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Original Research Article

Evaluation of serum procalcitonin as a significant marker in cases of septic arthritis and osteomyelitis: a two year study

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ABSTRACT

Background: Acute bone infections like septic arthritis and osteomyelitis are a serious threat in management and diagnosis in the department of orthopaedics. Biochemical marker is needed with good sensitivity and specificity in diagnosing acute bone and joint infections. The aim of the present study was to study the role of PCT in conditions of septic arthritis and osteomyelitis.
Methods: A two year prospective study was done and cases were grouped into three group and laboratory parameters TC, ESR, CRP and PCT were measured. The sensitivity, specificity and predictive values were compared using SPSS software version 20.
Results: 238 patients, (males- 154 & Females– 84) with mean age 34.1±8.20 years. Group-1 included 52 patients with raised PCT and MRSA and *Klebsiella* as the common isolates. Group-2 with 89 patients and mean PCT in the study group was 4.99 ng/ml. Ninety seven were included in Group-3. The mean PCT value was 2.6 ng/ml. In group-1, the specificity of PCT (comparing Group-1 & 3) was 96.8 [95% CI, 94.2 -98.4], the sensitivity (26% [3.2-60.1], the PPV 16.1% [95% CI 2.3-48.3] and the NPV was 98% [95% CI, 95.5-99.8].
Conclusions: To conclude our study, highlights the role of PCT as a sensitive and specific marker in diagnosing cases of septic arthritis and Osteomyelitis. This opens a gateway to further research in evaluating the PCT effectiveness as a response marker to treatment. PCT is more sensitive than CRP in acute bone and joint bacterial infections and raises early and faster.

Keywords: Procalcitonin, MRSA, *Klebsiella*, C - reactive protein

INTRODUCTION

Acute bone infections like septic arthritis and osteomyelitis are a serious threat in management and diagnosis in the department of orthopaedics. Rapid management and prompt diagnosis are initial crucial things to establish in cases of acute bone and joint infections. The outcome of these conditions depends largely upon the diagnosis. The disabling sequelae are in response to delayed diagnosis and management.[1] Despite advances in management and diagnosis few of the cases progress towards chronicity requiring prolonged hospitalization, extensive antibiotic administration, repeat surgery and management of long term functional sequelae. Laboratory parameters which may aid in diagnosis of acute conditions include total count, ESR and C- reactive protein were the last is an acute inflammatory marker which is raised in all other conditions of inflammation. These factors lack sensitivity and specificity, where isolation of organism from pus aspirate or synovial fluid still remains the gold standard.[2] The lack of sensitive laboratory tests makes the surgeon for an overuse of antibiotics for long duration and development of microbial resistance. In this context, there is a grave need for biochemical marker which shows good sensitivity and specificity in diagnosing

acute none and joint which can diagnose and lessen the overuse of antibiotics and development of resistance.[3]

Serum procalcitonin which is an acute inflammatory marker has been studied extensively and found to be low in normal healthy individuals. In conditions of inflammation associated with bacterial endotoxins the levels of PCT are raised.[4] However studies pertaining to relation of PCT with acute bone and joint infections are limited. The advantage of PCT is half-life with 22-29 hours which makes it to differentiate bacterial infections from viral and non-inflammatory causes. Few studies have already established the role of procalcitonin as a prognostic and diagnostic marker in bacterial indications and as a tool to start antibiotic administration.[5]

The aim of the present study was to study the role of PCT in conditions of septic arthritis and Osteomyelitis with comparison to other markers like CRP. We also intend to calculate the sensitivity, specificity and predictive values of PCT in cases of Septic arthritis and Osteomyelitis.

METHODS

The present prospective study was conducted at a tertiary care hospital of south India by Department of Orthopaedics for a period of two years from January 2015 to December 2107. The study was approved by the Institutional Research committee and the study was conducted as per the guidelines of the committee. Written and informed consent was obtained from all the participants in the study after explaining the details of the study.

All the patients above 18 years of age with history of acute (<2 weeks duration) synovitis, arthritis and osteomyelitis with no evidence of infection in other sites of the body attending the opd of orthopaedics department were included in the study.

Patient with history of chronic arthritis and chronic osteomyelitis, immune compromised sates, on history of oral or intravenous antibiotic administration and evidence of infection else were in the body were excluded from the study.

A detailed clinical examination with history of socio demographic factors with age, sex, duration of symptoms and swelling of the joint, movements, tenderness, warmth, restriction of movements were noted in a predesigned structured questionnaire sheet. Radiological investigations like X-ray (anteroposterior/lateral) and ultrasound of involved bone and joint were done.

In cases with swelling due to collection of fluid, aspiration was done using 18 G needle under adequate anaesthesia. The aspirate was processed immediately which included gram staining, culture and sensitivity. In all the cases with systemic symptoms of sepsis blood culture was also done. Laboratory analyses included CBP, ESR, CRP and procalcitonin. ESR was estimated by using Wintrobe's method, CRP by using nephelometric method. PCT was measured by an automatic quantitative method. [BRAHMS diagnostic, Germany] This method has a sensitivity of 0.06 ng/ml and results ranged from 0.06 to 50 ng/ml. Values of PCT levels >0.5 ng/ml was considered abnormal. All the other necessary investigations were done to rule out other possible causes of infection or febrile causes. Based upon the clinical examination and culture report all the cases in the study were categorized into three groups.

Group 1: Confirmed septic arthritis or osteomyelitis with positive culture from aspirate or blood.

Group-2: Presumed clinical septic or osteomyelitis but culture negative with raised WBC count, CRP >20 mg/l.

Group-3: Inflammatory group: Patients with acute symptoms pertaining to bone and joint but no suspicion of infection clinically. eg: rheumatoid arthritis, sickle cell crisis, non specific crisis.

Statistical analysis

All the data collected was entered initially into Microsoft excel spread sheet and corrected. The corrected data was entered and analyzed suing SPSS software version 20 [IBM group, Newyork]. The sensitivity, specificity and predictive values were analyzed and compared between the three groups for ESR, CRP and PCT. P value <0.05 was considered significant in our study.

RESULTS

In the present study conducted for a period of two years, 238 patients who fulfilled the inclusion criteria were included in the study. One hundred and fifty four were males (64.71%) and eighty four (35.29%) were females. The range of age in the study was 21 years with youngest and the oldest was 81 years. The mean age of the study group was 34.1±8.20 years.

Group-1 (Confirmed SA or OA with positive aspirate or blood culture) comprised 52 patients with mean age of 37.12±4.50 years; males were 38 in number and females 14 in number. Knee was the most common joint involved in 20 cases followed by ankle in 10 cases. Pain was associated with 100% of the cases followed by swelling and redness. Culture of the aspirate was positive in 48 cases, blood culture in 8 cases and both in 4 cases. MRSA was the most common isolate from the aspirate followed by *Klebsiella pneumoniae, Pseudomonas*. In cases of blood culture, *Pseudomonas* was the commonest followed by MRSA. In all the cases of Group-1, ESR, leukocyte count, CRP and PCT were raised and correlating with systemic signs and symptoms clinically confirmed as septic arthritis or OA. The mean values with Inter-quartile ranges are represented in Table-1. The mean PCT value in Group–1 was 6.87 ng/ml.

Group-2 (Presumed clinical septic or OA with raised WBC and CRP values) comprised 89 patients with 54 males and 35 females. The mean age of the group was 38.20±8.24 years knee and ankle joints collectively accounted for >50% of cases in Group-2. The mean PCT value in Group-2 was 4.99 ng/ml (2.5-5.6). Swelling of the joint was the commonest clinical manifestation and fever was the least.

Table 1: Baseline characters of cases in the study.

Character	Group-1 (n= 52)	Group-2 (n= 89)	Group-3 (n=97)
Gender			
Male	38	54	62
Female	14	35	35
Mean age (SD) years	37.12±4.50	38.20±8.24	28.10±4.2
Joints involved			
Wrist	6	5	4
Elbow	7	5	10
Finger	2	6	6
Shoulder	2	5	8
Ankle	10	20	24
Knee	20	47	42
Hip	5	1	3
Clinical presentation			
Fever	22	2	0
Redness	44	56	23
Pain	52	53	34
Swelling	48	68	46
Laboratory findings			
ESR (mm/h)	68 (57-85)	34 (24-40)	16 (18-22)
Leucocytes ($\times 10^9$/l)*	18 (14-18)	17 (16-19)	5.6 (6-8)
C-reactive protein (mg/l)*	182 (128-224)	174 (132-220)	134 (120-128)
PCT (ng/ml)*	6.87 (2.5-7.42)	4.99 (2.4-5.6)	2.6 (2.4-3.0)

*Median (Inter Quartile range).

Table 2: Mean with SD of all the parameters in the study.

Parameter	Group	N	Mean	S.D	P value
Total count	1	52	8412.21	1312.05	0
	2	89	8018.24	1063.12	
	3	97	7812.21	964.21	
ESR	1	52	63.21	11.21	0
	2	89	49.32	12.4	
	3	97	24.12	10.71	
CRP	1	52	12.14	5.01	0.012
	2	89	11.01	3.25	
	3	97	5.24	2.12	
PCT	1	52	1.65	0.84	0
	2	89	0.65	0.54	
	3	97	0.15	0.14	

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; PCT: Procalcitonin.

Group-3 (Non-inflammatory group) comprises 97 cases with 62 males and 35 females. The mean age of the study group was 28.10±4.2 years. Knee and ankle joints accounted for >60% of joints in the group. The mean PCT value was 2.6 ng/ml which is lower than the value in Group-1 and 2. Swelling was the commonest clinical manifestation in the study.

Table 2 summarizes the mean values of all the laboratory parameters and the statistical significance among the three groups in the study. All the laboratory parameters are increased in Group-1 patients when compared with group 2 & 3. A statistically significant correlation was observed with CRP among all the groups in the study.

In this study, the specificity of PCT was compared among all the groups. In group-1, the specificity of PCT (comparing Group-1 & 3) was 96.8 [95% CI, 94.2 -98.4], the sensitivity (26% [3.2-60.1], the PPV 16.1% [95% CI 2.3-48.3] and the NPV was 98% [95% CI, 95.5-99.8] When comparing Group 1 and Group 2 with Group 3 the sensitivity was 13% [95% CI, 4.7- 24.8], specificity was 96.9% [95% CI, 95 -98.9], PPV was 41% [95% CI, 16.3-68] and NPV was 88% [95% CI, 83-90]. When comparing Group 3 with confirmed cases of Septic arthritis the sensitivity was 22% [95% CI, 4.1-41.8], specificity was 97% [95% CI, 94.4-98.8], PPV was 31% [95% CI, 13.9-48] and NPV was 95 [95% CI, 91.2-97.5] (Table 3).

Table 3: Sensitivity, specificity, positive predictive and negative predictive value of PCT with the 95% CI.

Groups	Sensitivity	Specificity	PPV	NPV
1 vs 3	26 [3.2- 60.1]	96.8 [94.2- 98.4]	16.1 [2.3- 48.3]	98 [95.5- 99.4]
1+2 vs 3	13 [4.7- 24.8]	96.9 [95 -98.9]	41 [16.3- 68]	88 [83-90]
1+2 vs 3 (SA)	22 [4.1-41.8]	97 [94.4-98.6]	31 [13.9-48]	95 [91.2-97.5]
1+2 vs 3 (OA)	7.1 [4.8-20]	96.9 [94.2-98.6]	19 [5-38.6]	92 [87.6-97.3]

DISCUSSION

Early identification of acute bone and joint infection is still a challenge to the surgeons which helps in early management with favourable outcome. The problems encountered in accurate diagnosis are inadvertent use of antibiotics by the physician, low positivity rates of pus culture and sensitivity, absence of a good laboratory parameter with good specificity and sensitivity and spurious presentations at time of diagnosis. Various methods have been identified for the diagnosis but without lack of specificity.[6] Various acute phase markers have been evaluated in bacterial infections and procalcitonin (PCT) has been reported as a biochemical marker with clear specificity and sensitivity. Procalcitonin rises rapidly in bacterial infections and is also a prognostic marker for various bacterial infections like pneumonia, meningitis etc.[7] There are many of the studies comparing CRP, ESR with PCT in diagnosing other infections like meningitis etc but studies comparing PCT with ESR, CRP are limited in cases of acute bone and joint infections. With this background this study was done that PCT can be an accurate marker in diagnosing septic arthritis and osteomyelitis from other viral bone infections and on infective bone and joint infections. Our study also evaluates the sensitivity, specificity and predictive values of PCT in diagnosing SA and OA.[8]

As observed in earlier studies Knee joint was the most common joint involved followed by ankle joint in all the cases. However findings in the study of Mathews CJ, et al phalanges were more commonly involved than the ankle joint.[9] In group I cases, culture positivity was 92% with MRSA being the commonest isolate in pus and Pseudomonas from the blood. The results of our study are in concordance with the findings of Li SF et al who reported MRSA as the predominant isolate from their study.[10] In our study, levels of TC, ESR, CRP and PCT were elevated in all the cases. The level of PCT was 6.87ng/ml which is similar to the findings of Butbul-Aviel et al who reported that PCT was raised in cases of SA and OA and was more sensitive and specific than CRP and ESR.[11] In the present study the sensitivity, specificity and predictive values (positive and negative) was assessed at 0.5 ng/ml and 0.4 ng/ml. In our present study, when compared Group-1 with Group– 3 the sensitivity of PCT was 26%, specificity was 96.8%, positive predictive value was 16.1% and NPV was 98%. Findings of our study were in par with Hugle et al but with specificity were 98%, sensitivity was 32%.[12]

In cases of Group-2, the level of PCT was 4.99 ng/ml and CRP was 174 mg/ml and was raised but the levels were lesser than Group-1 confirmed cases of SA and OA. For Group-2 cases in our study, PCT is 100% specific and 94% sensitive with a PPV of 100% and 98% NPV. These findings of our study were on par with the findings of many studies conducted but in contrast with findings of Delevaux et al who reported that PCT was 100% sensitive and 100% specific with 100% PPV.[13] However there are only few studies in Indian scenario comparing the efficacy of PCT in diagnosing septic and OA in adults.

In Group-3 cases in our study, PCT levels were not elevated than cases in Group-1 and 2. The mean level of PCT was 2.6 ng/ml. The levels of other markers CRP, ESR were also lesser than other cases in the study. This is on par with the findings of Faesch and his co-workers who reported the same in their study.[14] The results of this group show that PCT and CRP levels are lower in non infectious causes than in cases of bacterial infections.

CONCLUSION

To conclude our study, highlights the role of PCT as a sensitive and specific marker in diagnosing cases of septic arthritis and Osteomyelitis. This opens a gateway to further research in evaluating the PCT effectiveness as a response marker to treatment. PCT is more sensitive than CRP in acute bone and joint bacterial infections and raises early and faster.

Limitations of the study

The limitation of the study was low sensitivity in Group-1 cases with PCT hence all the other markers may be

required to support the role of PCT as a single diagnostic aid in diagnosis of infections of bone and joint.

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