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Original article:

Role of serum procalcitonin as a diagnostic and prognostic marker in bacterial and non bacterial meningitis in children admitted at tertiary care centre, Bikaner

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ABSTRACT

Introduction: Meningitis is an extremely severe and life threatening infection that necessitates immediate diagnosis and prompt therapy. Level of serum procalcitonin(PCT) was found to be increase in presence of bacterial infection.

Aim & Objectives: To study the role of serum procalcitonin in differentiation of bacterial and non bacterial meningitis and their prognosis.

Material & Method: It was a hospital based observational study including 3 months to 12 years age children after excluding other non-CNS bacterial infection. Diagnosis of Meningitis and differentiation in bacterial and non bacterial group was made by CSF parameters. The serum procalcitonin level were sent at the start of treatment and repeated after 72 hours in those cases who had raised level of it (>0.5ng/dl). Written consent was obtained from parents of all participants.

Results: Out of total 50 meningitis cases mean age (6.84±4.14), 60% (30) were females. The level of serum procalcitonin was found increased in 57% (13/23) of bacterial meningitis and normal in children of all non bacterial meningitis (n-27) ($p<0.001$). Mean pre antibiotic procalcitonin in bacterial group was 7.15 ±21.25 while in non bacterial group it was 0.15±0.14 ($p>0.05$). After 72 hours of adequate therapy, in bacterial group 85% (11/13) patients had their procalcitonin level <0.5 (0.06±0.07) ($p<0.001$).

Conclusion: Serum PCT has good sensitivity and high specificity for early diagnosis of bacterial meningitis & useful in prognosis of bacterial meningitis in children.

Keywords: Meningitis, Procalcitonin

INTRODUCTION

Meningitis is an extremely severe and life threatening infection that necessitates immediate diagnosis and prompt therapy. There is now good evidence that mortality from this disease is falling, but a high index of suspicion, prompt diagnosis and aggressive management are essential to reduce mortality and morbidity.[1] Clinically, Gram staining and bacterial antigen testing of CSF as well as the classic biological markers in the blood or CSF used alone do not offer 100% sensitivity with high specificity for distinguishing bacterial and aseptic meningitis. To identify bacterial growth in CSF cultures at least 2 days was recommended and 3-8 days for viral cultures.[2] Among the new markers,

the serum PCT level appears to be one of the most sensitive and specific predictors to discriminate between bacterial and aseptic infections.[3] Procalcitonin (PCT) a calcitonin propeptide, is synthesized in C cells of the thyroid gland and secreted from leukocytes of the peripheral blood. Circulating concentrations of procalcitonin is very low, usually below 0.01ng/ml and in viral infection and inflammation, the concentrations increases lightly but rarely above 1.0ng/m.[4] It increases dramatically and quickly after single endotoxin injection, and this response is very rapid and the molecule is stable, making it a potentially useful marker for distinguishing bacterial from non bacterial infection.[1] However several authors have postulated that procalcitonin measurement might be superior to commonly used tests, such as C reactive protein measurement,[5-8] others stated that procalcitonin values should be interpreted with caution in the early neonatal period, because of the transient physiological rise in procalcitonin in apparently well newborns.[5,9,10]

AIM

To study the role of serum procalcitonin in differentiation of bacterial and non bacterial meningitis and their prognosis.

METHODS

The study was hospital based observational study including 3 months to 12 years age children after excluding other non-CNS bacterial infection during nine months (January 2019 to September 2019) conducted in Department of Paediatrics, S.P. Medical College and P.B.M. AGH, Bikaner, Rajasthan. After obtaining permission from Ethical Committee and informed consent from guardian of each participant of study population selected through analyzing inclusion and exclusion criteria. Detailed history was taken and thorough clinical examinations were done. All the findings were recorded in predesigned proforma. Blood samples were collected from patients suffering from bacterial and nonbacterial meningitis, confirmed by CSF examination, at admission and after 72 hours of initiation of treatment and further tested for serum procalcitonin level on sandwich ELISA. The serum procalcitonin level were sent at the start of treatment and repeated after 72 hours in those cases who had raised level of it (>0.5ng/dl). All data collected was entered into Microsoft Excel and was analyzed with help of Epi info software from CDC and tests of significance considering level of significance as $p<0.05$.

RESULTS

Out of total 50 meningitis cases mean age (6.84±4.14), 60% (30) were females 60.9% were from rural area among bacterial meningitis cases. 100% of bacterial & 96.3% of non bacterial meningitis patients reported with fever. Occurrence of vomiting, neck pain, headache, convulsion, myalgia, decreasing feed frequency and fatigue was higher among bacterial meningitis patients whereas occurrence of abnormal behavior ingitis, excessive cry, loss of consciousness, and pain abdomen was higher among non-bacterial meningitis cases. Occurrence of symptoms among bacterial and non-bacterial meningitis was found to be statistically insignificant. Mean Glasgow Coma score was 11.35±3.27 & 12.30±2.83 among bacterial and non-bacterial meningitis respectively ($p>0.05$). Mean TLC Count was 15734.78±6816.66 & 10007.41±5146.39 among bacterial and non-bacterial meningitis respectively ($p<0.05$). Mean DLC (lymphocyte) was 34.69±17.46 & 44.05±20.05 among bacterial and non-bacterial meningitis respectively ($p>0.05$). Mean DLC (neutrophil) was 58.52±17.47 & 48.43±19.99 among bacterial and non-bacterial meningitis respectively ($p>0.05$). Mean CRP was 38.62±35.89 & 4.13±3.64 mg/dl among bacterial and non-

bacterial meningitis respectively (p<0.001). Mean ESR was 31.30±18.24 & 11.56±6.74 mm/hr among bacterial and non-bacterial meningitis respectively and this difference was found to be statistically highly significant (p<0.001). The CSF parameters among both groups had statistically insignificant difference except protein with mean (151.88±249.77) in bacterial group and (58.93±12.17) in nonbacterial group (p<0.05). The both study groups were compared according to serum procalcitonin level less than and more or equal to 0.5ng/ml. The level of serum procalcitonin was found increased in 57% (13/23) of bacterial meningitis and normal in children of all non bacterial meningitis (n-27) (p<0.001). Mean pre antibiotic procalcitonin in bacterial group was 3.52±6.71 while in non bacterial group it was 0.15±0.14 (p>0.05). After 72 hours of adequate therapy, in bacterial group 85% (11/13) patients had their procalcitonin level <0.5 (0.06±0.07) (p<0.001). The mortality rate was 4.3% among bacterial meningitis group.

Table: 1. Socio demographic profile

AGE GROUP	**Final Diagnosis group**	
	Bacterial (N=23)	**Non Bacterial (N=27)**
	No. (%)	No. (%)
<5	11 (47.8)	9(33.3)
6-10	6 (26.1)	11(40.7)
11-14	6 (26.1)	7(25.9)
GENDER		
Female	14(60.9)	16(59.3)
Male	9(39.1)	11(40.7)
AREA		
Rural	14(60.9)	14 (51.9)
Urban	9(39.1)	13(48.1)

Table: 2. Investigations

GCS	Final Diagnosis group		P value
	Bacterial	Non Bacterial	0.277
	No. (%)	No. (%)	
<8	3 (13)	1 (3.7)	
8-12	10 (43.5)	12 (44.4)	
>12	10 (43.5)	14 (51.9)	
TLC			
<4000	1 (4.3)	0	0.001*
4000-11000	4 (17.4)	18 (66.7)	
>11000	18 (78.3)	9 (33.3)	
DLC (Lymphocyte %)			

<20	3 (13.0)	4 (14.8)	0.087
20-40	13 (56.5)	7 (25.9)	
>40	7 (30.4)	16 (59.3)	
DLC (Neutrophil %)			
<40	4 (17.4)	11 (40.7)	0.066
40-80	17 (73.9)	14 (51.9)	
>80	2 (8.7)	2 (7.4)	
CRP (mg/dl)			
<6	4 (17.4)	21 (77.8)	<0.001*
≥6	19 (82.6)	6 (22.2)	
ESR (mm/hr)			
<15	4 (17.4)	20 (74.1)	<0.001*
>15	19 (82.6)	7 (25.9)	

Table: 3. Correlation of CSF Parameters with Final Diagnosis group

Investigations	Final Diagnosis group		p
	Bacterial (n=37)	Non Bacterial (n=13)	
	Mean ± SD	Mean ± SD	
Cell Count (thousands)	3551.13±14577.77	123.41±187.25	0.227
Cell Type (L)	55.22 ±25.58	58.56±22.24	0.624
Cell Type (N)	43.78 ±25.66	39.85±22.44	0.566
Protein	151.88 ±249.77	58.93±12.17	0.059
Sugar	56.69 ±23.15	67.84±23.16	0.096

Graph: 1.

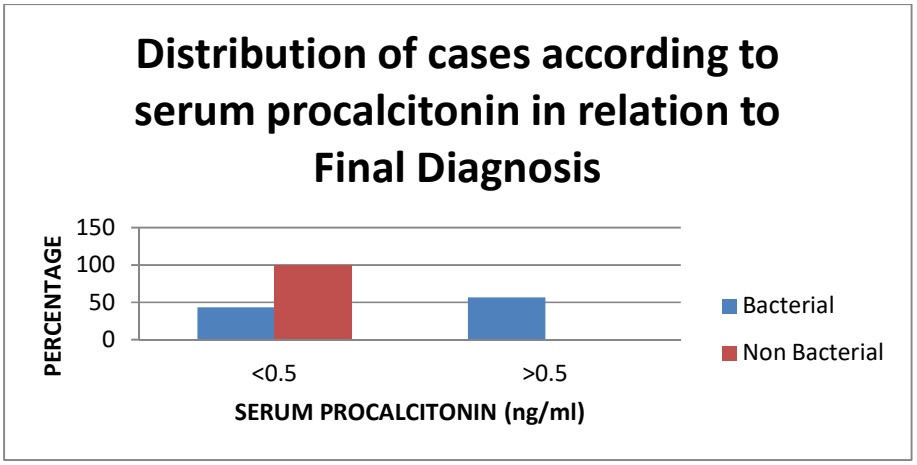

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Table: 4.

Procalcitonin				P
Initial		After 72 hrs		
Mean	SD	Mean	SD	
3.52	6.72	0.14	0.29	0.021

DISCUSSION:

This was a hospital based observational study conducted in Department of Paediatrics, S.P. Medical College and P.B.M. Associated Group of Hospitals, Bikaner, Rajasthan. Total 50 cases meeting criteria were included and divided in bacterial and non-bacterial group by CSF examination before starting the therapy. Serum procalcitonin level was checked before starting the therapy and after 72 hours of treatment. Out of total 50 cases, 23 (46.0%) were bacterial and 27 (54%) were non-bacteria. Similar results were observed by Dubos et al[2] (2008) and contrary was found by Gendrel et al[11] (1997).

Out of 23 bacterial meningitis cases, 47.8% were in <5 year age group whereas equal frequency (26.1% each) was observed in 6-10 years age group as well as 11-14 years age group. Similar findings were observed by Korczowski et al[12] (2000), Schwarz et al[13] (2000).

Mean age of children suffering from bacterial meningitis was 6.39±4.15 years and of those suffering from non bacterial meningitis was 7.22±4.18 years. Among 23 bacterial meningitis cases 60.9% were females where as among 27 non bacterial meningitis cases, 59.3% were females. The effect of gender on final outcome was found to be statistically insignificant (p>0.05). Chaudhary et al[14] (2018) and Alkholi et al[15] also observed similar results.

Among 23 bacterial meningitis cases 60.9% were from rural area where as among 27 non bacterial meningitis cases, 56% were from rural area. 100% of bacterial & 96.3% of non bacterial meningitis patients reported with fever. Occurrence of vomiting, neck pain, headache, convulsion, myalgia, decreasing feed frequency and fatigue was higher among bacterial meningitis patients whereas occurrence of abnormal behavior ingitis, excessive cry, loss of consciousness, and pain abdomen was higher among non-bacterial meningitis cases. Occurrence of symptoms among bacterial and non-bacterial meningitis was found to be statistically insignificant. Mean Glasgow Coma score was 11.35±3.27 & 12.30±2.83 among bacterial and non-bacterial meningitis respectively and this difference was found to be statistically insignificant. Chaudhary et al[14] also found insignificant correlation.

Mean TLC Count was 15734.78±6816.66 & 10007.41±5146.39 among bacterial and non-bacterial meningitis respectively (p<0.05) similar results were observed by Alkholi et al[15] (2011) and Ibrahim et al[16] (2011) whereas Schwarz et al[13] (2000) observed higher TLC levels with bacterial meningitis as compared with those with non bacterial meningitis (p<.001).

Mean DLC (lymphocyte) was 34.69±17.46 & 44.05±20.05 among bacterial and non-bacterial meningitis respectively (p>0.05). Mean DLC (neutrophil) was 58.52±17.47 & 48.43±19.99 among bacterial and non-bacterial meningitis respectively and this difference was found to be statistically insignificant (p>0.05).

Mean CRP was 38.62±35.89 & 4.13±3.64 mg/dl among bacterial and non-bacterial meningitis respectively (p<0.001). Similar results were observed by Schwarz et al[13] (2000) with higher CRP in bacterial meningitis whereas

Gendrel et al[11] (1997), Alkholi et al[15] (2011), Ibrahim et al[16] (2011) and Liu et al[17] (2006) observed a zone of overlapping insignificant values between the two groups.

Mean ESR was 31.30±18.24 & 11.56±6.74 mm/hr among bacterial and non-bacterial meningitis respectively and this difference was found to be statistically highly significant ($p<0.001$). Liu et al[17] (2006) observed higher but significant levels of ESR (50.44+/-8.95mm/h) than those with non-bacterial meningitis (16.75+/-13.23mm/h,$P<0.01$). The similarity pattern in results and significance is contributed to clinical profile of patients with bacterial meningitis.

The CSF parameters among both groups had statistically insignificant difference except protein with mean (151.88±249.77) in bacterial group and (58.93±12.17) in nonbacterial group ($p<0.05$). Gendrel et al[11] (1997) observed that cerebrospinal fluid (CSF) showed a zone of overlapping values between the two groups. Alkholi et al[15] (2011) and Ibrahim et al[16] (2011) observed that all CSF parameters showed overlapping values between the two groups.

Serum PCT levels were significantly higher in bacterial meningitis (BM) compared with non-bacterial meningitis (NBM). The values among both groups differed significantly ($p<0.001$). Thirteen out of 23 bacterial cases have serum PCT level >0.5 ng/ml while none of non bacterial cases have serum PCT level >0.5ng/ml, so sensitivity and specificity were 56% and 100% respectively. Gendrel et al[11] (1997), Hatherill et al[18] (1999), Dubos et al[2] (2008), Liu et al[17] (2006), Alkholi et al[15] (2011), Ibrahim et al[16] (2011), Alaviand Shokri et al[19] (2012), Umranand Radhi et al[20] (2014), Chaudhary et al[14] (2018) observed similar findings.

Mean initial procalcitoninin bacterial group was 3.52±6.71 while in non-bacterial group it was 0.15±0.14 and the difference was found statistically significant ($p<0.05$). Similar pattern of higher significant values among bacterial meningitis was observed by El Shorbagy et al[21] 63(2018), Hatherill et al[18] (1999), Korczowski et al[12] (2000) and Schwarz et al[13] (2000).

When we compared procalcitonin level in bacterial group at initial and after 72 hours, mean initial procalcitonin was 3.52±6.71 and after 72 hours it was 0.14±0.29 and the difference was found statistically significant ($p<0.05$). Alkholi et al[15] (2011) also showed rapid fall in PCT level. The mortality rate was 4.3% among bacterial meningitis group.

CONCLUSION:

Serum PCT has good sensitivity and high specificity for early diagnosis of bacterial meningitis & useful in prognosis of bacterial meningitis in children. It is easily available investigation and still underutilized. It will definitely help to improve quality care of meningitis patients, so our study can be used as base for conducting more studies on large community.

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