng/ml	Severe BI :n= 2 - 10 ng/ml	Septic Shock >10 ng/ml	P-value
Sex									
Male			0,13196	45	5	19	21	32	0,6926
Female				41	9	17	27	37	
Age									
0 – 5	24	2,72	0,00000	11	5	2	5	1	0,2933
5 – 15	6	29,19		3	0	1	0	2	
15 – 30	39	17,90		13	1	7	8	10	
30 – 45	72	15,70		25	5	6	16	20	
45 – 60	63	15,43		14	2	13	13	21	
>60	49	21,55		19	2	7	6	15	
Clinical Information									
Kidney failure	84	7,38	0,00000	13	3	12	27	29	0,0017
Febrile state	60	5,45		33	4	9	7	7	
Renal assessment	29	23,46		6	2	4	4	13	
Infectious balance sheet	28	19,04		8	1	5	3	11	
Arthromyalgia	11	0,04		11	0	0	0	0	
Lung infection	5	7,38		2	1	0	1	1	
Collapse	2	8,15		0	1	0	0	1	
Other*	13	27,29		3	0	1	4	5	
No information	20	163,05		9	2	5	2	2	

BI: bacterial infection

*Other: hydrops, meningoencephalitis, coma attack, diabetes on hypertension, diarrhea and vomiting, chest pain, dysuria, shock, hemoptysis, altered consciousness, systemic inflammatory response syndrome (SIRS), neck stiffness, hypersudation.

DISCUSSION

Characteristics of the study population

PCT was prescribed for subjects aged 3 days to 90 years with a mean age of 41.68 ± 22.66 years for men and 40.99 ± 19.14 years for women. There was no statistically significant difference between the two sexes according to PCT concentration (p=0.13196). This finding of the similarity of the average PCT concentration by gender is comparable to that in the literature[4]. The mean PCT concentration increased with age, with a statistically significant difference (*p=0*.0000). Some studies on the diagnostic value of PCT and CRP for detecting severe bacterial infections in patients with unknown fever by systematic review and meta-analysis show a difference in value according to age, positive predictive values for PCT were: 0.12 to 0.26 µg/L for children aged 0 to 3 months, and greater than 0.50 µg/L for other ages (adolescents and adults) [5]. The male gender dominated in our series, at 52%, and the same trend has been observed in some studies [6, 7].

Prescription of PCT

Interest in prescribing PCT was observed in order of frequency in nephrology, internal medicine, rheumatology and cardiology. In our study the most frequently mentioned clinical information was renal and infectious tests respectively 33.20% and 23.71%, the least frequent were lung infections and shock. In haemodialysis (HD) patients who were the majority in our series, the literature reports that the level of PCT was significantly higher in stable HD patients without overt bacterial infection [9]. However, any increase above baseline PCT levels could diagnose a bacterial infection in these patients [10]. PCT and β2-MG could also be used to determine upper urinary tract infections. This combination may increase the sensitivity and specificity of the diagnosis of UTIs in clinical practice [8]. In cardiology, a high PCT concentration may be a factor in poor prognosis in a patient with heart failure with reduced systolic ejection fraction [6].

In rheumatology, almost all of these patients in our series had PCT levels below the limit of prediction of infection; unlike other markers of inflammation (CRP, SV, fibrinogen) according to the literature, PCT remains low in the flare-ups of certain inflammatory diseases such as systemic lupus erythematosus, inflammatory rheumatism [1]. One patient was monitored for systemic inflammatory response syndrome (SIRS) in our series with a PCT level of 83.01 ng/mL. According to the literature, the diagnostic value of soluble plasminogen urokinase activating receptor (suPAR) in relation to C-reactive protein (CRP) and procalcitonin (PCT) in children with systemic inflammatory response syndrome (SIRS) has been proven, the SIRS group had a mean PCT of 12.70 ± 21.88 ng/mL [11].

Several studies have shown that PCT is particularly indicated for use in intensive care and emergency medicine for early, rapid diagnosis and appropriate therapy. PCT, CRP and lL-6 can be used as early diagnostic markers of bacterial infections in patients with septicaemia [3]. Prescription for lung infection was rare in our series, PCT was positive in 3/5 cases. According to the literature, PCT has shown its value in monitoring the therapeutic efficacy of tuberculosis and bacterial pneumonia [12, 13].

Biological characteristics

The mean PCT in our series for all categories was 16.17 ± 31.78 ng/mL, with a median of 1.04 ng/mL, a minimum of 0.01 ng/mL and a maximum of 110.00 ng/mL. Plasma PCT is a good indicator of the inflammatory response associated with bacterial infection, and is higher in gram-negative than in gram-positive bacterial infections [14, 15]. According to the algorithm of Christ-Crain *and colleagues*, [16] for initiating or not initiating antibiotic therapy, we found that 33.99% of our subjects had a PCT value less than or equal to 0.25 ng/ml. In children under five years of age, the mean minimum PCT value was 2.72 ng/mL. It was higher in children aged five to 15 years (29.19
ng/mL). There appeared to be a statistically significant difference (p=0.00) in the variation in PCT concentration between age groups. According to one study, the serum procalcitonin level of patients with early-stage sepsis is significantly elevated and is of diagnostic value for different groups of pathogenic bacteria. It may also reflect the severity of the disease and predict patient prognosis [15].

The mean PCT in patients monitored for renal failure was 7.38 ng/mL, of whom 15.48% had a PCT level of less than or equal to 0.25 ng/mL (the threshold for predicting infection). PCT levels above 10 ng/mL were predominantly 34.52% in patients with renal failure. This interest in PCT for kidney disease has been confirmed by some studies [17, 18].

In the exploration of the infectious state, the mean PCT level was 19.04 ng/mL; and 28.57% had a PCT level of 0.25 ng/mL or less, and 39.29% had a level greater than 10 ng/mL. Apart from its interest in monitoring bacterial and fungal infection [14], PCT has shown interest in monitoring severe *Plasmodium falciparum* malaria, where PCT levels correlate with parasite density and decrease proportionally with parasite density [19].

The average rate during the lung infections in our series was 7.38 ng/L, of which 40% were below the threshold of negativity. Some studies have shown the usefulness of PCT in monitoring the treatment of tuberculosis and pneumonia, and its effectiveness has been shown to be associated with decreases in serum PCT levels, sedimentation rate (SV) and CRP [12]. Dynamic changes in serum CRP and PCT levels could potentially be used as a moderate predictive marker for the prognosis of communityacquired pneumonia in hospital patients [13].

CONCLUSION

PCT was prescribed as part of the renal workup, and febrile states were monitored in the majority of cases. The indications for its prescription have been diverse, with nephrology being the largest prescribing service for PCT for monitoring patients with renal failure. PCT values were mostly above the positive predictive threshold for infection in the majority of cases. Procalcitonin was a good marker for differential diagnosis between bacterial infection and rheumatic inflammatory disease where PCT values remained below the threshold for positivity. The prescription of PCT offers the potential for a significant reduction in antibiotic exposure, both at initiation and over time.

This descriptive study could be supplemented by a prospective analytical study to study the contribution of this marker in the diagnosis and surveillance of infections during certain pathologies associated with the risk of infections.

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