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Procalcitonin Role in Musculoskeletal Infection: A Comparative Prospective Study

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ABSTRACT

Early diagnosis of musculoskeletal infections is of vital importance to avoid devastating complications. There is no single laboratory marker which is sensitive and specific in diagnosing these infections accurately. White blood cell count, erythrocyte sedimentation rate and C-reactive protein are not specific as they can also be elevated in conditions other than bacterial infections. Materials Culture and sensitivity is not a true gold standard due to its varied positivity rates. Serum Procalcitonin (PCT) is one of the new laboratory markers for pyogenic infections. The objective of this study is to assess the value of PCT in diagnosis of soft tissue, bone and joint infections.

Patients and Methods: Patients of all age groups (seventy-four patients) with diagnosis of musculoskeletal infection are prospectively included in this study. All patients were subjected to White blood cell count, erythrocyte sedimentation rate, C-reactive protein and serum Procalcitonin measurements. Healthy non infected outpatient group (twenty-two patients) taken as a control group and underwent the same evaluation steps as the study group.

Results: The study group showed mean Procalcitonin levels of 1.3 ng/ml. Procalcitonin, at 0.5 ng/ml, was (42.6%) sensitive and (95.5%) specific in diagnosing of musculoskeletal infections with (positive predictive value of 87.5% and negative predictive value of 48.3%) and (positive likelihood ratio of 9.3 and negative likelihood ratio of 0.6).

Conclusion: Serum Procalcitonin, at a cut – off of 0.5 ng/ml, is a specific but not sensitive marker in the diagnosis of musculoskeletal infections, and it can be used effectively to rule in the diagnosis of infection but not to rule out it.

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Introduction

Infections involving the musculoskeletal system can cause damage to soft tissue and bones, resulting in significant destruction of the skeleton. The consequential effects of an orthopedic infection can cause significant residual pain and deformity. Despite the expanding growth of antibiotics and antibiotic classes, musculoskeletal infections remain problematic issue. Early identification and prompt treatment of musculoskeletal infections are necessary to improve the poor outcomes and avoid the permanent sequelae that continue to affect a large number of patients with musculoskeletal infections. Musculoskeletal infections in general can be divided into the following major categories

- Soft tissue infections (cellulitis, necrotizing fasciitis, diabetic foot infections etc.).
- Infections of bone (osteomyelitis)
- Infections of joints (septic arthritis)

These infections have specific pathophysiology, particular characteristics and specific organisms that are associated with each infection. For any type of musculoskeletal infection, the orthopedic surgeon usually follows the classical sequence of diagnostic aids, namely; clinical symptoms and signs, laboratory investigations, imaging modalities and lastly microbiological studies.

An ideal marker for bacterial infections should allow an early diagnosis, inform about the course and prognosis of the disease and facilitate therapeutic decisions [1]. For diagnosis of soft tissue infections, the physician should start from clinical features (history and physical examination) which may be sufficient to make diagnoses of superficial non necrotizing infections. On the other hand, the necrotizing deep infections sometimes need laboratory investigations, imaging modalities and microbiological studies for assessment of the extent of the pathology and guide the management [2].

In endocrinologically normal person the Calcitonin is produced from the parafollicular C- cells of the thyroid. Calcitonin act to

reduce blood calcium opposing the effect of parathyroid hormone. Procalcitonin (PCT) is a precursor peptide for the hormone calcitonin [3]. After translation from calcitonin-messenger RNA\ (mRNA), PCT is cleaved enzymatically into smaller peptides, finally to yield the thirty-two amino acid mature calcitonin [1].

Patients and Methods

This is a prospective study which was conducted in the Department of Orthopedic Surgery, in Al-Basrah Teaching Hospital from March 2017 to March 2018. The sample included 47 patients that were presented to the Department with musculoskeletal infections (soft tissue, bone or joint infections) of male and female genders, their mean age was (35.9 years ± 24 SD), with no evidence of other infection elsewhere in the body. The criteria for inclusion depended on the presence of clinical symptoms and signs of infection.

A detailed informed consent was taken from the patients themselves or from their next of kin (if they were children) to be included in this study.

We included all patients with musculoskeletal infection except: Newborns during first three days of life, patients with history of systemic fungal infections (e.g., candidiasis, aspergillosis), severe mechanical trauma, cardiac or respiratory failure and cases with chronic osteomyelitis.

All patients were evaluated for clinical parameters of acute infection which includes presence of pain, swelling; redness, tenderness warmth; tenderness and restriction of range of movement. Vital signs measured and recorded. Any finding in the bacteriological examination (if available) or imaging modalities supporting the presence of infection is noticed. All these data were recorded in the pre-formulated questionnaire.

Adequate amount of venous blood sample has been drowned from every patient at time of admission under aseptic conditions, part of this sample was taken for ESR and WBC count measurement and the remaining blood placed in a clot activated tube; and then taken to the Lab for centrifuge and isolation of serum.

Statistical Analysis

Sensitivity, specificity, positive and negative predictive values and the likelihood ratio (positive and negative) were performed to compare the performance of laboratory test in question between cases and control groups.

Results

A total of 73 patients presented to the orthopedic department were included in the study, 47 of those patients have a clinically diagnosed acute musculoskeletal infections (soft tissue infections, septic arthritis, osteomyelitis or diabetic foot infections) as shown in Figure 1.

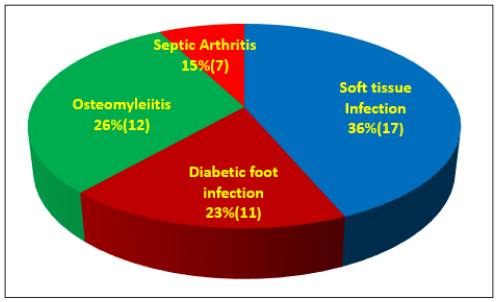

Figure 1: Types of musculoskeletal infections studies

Four patients found to have a chronic osteomyelitis, the results of all of them were below the cutoff value of PCT and they were excluded from the study. The remaining 22 patients were out patients with no features suggestive of any infection (control group).

The mean age of the study group was (35.6 years ± 24 SD). The youngest was 1 month old and the oldest was 80 years old. Out of 47, there were 28 males (59.6%) and 19 females (40.4%).

Table 1: Mean PCT level for each age group

Age group	No of patients	Mean PCT level
4 days – 10 years	7	3.9
11 years - 20 years	10	0.352
21 years – 50 years	15	1.31
>50 years	15	0.778

We divided the sample into 5 groups based on the diagnoses of the pathology:
Group 1 soft tissue infections
Group 2 septic arthritis
Group 3 osteomyelitis
Group 4 diabetic foot infections
Group 5 the control group

Statistical analyses including sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios calculated for PCT (at a cutoff value of 0.5 ng/ml), CRP (at a cutoff value of 2 mg/dl), ESR (at a cutoff value of 45 mm/hr) and WBC (at a cutoff value of 10×10^9 cell/ mm^3).

By comparing the results as shown in table 2; CRP has the highest sensitivity compared to the rest of the variables; however, PCL has the highest specificity. Despite PCL and WBC have the same PPV, Procalcitonin PLR is much higher than that of the WBC; this means than PCL can be an accurate investigation in ruling in infection rather than ruling infection out.

Table 2: Comparison among statistical data of all studies investigations

Type of Investigation	Sensitivity	Specificity	PPV	NPV	PLR	NLR
PCL	42.6%	95.5%	87.5%	38.4%	9.3	0.6
CRP	91.5%	54.5%	81.1%	75%	2	0.15
ESR	76.2%	83.3%	84.2%	75%	4.5	0.08
WBC	65%	77%	87.5%	48.5%	2.9	0.16

PCL: Procalcitonin, CRP: C-Reactive protein, ESR: Erythrocyte sedimentation rate, WBC: White blood cells, PPV: Positive predictive value, NPV: Negative predictive value, PLR: Positive likelihood ratio, NLR: Negative likelihood ratio.

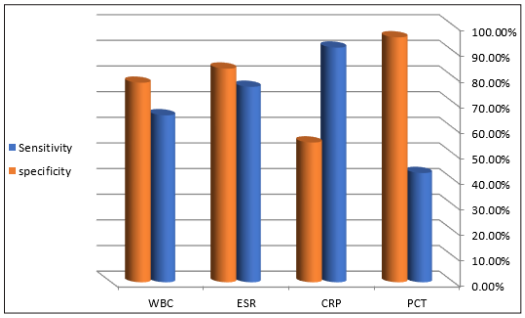

Figure 2: Analysis of the studies Lab markers

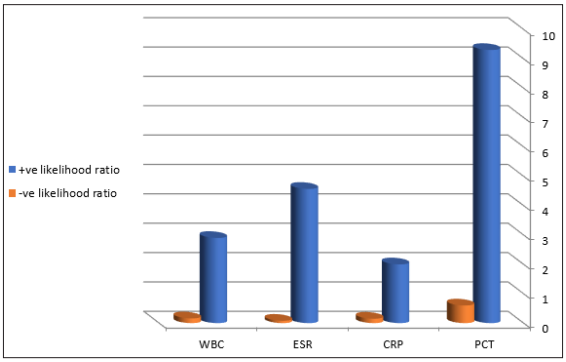

Figure 3: Positive and negative likelihood ratio of the studied Lab markers

Table 3: Values of infection markers in different MSK infections

Marker	Type of infection	Mean
ESR (mm/hr)	Soft tissue Infection	61.25
	Acute Septic Arthritis	76.40
	Acute Osteomyelitis	83.43
	Diabetic foot	67.80
WBC (10×10^9 cell/ mm^3)	Soft tissue Infection	11.92
	Acute Septic Arthritis	9.90
	Acute Osteomyelitis	14.69
	Diabetic foot	13.07
CRP (mg/dl)	Soft tissue Infection	4.78
	Acute Septic Arthritis	11.87
	Acute Osteomyelitis	23.00
	Diabetic foot	4.46
PCT "ng/ml"	Soft tissue Infection	0.99
	Acute Septic Arthritis	0.58
	Acute Osteomyelitis	2.76
	Diabetic foot	0.75

Discussion

Musculoskeletal infections are a common problem facing orthopedic, rheumatology specialists in addition to general practitioners and other health care providers. The diagnosis of musculoskeletal infections sometimes represents a dilemma, with serious sequels of delaying diagnoses and treatment, or treating empirically the wrongly diagnosed patient as having infection, which raise another problem in medical practice of bacterial resistance and expose the patients for the adverse effects of antibiotics that he/she may not need.

For the sake of making solution for those problems, the medical community is in need for a diagnostic test that increase the accuracy of diagnoses so as to decrease the delay in treatment or the use of unneeded treatment for cases suspected to have musculoskeletal infections. In the presented study we took Procalcitonin as a new marker for infection and evaluate its performance in cases of acute musculoskeletal infections.

We select the cases of musculoskeletal infections on the bases of clinical criteria of presence of the signs and symptoms of infection like, pain, redness, tenderness, swelling, loss of function and presence of discharge. These parameters were used by Butbwl-Aviel et al (2005) in their study on Procalcitonin as a diagnostic aid in osteomyelitis and septic arthritis, but they include microbiological studies in their series [4]. Unlike our study, we depended completely on clinical criteria without any microbiology study.

Unfortunately, our circumstances did not allow such microbiological studies to fulfill the diagnostic criteria of infection adopted in comparable studies. In addition to that, most of our presented patients with musculoskeletal infections (33 patient out of 47), have been kept on systemic antibiotic before presentation, this might explain the negative bacteriological results. Microbiological studies will not be so reliable unless we stop the antibiotic for at least 2-5 days, which is probably unethical in patient requiring active measures.

The cutoff value of PCT is not agreed upon among the health community till now. Bottner F et al [5]. Have used a cutoff value 0.3 ng/ml, while Faesch S. et al [6]. and Hugle T. et al [7]. Took 0.5 ng/ml as a cut off value; this reflects the absence of consensus about the optimal cut off for procalcitonin level.

In our study, the test was done at two cutoff values (0.3 and 0.5 ng /ml). We found no significant difference in the results of sensitivity and specificity between the two cutoff values.

In our study, at 0.5 ng/ml cutoff value, the sensitivity was 42.6% and the specificity was 95.5%. These values were comparable to what was found by Maharajan K. et al [8]. in their study of septic arthritis and osteomyelitis; the sensitivity was 66.7% and specificity 91% which is better than our results; probably because of the larger sample size. Wang C, et al [9]. in their study of procalcitonin in septic arthritis; the sensitivity was 34.79% and the specificity was 98.61%, and these results are comparable to the results in our series.

Contrary to these results Jeong D-K et al [10]. In their study found that the sensitivity of PCT was 95%, and this can be attributed to that their inclusion criteria in which they select critically ill patients with severe bacterial infection of two body systems while our sample include only infections in musculoskeletal system with generally stable conditions.

In regard to the positive and negative likelihood ratio, C.-J. Shen et al [11]. in their meta-analysis showed that the positive likelihood ratio of the Procalcitonin in bone and joint infection was 4.8 while the negative likelihood ratio was 0.6 which were comparable to what was found in our study. The high positive likelihood ratio gives us a clue that PCT can be used effectively to rule in infection (high positive likelihood 9.3 in our study, means high probability of infection in positive test results) but not to rule out infection, due to the fact that negative likelihood ratio was 0.6 in our study, which is obviously poor.

In regard to the mean level of procalcitonin in different types of infection; our study showed that it was higher in cases of osteomyelitis than in cases of septic arthritis which is consistent to what is found by Butbul-Aviel et al [4]. In their series and this can be explained by the fact that PCT levels increase to higher levels in conditions of bacteremia and\or septicemia than in cases of localized infections.

Conclusion

Serum Procalcitonin is an infection marker that show high specificity but low sensitivity at a cutoff value of 0.5 ng/ml, and it gives a very good positive likelihood ratio; so, it can be used to rule in musculoskeletal infection when it come as positive (i.e., low false positive results), but not to rule out the presence of infection when it come as negative due to its low sensitivity and poor negative likelihood ratio (i.e., high false negative results). In comparison to the available laboratory markers for infection (namely, CRP, ESR and WBC) serum Procalcitonin represent a better diagnostic tool in conjunction with clinical evaluation for diagnosis of musculoskeletal infections.

Conflict of Interests

The authors declare no conflict of interests regarding this study

Funding

This research did not receive any specific funding

Informed Consent

In accordance with the Helsinki Declaration as revised in 2013 an informed written consent were given to all patients explaining the study and the aim of the study and any possible complication can occur from the phlebotomy.

References

1. Christ-Carin MJSmw, Beat Müller (2005) Procalcitonin in bacterial infections-hype, hope, more or less? 13: 451-460 .
2. Anaya DA (2007) Dellinger EPJd and management. Necrotizing soft-tissue infection 44: 705-710.
3. Becker K, Nylen E, White J, B Müller, R H Snider (2004) Procalcitonin and the calcitonin gene family of peptides in inflammation, infection, and sepsis: a journey from calcitonin back to its precursors 89: 1512-1525.
4. Butbul-Aviel Y, Koren A, Halevy R, Waheeb Sakran (2005) Procalcitonin as a diagnostic aid in osteomyelitis and septic arthritis 21: 828-832.
5. Bottner F, Wegner A, Winkelmann W, K Becker, M Erren, et al. (2007) Interleukin-6, procalcitonin and TNF-α: markers of peri-prosthetic infection following total joint replacement 89: 94-99.
6. Faesch S, Cojocaru B, Hennequin C, Stéphanie Pannier, Christophe Glorion, et al. (2009) Can procalcitonin measurement help the diagnosis of osteomyelitis and septic arthritis? A prospective trial 35: 1-6.
7. Hugle T, Schuetz P, Mueller B, G Laifer, A Tyndall, et al. (2008) Serum procalcitonin for discrimination between septic and non-septic arthritis 26: 453-456.
8. Maharajan K, Patro DK, Menon J, Ananthanarayanan Palghat Hariharan, Sabhash Chandra Parija, et al. (2013) Serum Procalcitonin is a sensitive and specific marker in the diagnosis of septic arthritis and acute osteomyelitis 8: 1-7.
9. Wang C, Zhong D, Liao Q, Lingyu Kong, Ansong Liu, et al. (2014) Procalcitonin levels in fresh serum and fresh synovial fluid for the differential diagnosis of knee septic arthritis from rheumatoid arthritis, osteoarthritis and gouty arthritis 8: 1075-1080.
10. Jeong D K, Lee HW and Kwon Y-MJJoKNS (2015) Clinical value of procalcitonin in patients with spinal infection 58: 271.
11. Shen CJ, Wu MS, Lin KH, WL Lin, HC Chen, et al. (2013) The use of procalcitonin in the diagnosis of bone and joint infection: a systemic review and meta-analysis 32: 807-814.