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Utility Of The Serum C - Reactive Protein And Procalcitonin For Detection Of Occult Bacterial Infection In 3-36 Month Old Children

Üç-36 Ay Arası Çocuklarda Gizli Bakteriyel Enfeksiyonları Saptamada C-reaktif Proteinin Ve Prokalsitoninin Kullanılabilirliği

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Aim: To assess the utility of serum C-reactive protein (CRP) and Procalcitonin (PCT) as a screening method for occult bacterial infection (OBI) in 3-36 month old children.

Materials and Methods: Febrile children, who were admitted to emergency department with ages ranging from 3 to 36 months, temperatures > 38.3°C, and clinically undetectable source of fever, were enrolled in this study. Sex, age, degree of fever, Yale Observation Scale (YOS) score, antibiotic treatment and hospitalization were recorded at the time of the initial evaluation. Routine urine analysis, white blood cell count (WBC) count, CRP and PCT determination tests were performed at the initial evaluation. Viral serology was done and patients having specific IgM positivity during the acute phase and/or a four-fold increase in specific IgG titer during convalescence phase were considered to be positive. A chest radiograph, blood culture and urine cultures were taken from all patients. The patients were divided into two groups: OBI group and viral infection group. These two groups were compared for each predictor.

Results: There were 10 patients with OBI, six with urinary tract infection two with pneumonia, one with bacterial meningitis and one with bacteremia and 16 patients with viral infection, (five Adenovirus, five Respiratory syncytial virus, four Enterovirus, one Parainfluenza type 1, one Epstein-Barr virus. Regarding the CRP values, there was no statistical difference between OBI and viral infection groups (respectively, median 44.84 mg/L and 23.3 mg/L, p=0.097), but PCT values were significantly higher in OBI group (respectively, median 2.38 ng/mL and 0.28 ng/mL, p=0.014).

Conclusion: This study showed that PCT is superior than CRP in detecting OBI and could be used for screening purposes in pediatric emergency departments while elevated levels might be found in some viral infections.

Key Words: ***Occult bacterial infection, C-reactive protein, Procalcitonin***

Amaç: Üç–36 ay arası gizli bakteriyel enfeksiyon riski taşıyan hastaların saptanmasında C-reaktif proteinin (CRP) ve Prokalsitoninin (PCT) kullanılabilirliğini saptamak.

Gereç ve Yöntem: Yaşları 3-36 ay arası olan, 38.3°C üzerinde ateş yüksekliği şikayeti ile acil servise başvuran ve ateş odağı saptanamayan hastalar çalışmaya alındı. Başvuru anında, cinsiyetleri, yaşları, ateş yüksekliğinin derecesi, Yale Gözlem Ölçeği (YGÖ) skoru, hastaneye yatma ve antibiyotik başlanma durumları kaydedildi. Başvuru anında, rutin idrar analizi, beyaz küre sayıları, CRP ve PCT'nin düzeylerinin ölçümü için testler yapıldı. Viral serolojik inceleme yapıldı ve akut faz dönemindeki spesifik IgM pozitifliği ve/veya konvalasan fazda spesifik IgG düzeylerinde 4 katlık artış pozitif olarak kabul edildi. Tüm hastalardan kan kültürü, idrar kültürü yapıldı ve akciğer grafileri çekildi. Hastalar gizli bakteriyal enfeksiyon ve viral enfeksiyon grubu olmak üzere ikiye ayrıldı. İki grup verileri her bir belirleyici açısından karşılaştırıldı.

Bulgular: Gizli bakteriyel enfeksiyonlu 10 hastada, altı idrar yolu enfeksiyonu, iki bronkopnömoni, bir menenjit, bir bakteriyemili hasta saptanırken, viral enfeksiyon saptanan 16 hastada, beş Adenovirus, beş Respiratory syncytial virus, dört Enterovirus, bir Parainfluenza Tip1 ve bir Epstein-Barr virus enfeksiyonlu hasta saptandı. Gizli bakteriyel enfeksiyon grubu, viral enfeksiyon grubu ile CRP değerleri açısından karşılaştırıldığında istatistiksel olarak anlamlı fark saptanmazken (sırasıyla, ortanca 44.84 mg/L ve 23.3 mg/L, p=0.097), PCT değerleri istatistiksel olarak anlamlı saptandı (sırasıyla, ortanca 2.38 ng/mL, 0.28 ng/mL, p=0.014).

Sonuç: Bu çalışma, çocuk acil bölümlerinde PCT'nin gizli bakteriyel enfeksiyonları saptamada CRP'ye göre daha üstün bir belirleyici olduğunu ve tarama amaçlı kullanılabileceğini, ancak bazı viral enfeksiyonlarda yüksek saptanabileceğini göstermiştir.

Anahtar Kelimeler: ***Gizli Bakteriyal Enfeksiyon, C-reaktif protein, Prokalsitonin***

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Febrile infants and children frequently present to primary care and emergency physicians. The majority of these children are younger than 3 years. Most have an apparent source of infection (ie, a viral respiratory infection, acute otitis media, or enteritis). However, 20% of febrile children have fever without source of infection after history and physical examination and occult bacterial infections (OBI) (urinary infection, pneumonia, occult bacteremia, early bacterial meningitis, etc.) develop in 11.3% of them (1-4).

The most important feature of Procalcitonin (PCT) is that it increases in bacterial infections, it does not increase or slightly increases in viral and local infections and it decreases in a very short time upon a successful antibiotic treatment (5-13). It has been found out that PCT starts to increase in the first 2-3 hours, reaches the peak level in 6-8 hours, stays high for 24 hours and it has an half-life of approximately 25-30 hours because of its rapid kinetic effect (12-14). The kinetic of serum C-reactive protein (CRP) is slower than that of PCT and to increase within 4 – 6 h after onset of inflammation. It then doubles every 8 h and peaks at approximately 36 – 50 h (15). Due to this feature of PCT, the monitoring of the patient is more reliable and the early differential diagnosis of bacterial and viral infections is possible (16,17).

The objective of this study was to investigate the utility of PCT and CRP and to compare them in the differential diagnosis of OBI and viral infections in the patient group of 3-36 month old children who are admitted to pediatric emergency services for high fever complaints with fever without a focus despite medical history and physical examination.

Materials and Methods

Children aged 3 to 36 months of age consulting the Pediatric Emergency Department of the Dokuz Eylul University, Faculty of Medicine (Izmir/Turkey) with an axillary temperature ≥ 38.3°C and without localizing signs of infection in their history or at physical examination were prospectively enrolled. Each infant was examined by a pediatric resident who took a complete history, performed a physical examination, recorded the degree of fever and determined a clinical score according to Yale Observation Scale (YOS) scores (18).

Routine urine analysis, white blood cell (WBC) count and CRP determination were performed at the initial evaluation. Chest radiography was taken for all study patients regardless of respiratory symptoms.

Pyuria was defined as ≥5 white blood cells/high-power field in a centrifuged urine sample. Urine for culture was obtained by urethral catheterization using standard sterile technique from all the patients having pyuria and the patients under the age of 12 months without pyuria. Blood culture, viral serology panel and 2 mL blood were taken from all patients for the study of PCT levels. Blood taken was centrifuged for viral serology and PCT examinations for 10-15 minutes in 3000 rpm and then serums were separated and stored in - 70°C. At the initial admission, lumber puncture was done in all patients with poor general condition (fever with convulsion, sleepiness, toxic appearance etc.). Patients with good general condition were followed clinically.

The exclusion criteria for potential study subjects were: having high fever for more than a week with clinical localization symptoms; antibiotic treatment within 48 hours prior to admission to the hospital; vaccination in the days before the study, which may have caused the febrile syndrome; surgery performed within 7 days before the start of the study; any chronic pathology that could alter CRP values; a history of prior urinary tract infection, pathology involving malformation of the kidney or of the urinary tract and vesicoureteral reflux.

Patients with more than $>10^4$ CFU/mL pathogenic bacteria in urine cultures obtained by catheter (19), having a reproduction in blood and cerebrospinal fluid (CSF) cultures, having infiltration in chest radiography and having negative test results for viral serology formed the OBI group. Patients with positive Immunoglobulin M (IgM) upon examination of viral serology and/or having a fourfold increase of antibody in Immunoglobulin G (IgG) titer of control serum taken in the second week and having no positive bacteriologic cultures formed the viral infection group.

Phone numbers of patients in both groups whose general condition seemed good were taken for monitoring future complications and data about the prognosis was collected by getting into touch with the patients on 1st, 2nd, 3rd, 7th and 15th days. Physical examinations and laboratory analysis for etiologic diagnosis of patients with high fever and with new symptoms or diagnosis were repeated. Antibiotic treatment was started in both patients with occult bacterial infections and patients who have been recalled for reexamination and found having an infection focus.

Informed consent was obtained from parents or guardians and the study was approved by board of ethics.

Radiological Evaluation

The diagnosis of "occult pneumonia" was based on a radiologic diagnosis of lobar infiltrate or pneumonia in a patient with no abnormalities noted on physical examination.

Evaluation of Blood Cultures

Blood culture samples were taken after systemic examination of patients and before decreasing the temperature. The area was cleaned by povidon iodine and 3 mL blood was taken after waiting for 30 seconds. The blood taken was cultured in BACTEC which is blood culture medium and evaluated by BACTEC 9240 device (Becton Dickinson Canada U.S.A).

Organisms which reproduce within the first 48 hours were passaged to their mediums like bloody agar and chocolate agar. The samples were examined in terms of newly reproduced colonies after incubation of samples at 35-37°C for 24 hours. Samples having more than one different colony were determined as contaminated.

Serologic Diagnosis of Viral Infections

Adenovirus, Enterovirus, Parainfluenza type 1,2,3, Epstein-Barr virus (EBV), Respiratory syncytial virus (RSV), Influenza A and B viruses were investigated in serums of the patients by using Respiscreen Clinikit (Orgenium Helsinki, Finland), an indirect commercial EIA kit. Patients having specific IgM positivity during the acute phase and/or a four-fold increase in specific IgG titer during convalescence phase were included in the viral infection group. The sensitivity and specificity values of viral serologic markers were all above 89% (range, 89.2-95%) (according to manufacturer's catalog: http://www.orgenium.com/Orgenium%20Catalog %202008.pdf).

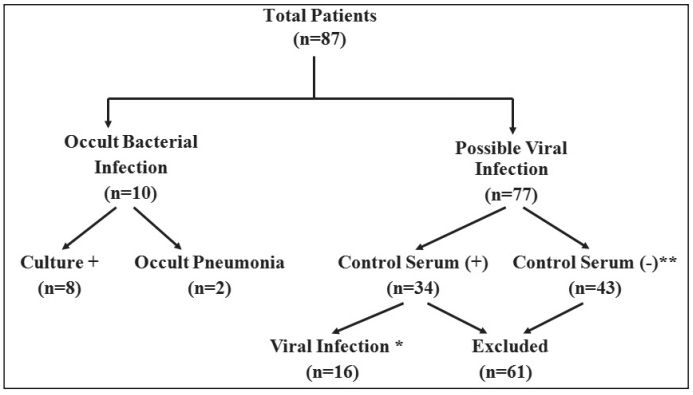

Figure 1. Flow chart of the present study

* Four fold IgG antibody increment of control serum

** Did not give permission us for taking control serum because their children had already ben recovered

White Blood Cell Count and Measurement of CRP and PCT Levels

Number of white blood cells was counted by STKS coulter LH 750 device (Coulter Electronics, Miami, Florida). Plasma concentrations of CRP were measured by means of particle-enhanced immunonephelometry with the Behring nephelometer using N Latex CRP mono reagent (Dade Behring Marburg GmbH, Germany). An immunoluminometric assay for the measurement of PCT serum concentration was performed with LUMItest PCT kit (Brahms Diagnostica GmbH, Berlin, Germany). The cut-off values for determination of OBI were accepted as ≥15 000 cell/mm3 for WBC, ≥40 mg/L for CRP, ≥0.5 ng/mL for PCT (13,19).

Statistical Analysis

Statistical analysis was made by using SPSS Software 11.0. Comparison between group averages was made by non-parametric tests. To this aim, Mann-Whitney U-test was used for comparison between the averages of two groups. Data were given as median (range). Spearman correlation analysis was used to determine the correlation between the two groups. The determined value of $p<0.05$ was considered significant.

Results

A total of 87 patients participated in the study and 10 patients were determined as having OBI and 16 patients were determined as having a viral infection (Figure 1).

There were six patients with urinary tract infection, two with bronchopneumonia, one with meningitis, one with bacteremia among 10 patients with OBI, there were five patients with Adenovirus, five with Respiratory syncytial virus (RSV), four with Enterovirus, one with Parainfluenza type 1 and one with Ebstein–Barr virus (EBV) infection among 16 patients with viral infection (Table 1 and 2). Escherichia coli was responsible for most of the urinary tract infections, Streptococcus pneumoniae was isolated in the bacteremia patient and Haemophilus influenzae was isolated in CSF culture in the patient with meningitis.

Both groups were compared in terms of average ages, genders, YOS scores, antibiotic treatment, and hospitalization, degree of fever, WBC count, PCT and CRP

Table 1: Clinical and laboratory finding of patients with occult bacterial infection

Patient with OBI	Fever (°C)	YOS score	WBC (cell/mm^3)	CRP (mg/L)	PCT (ng/mL)	Culture	Diagnosis
Patient 1	39.0	6	16700	41.00	2.38	10^5 *E.coli*	UTI
Patient 2	39.5	10	30500	48.68	1.00	*Streptococcus pneumoniae*	Bacteriemia
Patient 3	38.5	10	32500	3.00	5.96	10^5 *E. coli*	UTI
Patient 4	39,0	7	16400	9.00	2.39	10^5 *E.coli*	UTI
Patient 5	39.2	7	13200	150.00	2.58	10^5 *E. coli*	UTI
Patient 6	38.7	7	7600	38.00	0.55		Bronchopneumonia
Patient 7	39.0	6	15600	102.00	2.09	10^5 *E. coli*	UTI
Patient 8	38.8	14	4200	363.00	445.00	*Haemophilus influenzae*	Meningitis
Patient 9	38.5	7	16200	35.00	0.26		Bronchopneumonia
Patient 10	40.0	7	8600	244.00	2.59	10^5 E.coli	UTI

UTI: Urinary Tract Infection, YOS: Yale observation scale, CRP: C-reactive protein, PCT: Procalcitonin,
OBI: Occult Bacterial Infection, WBC: White blood cell

levels. Regarding the CRP values, there was no statistical difference between occult bacterial infection and viral infection groups (median 44.84 mg/L [range 2.56 to 363.47], 23.3 mg/L [range 0.50 to 79.2], p=0.097), but PCT values were significantly higher in OBI group (median 2.38 ng/mL [range 0.26 to 445], 0.28 ng/mL [range 0.12 to 6.28], p=0.014) (Table 3). There was no statistically significant difference between the two groups with regard to YOS scores, application ratio of antibiotic treatment, degree of fever and WBC count (p>0.05). There was a statistically high hospitalization ratio in OBI group than viral infection group (62.5%, 32.5%, p=0.03). It was determined that all patients in OBI group and 81.3% of those in viral infection group had antibiotic treatment. There was no statistically significant difference between the two groups with regard to treatment (p=0.262).

While there was a positive correlation between PCT levels and YOS score and CRP levels (r=0.778, p=0.001; r=0.759, p=0.001, respectively) determining OBI, there was no significant correlation between PCT and WBC count, degree of fever (p > 0.05).

Procalcitonin level was found to be more than 0.5ng/mL for 90% of patients in the OBI group and 37.5% of the viral infection group. Overall, two patients were diagnosed ashaving Adenovirus, one patient as having EBV, two patients as having Enterovirus, two patients as having RSV who were among the patients with viral infection and who have high PCT values. CRP was found to be greater than 40 mg/L in 60% of OBI cases and in 30% of viral infection cases. While the number of patients with CRP below 40 mg/L was 4 (40%), PCT level of one of the patients with OBI was found to be below 0.5 ng/mL.

Discussion

The management of febrile young children without apparent source of infection and the use of accurate diagnostic laboratory methods remains controversial. In 1993, Baraff published a consensus practice guideline for management of febrile infants aged 3-36 months and two options were suggested for febrile nontoxic-appearing infants: obtaining a blood culture and giving empirical antimicrobial therapy (ceftriaxone) or obtaining a blood culture and giving empirical antimicrobial therapy in case of a WBC count equal to or greater than 15000 cell/mm^3 (20). In spite of the fact that a consensus has not been reached on the evaluation and management of fever in young infants without an obvious focus of infection, most would agree that no single laboratory test has been shown to reliably identify young infants at high or low risk of having bacterial illness. Many inflammatory determinants such as Interleukin (IL)-1, IL-6, tumor necrosis factor-, fibronectin, -integrin, CRP have been studied up to now for evaluation and true diagnosis of children between 3-36 months with fever and with fever without a focus (2,6,7). However, the developed clinical scoring methods and assaying methods of many inflammatory determinants are neither useful nor cheap and simple and they take a long time to obtain the results. With the identification of reliable determinants providing the diagnostic accuracy of OBI, the use of antibiotics will be limited, development of bacterial resistance to antibiotics and complications will be reduced and unnecessary hospitalization for the administration of parental antibiotics in viral infections will be prevented.

It has been reported that the risk of

Table 2: Clinical and laboratory finding of patients with viral infections

Patient with Viral Infections	Fever (°C)	YOS score	WBC (cell/ /mm^3)	CRP (mg/L)	PCT (ng/mL)	Culture	Determined infectious agent
Patient 1	39.5	7	15600	60.0	2.53	-	Enterovirus
Patient 2	39.2	6	16800	35.7	1.59	-	Adenovirus
Patient 3	39.5	7	7600	0.50	0.28	-	RSV
Patient 4	38.3	6	10900	13.0	0.20	-	Adenovirus
Patient 5	38.5	8	15100	24.0	0.12	-	Enterovirus
Patient 6	38.5	6	5800	1.50	0.93	-	RSV
Patient 7	39.0	7	14000	5.50	0.20	-	Enterovirus
Patient 8	40.0	8	40000	34.4	6.28	-	Epstein-Barr virus
Patient 9	38.5	6	4500	1.45	0.17	-	Enterovirus
Patient 10	39.0	7	13200	9.31	0.38	-	Adenovirus
Patient 11	39.5	6	29500	22.6	0.13	-	Adenovirus
Patient 12	39.0	8	30600	75.0	0.28	-	RSV
Patient 13	39.8	7	7200	4.99	0.21	-	Parainfluenza Type 1
Patient 14	40.0	6	17400	47.7	5.75	-	Adenovirus (Bronchopneumonia)
Patient 15	39.2	6	22100	79.2	1.10	-	RSV
Patient 16	38.5	8	16200	34.9	0.24	-	RSV (Bronchopneumonia)

YOS: Yale Observation Scale, CRP: C-reactive protein, PCT: Procalcitonin, WBC: White blood cell, RSV: Respiratory Syncytial Virus

bacteremia is 6% in patients with a WBC count of 15000 cell/mm3 or greater, and this risk decreases to 0.7% in those patients with a WBC count of 15000 cell/mm^3 or below (21). However, studies in the past have indicated that WBC count is not a reliable indicator of severe bacterial infection (SBI) in febrile infants (1,16,22). Pulliam et al. examined a febrile pediatric population with SBI and found that WBC count was not an ideal indicator than CRP (1). Although, it is suggested that the blood cultures should be taken from patients whose number of white blood cells is 15000 cell/mm^3 and above and their empiric antibiotic treatments should be started (23). In our study, it has been determined that 30% of patients whose number of WBC is above 15000 cell/mm^3 and 81.3% of the patients who had viral infection have had unnecessary antibiotic treatment.

It was reported that the CRP levels do not increase until 12 h after the onset of fever (1,24,25). In addition, CRP levels can be elevated in minor or viral infections and do not always enable confirmation of the severity of an infection, especially in the first 12 h of the process (16). In our study, it was ascertained that 4 of the patients in the OBI group were not detected when the cut-off value for CRP was taken as ≥40 mg/L. Pulliam et al. determined that CRP level of 3 patients, who had serious bacterial infection with a fever lasting less than 9 hours, was below 7 mg/L (1). Nevertheless, the duration of degree of fever of our patients was not recorded. Therefore, it has been thought CRP is an inadequate determinant in identifying patients with OBI in early stage. It has been reported that the serum CRP is not specific and sensitive enough for bacterial infections since it can remain at low concentrations in bacterial infections and can increase significantly in viral infections (15,25,26).

Recently, it has been emphasized that PCT is a more specific and sensitive method than CRP in the early diagnosis of patients having risk of bacterial infection and in the differentiation of viral and bacterial infections (6,7,9,25,27). It is known that the serum PCT level low in the healthy people (<0.5 ng/mL) and rises slightly in viral infections (13,16,22). This increase often correlates with the severity of the disease and can increase nearly a thousand-fold in bacterial infections (22,28-30). In 2003, Galetto-Lacour et al. have reported that PCT was the single most sensitive test (31). Fernandez et al. evaluated the usefulness of PCT as well as CRP as predictors of bacterial infections in febrile children aged 1 to 36 months. In this study, the authors found PCT to be the best predictor of bacterial infection. Using a calculated optimum cutoff as 0.53 ng/mL the authors noted a sensitivity of 65.5% and a specificity of 94.3% (16). In our study, the sensitivity and specificity values were not calculated because of small sample population.

Table 3: Comparing the laboratory and clinical features of occult bacterial infection and viral infection groups

	OBI* (n= 10)	Viral Infection* (n= 16)	p**
Age (months)	9.2 (4.0-15.0)	8 (3.0-28.0)	0.698
Fever (°C)	39.0 (38.5-40.0)	39.1 (38.3-40.0)	0.897
YOS scores	7 (6.0-14.0)	7 (6.0-8.0)	0.262
WBC (cell/mm^3)	15600 (4200-32500)	15350 (4500-40000)	0.979
CRP (mg/L)	44.84 (2.56-363.47)	23.3 (0.50-79.2)	0.097
PCT (ng/mL)	2.38 (0.26-445)	0.28 (0.12-6.28)	**0.014**

* Data are given as median (range)
** Mann-Whitney U-test

During the first 12 hours of the fever CRP level does not reach the peak level and most of the children with fever are generally admitted to emergency services in the first 12 hours. Therefore, CRP levels do not provide sufficient information about the seriousness of the infection (1,24). In our study, it has been found that PCT level of 3 cases, which have been diagnosed of OBI, have been calculated above 0.5ng/mL although their CRP levels have been below 40 mg/L. The duration of the fever before the admission of the patients to the emergency department was not recorded. However these results indicated that this duration should have been less than 12 hours in 3 patients diagnosed with OBI and who had low CRP levels.

Many studies have compared the OBI groups with control groups without infection or with patient groups who are thought to have a probable viral infection. Lacour et al. compared the patients in the OBI group with the patients who were thought to have clinically probable viral infection which was not confirmed with viral serological evaluation (7). Fernandez et al conducted a prospective, observational and multi-centered study (among patients aged 1 to 36 months) in which invasive bacterial infection groups were compared with the viral infection groups of which the diagnoses were confirmed with serologic viral evaluation (16).

Therefore, a significant difference of our study from the others is the comparison of the patients with OBI (3-36 month age) with the patients with viral infection whose diagnoses have been confirmed with serological methods similar to those in the study of Fernandez et al. (16).

It was reported that bacterial pneumonia cannot be differentiated from viral pneumonia on the basis of a patient's characteristics, routine laboratory tests, or chest radiographic findings (32,33). White blood cell count or serum CRP levels sometimes help to differentiate between bacterial or viral infection (1,3). In a prospective study carried out by Toikka et al. which aimed the differential diagnosis of viral and bacterial pneumonia, the levels of CRP, PCT and IL-6 were investigated in the sera of patients aged 1 month to 17 years (2.6 years average). Although there was no statistically significant difference between the PCT and CRP values of the patients, the patients with specific pneumonic infiltration of bacterial origin which was confirmed with chest radiography had higher PCT and CRP values than the patients with viral pneumonias (34). In the same study, a viral agent was identified in only 18% of the patients who had changes in their specific whole chest radiography, while it was determined that the agent was a virus in 45% of the patients who had moderate radiologic changes (34). In our study, viral agents (Adenovirus (patient 14), RSV (patient 16) Table 2) was identified in only 2 of the patients while there were moderate radiologic changes in the whole chest radiography of 3 patients who were thought to have pneumonia. It has been found out that PCT level was low in one of the 2 patients in the OBI group in which bronchopneumonia was diagnosed. The PCT level of this patient was low and although the viral serologic examination of this patient was negative, the patient was thought as having viral bronchopneumonia as a result of the low CRP and PCT levels and moderate infiltrations in the whole chest radiography.

Appenzellera et al. have reported that CRP may increase in adenoviral infections (35).Kawasaki et al. have demonstrated that there might be some increases in the

levels of CRP and IL-6 which are inflammatory determinants in respiratory diseases caused by adenoviruses (36). Ruuskanen et al. have found that increases in the levels of CRP may be seen in adenovirus and influenza infections similar to invasive bacterial infections (37). In a different study, it has been shown that PCT did not increase in severe acute respiratory syndrome (SARS) infection of viral etiology (38). Korczowski et al. have found that PCT could be increased in 7% of the gastroenteritis related to rotavirus infection (39). In this study, a wide viral serologic study has been carried out for the first time and it has been showed that the level of the PCT could be increased in viral infections. In our study, it has been identified that in 6 of the 16 patients (37.5%) the PCT level was above 0.5ng/mL. The reason for the high level of PCT in viral infections might be the fact that some viral infections that are strong immune stimulants (Adenovirus, RSV, EBV, Enterovirus) may increase the level of PCT.

In our study the first limiting factor was the small size of the study sample and the second limiting factor was that some viral pathogens (rhinovirus, coronavirus etc.) which are commonly encountered in this age group were not sought.

A recent study has shown that low PCT level cannot be used to exclude OBI in this population and suggested a combination of PCT, CRP and WBC count may be more useful in predicting OBI (11). However, we found that PCT is a better determinant than CRP in OBI diagnosis. Measuring PCT levels in fever without focus could reduce the number of hospitalizations and unnecessary antibiotic usage, hospital stays and finally the cost.

Finally;

1. High PCT levels were also found in viral infections such as Adenovirus, EBV, Enterovirus, RSV, which show clinical symptoms of bacterial infections. However, this study showed that studies with larger patient populations and studies to find out in which viral infections PCT is more elevated are needed.

2. Although PCT may increase in some viral infections, it still shows that PCT level is currently the most reliable and rapid method for the differentiation of viral infections from bacterial infections and for distinguishing occult bacterial infections according to CRP and the white blood cell count.

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