Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2019;44(Suppl 1):69-76
DOİ: 10.17826/cumj.551752

ARAŞTIRMA / RESEARCH

Comparison of procalcitonin, C-reactive protein, white blood cell and body temperature in the diagnosis of ventriculostomy-associated infection

Ventrikülostomi sonrası gelişen enfeksiyon tanısında prokalsitoninin C-reaktif protein, beyaz küre ve ateşle karşılaştırılması

Ali Arslan[1], Semih Kıvanç Olguner[1], Vedat Açık[1], Faruk İldan[2], Ali İhsan Ökten[1]

[1]Adana City Training Research Hospital, Department of Neurosurgery, Adana, Turkey
[2]Cukurova University of Medical School, Department of Neurosurgery, Adana, Turkey

Cukurova Medical Journal 2019;44(Suppl 1):69-76.

Abstract

Purpose: The aim of this study was to evaluate the effect of neurosurgical procedures on procalcitonin levels and the role of procalcitonin in distinguishing the inflammatory reaction due to surgery and postoperative infection.

Materials and Methods: This study was performed on 27 patients with hydrocephalus. Among these patients, 10 patients had ventricular drainage while 17 had ventriculoperitoneal shunt. The changes in the values of procalcitonin, white blood cell count, C-reactive protein and body temperature were examined in the preoperative 1st and during postoperative 7 days.

Results: All the patients had statistically significant increase in the body temperature values of the postoperative 1st day compared to preoperative values. C-reactive protein peaked in the postoperative 2nd day and, after that, followed a regular kinetic to show a decrease pattern. C-reactive protein was found to be 3 times higher in the postoperative 5th day compared to the preoperative value. Procalcitonin was found to remain in normal limits in all the patients that did not develop infection while the same was observed to increase in patients with infection.

Conclusion: Procalcitonin will be a serious and safer parameter for the follow-up of the systemic complications following surgery upon the conclusions obtained with studies that include a higher number of patients and varying types of operations.

Keywords: C-reactive protein, procalcitonin, ventriculostomy-associated infection

Öz

Amaç: Bu çalışmada beyin cerrahisinin prokalsitonin düzeylerine etkisini ve prokalsitoninin beyin cerrahisinin yaratmış olduğu enflamatuar reaksiyonla, postoperatif gelişen enfeksiyonu ayırt etme özelliği araştırılmıştır.

Gereç ve Yöntem: Çalışmamız 10'unda ventriküler drenaj, 17'sinde ventriküloperitoneal şant uygulanan 27 hidrosefalili hastada yapılmıştır. Preoperatif 1 ve postoperatif 7 gün boyunca Prokalsitonin, Beyaz küre sayısı, C-reaktif protein ve ateş değerlerindeki değişimler incelenmiştir.

Bulgular: Tüm hastalarda postoperatif 1. günde preoperatif değerlere göre ateş değerlerinde anlamlı yükseklik tespit edilmiştir. C-reaktif proteinin postoperatif 2. günde pik yaptığı ve daha sonra azalma paterni gösteren düzenli bir kinetik izlediği gözlenmiştir. Postoperatif 5. günde, C-reaktif proteinin halen preoperatif değerinin 3 katı kadar yüksek olduğu tespit edilmiştir. Prokalsitoninin enfeksiyon gelişmeyen tüm hastalarda postoperatif normal sınırları aşmadığı, enfeksiyon gelişen hastalarda ise arttığı gözlenmiştir.

Sonuç: Gelecekte daha fazla hasta sayısı ve farklı operasyon türlerini de içeren gruplarla yapılacak çalışmaların sonuçlarıyla prokalsitoninin beyin cerrahi sonrası sistemik komplikasyonları takipte ciddi ve güvenli bir parametre olacağını düşünmekteyiz.

Anahtar kelimeler: C-reaktif protein, prokalsitonin, ventrikülostomi ilişkili enfeksiyon

Yazışma Adresi/Address for Correspondence: Dr. Semih Kivanc Olguner, Adana City Training Research Hospital, Department of Neurosurgery Adana,Turkey E-mail: kivanc3olguner@hotmail.com
Geliş tarihi/Received: 10.04.2019 Kabul tarihi/Accepted: 07.05.2019 Çevrimiçi yayın/Published online: 23.09.2019

INTRODUCTION

It is known how the inflammatory response develops as the answer to the infections. Similar inflammatory responses can also develop after pancreatitis, major trauma, burns and autoimmune diseases. Systemic inflammatory response syndrome (SIRS) which includes systemic symptoms such as changes in body temperature, leukocytosis, tachycardia may have infectious or noninfectious etiology[1].

Acute phase reactants such as body temperature, white body cell (WBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) which are now used as infection parameters in the systemic inflammatory response are not infection specific markers. Inflammatory response due to surgical trauma in neurosurgery causes these parameters to increase without infection. Therefore, researches are still continuing on bacterial infection-specific markers which show infective complications that may develop in the early postoperative period, and which are not affected by surgical trauma, but also rapidly respond to treatment after appropriate antibiotic treatment. In recent years, procalcitonin has been investigated for these reasons[2-4].

Procalcitonin is a 116 amino acid glycopeptide produced by the C cells of the thyroid gland under normal conditions and is the precursor of calcitonin. Procalcitonin levels in healthy individuals are either too low (<0.5 ng/ml) or not detectable in serum plasma. It is known that in patients with sepsis and severe invasive bacterial infection, the serum procalcitonin levels increase significantly and fall rapidly with appropriate antibiotic therapy[4].

However, procalcitonin levels do not change in severe viral infections and other inflammatory diseases. There are few studies in the literature about the place of procalcitonin in determining infective complications following cranial surgery[5-7]. Therefore, we planned this research to determine whether procalcitonin is affected by surgical intervention, it helps to recognize the surgical complication and there is a superiority of procalcitonin to existing infection markers.

MATERIALS AND METHODS

This study was carried out on 27 patients with hydrocephalus who were treated at the department of Neurosurgery in the Medical Faculty of Cukurova University. The patients were informed prior to the medical applications, and the study was approved with 03072007/7 number by the Ethics Committee of Cukurova University.

The patients who were examined at the emergency room due to hydrocephalus were included in the study , and those who had chronic organic failure, terminal level oncologic disease, pregnancy, massive blood transfusion, patients with multiple trauma and fractures in more than one area (due to triggering of systemic inflammatory response), undergone a surgical operation within the previous three months, urinary tract, lung or skin infections or chronic rheumatic diseases (systemic lupus erythematosus, rheumatoid arthritis, familial mediterranean fever etc.) were excluded from the study. Fiftytwo patients charts were collected and 25 patients were exctracted from the study due to above mentioned exclusion criterias.

Two patients included in this study had chronic diseases (hypertension). One patient had meningomyelocele while 5 patients had concomitant intracranial mass (two had thalamo-mesencephalic, two in cerebellum and one in foramen magnum localization).

Clinical follow-up

The demographical data (age and gender etc.), clinical findings and previous antibiotic regiment of each patient were recorded upon first admittance. The patients were followed for infection and postoperative complication in the preoperative 1st day and following postoperative 7 days. The blood, urine and cerebrospinal fluid (CSF) specimens of the patients with body temperatures higher than 38°C and wound site swab materials of the patients with wound site discharge were added to the cultures.

Surgical procedures

The patients were applied two different operative procedures. These were ventricular drainage and ventriculoperitoneal shunt.

The patients who were applied to external ventricular drainage(EVD) consisted of 5 male and 5 female patients (10 patients, in total, (37.03%), and their mean age was 41.7. The patients who were applied ventriculoperitoneal (VP) shunt consisted of

10 male and 7 female patients (17 patients, in total, (62.96%), and their average age was 17.64. (Table 1).

Table 1. Demographical data of the patients

Patient No	Gender	Age	Type of ventriculostomy	Type of anesthesia
1	Male	5	VP shunt	General
2	Male	14	VP shunt	General
3	Male	16	VP shunt	General
4	Female	0	VP shunt	General
5	Male	11	VP shunt	General
6	Male	5	VP shunt	General
7	Male	0	VP shunt	General
8	Male	32	External ventricular drainage	Local
9	Male	60	External ventricular drainage	Local
10	Female	43	VP shunt	General
11	Female	1	VP shunt	General
12	Female	63	External ventricular drainage	Local
13	Female	42	External ventricular drainage	Local
14	Male	43	External ventricular drainage	Local
15	Male	74	VP shunt	General
16	Female	75	External ventricular drainage	Local
17	Female	35	VP shunt	General
18	Female	9	VP shunt	General
19	Male	3	VP shunt	General
20	Female	33	External ventricular drainage	Local
21	Female	48	External ventricular drainage	Local
22	Female	30	VP shunt	General
23	Female	16	External ventricular drainage	Local
24	Female	51	VP shunt	General
25	Female	9	VP shunt	General
26	Male	16	VP shunt	General
27	Male	35	VP shunt	General

*No: number, VP: Ventriculo-peritoneal

10 patients were locally anesthetized (37.03%) while 17 patients received general anesthesia (62.96%). All the patients were given cefazolin sodium 25mg/kg (MN Pharmaceuticals, Istanbul , TURKEY) prophylaxis 30 minutes prior to operations and throughout postoperative 7 days.

Table 2. Distribution of the patients with postoperative complications

Postoperative complication	n	(%)
Urinary tract infection	2	7.4
Pneumonia	1	3.7
Pneumonia+decubitus	1	3.7
Meningitis	1	3.7

Laboratory analysis

Blood samples were taken from all the patients between 07:00 and 08:00 a.m. In the preoperative 1st day and throughout postoperative 7 days, and their body temperatures were recorded 4 times a day in the same hours. The blood samples taken for CRP and PCT analyses were placed into dry tubes and were subjected to centrifuge at 4000 rpm for 10 minutes. The serums of these blood samples were removed after centrifuge. The serum samples intended for CRP examination were analyzed by nephelometric method (Dade Behring, Germany BN II device) at the central lab of our hospital in the same day.

On the other hand, the serum samples for procalcitonin examination were analyzed by kryptor method (BRAHMS Diagnostica-Berlin, Germany) at the central laboratory of our hospital in the same day. During the examination of the blood samples, Sysmex XT 2000-i (Roche Diagnostics GmbH Mannheim, Germany) device was used for WBC analysis.

Statistical analysis

The data were transferred to electronic media and were analyzed on SPSS 15.0 Computer Package Software. Categorical variables were expressed as numbers and percentages, and continuous variables were expressed as means and standard deviations (when necessary, median and minimum-maximum). In the intergroup comparison of the continuous variables, the distributions were controlled and, as the parameters did not show normal distribution, the Mann Whitney U test was used. The p values given in the tables were not corrected for multiple comparisons. In all tests, the statistical significance level was considered to be 0.05.

RESULTS

Among the 27 patients, 5 developed postoperative septic and aseptic complications. (Table 2) *E.coli* and *Proteus mirabilis* proliferated in the urine culture of a patient who developed urinary tract infection. Two patients developed pneumonia postoperatively and were entubated upon decreasing oxygen saturations. One of these patients remained in mechanical ventilation at intensive care unit for 10 days. The patient recovered with appropriate antibiotic treatment and was taken to ordinary follow-up. The other patient was exitus due to diffuse brain edema and pneumonia. One patient developed sacral and gluteal decubitus ulceritis due to extended period of bed rest. Decubitus ulceritis were treated with local dressing and did not develop any infective complication. The body temperature, WBC, CRP and PCT values of the patients are analyzed in various groups below in order to ensure a better comprehension.

No preoperative pathologic increase was observed in the axillary body temperatures of the patients. However, the comparison of preoperative and postoperative body temperatures indicated that body temperatures peaked in the postoperative 1st day and gradually decreased in the following period. The difference between the body temperature values of the preoperative and postoperative 1st days was found to be statistically significant(P<0.001). On the other hand, the comparisons for the other days did not produce any statistically significant difference. (Table 3).

There was an increase observed in the postoperative WBC values. However, the comparison of the preoperative and postoperative WBC values demonstrated that only the WBC values of the postoperative 1st day was significant (p=0,020).(Table 3)

The CRP values of all the patients showed increase after surgery. Despite the different surgical procedures that were applied, postoperative CRP followed a characteristic kinetic. It peaked especially in the postoperative 2nd day and then started to decrease gradually. The measurements 5 days after the operations showed that the CRP values were still 3 times higher than the preoperative ones. (Table 3)

There was no increase in the procalcitonin values of the patients following operations. (Table 3) Only 2 patients with infections showed increased procalcitonin levels.

Table 3. The comparison of preoperative values of variables with postoperative following days

		Preop	**Postop 1st day**	**Postop 3rd day**	**Postop 5th day**	**Postop 7th day**	**P time**
Body temperature (°C)	SD	36.76±36.95	37.42±37.66	36.97±37.25	36.77±36.92	36.6±36.8	p<0,001
	Median (min-max)	36.65 (36-37.7)	37.50 (36.6-38.4)	36.7 (36.4-38.9)	36.8 (36.3-37.6)	36.5 (36.0-37.7)	
	P value	reference	<0.001	0.093	0.901	0.241	
WBC	SD	8150±9838	9821±11736	8886±10462	7859±9134	7896±9831	0,098
	Median (min-max)	8650 (3200-16000)	9750 (4000-22000)	7900 (4300-15300)	7500 (3500-12900)	7200 (12.8-19500)	
	P value	reference	0.020	0.227	0.686	0.784	
CRP	SD	17.78±30.3	43.97±72.7	37.28±53.77	25.87±37.91	29.36±45.21	0,03
	Median (min-max)	5.0 (3-140)	18.0 (3.02-321)	23.6 (3.17-190)	15.4 (3.17-130)	14.0 (3-133)	
	P value	reference	0.003	0.001	0.064	0.148	
PCT	SD	0.05±0.07	0.13±0.23	0.15±0.29	0.38±0.92	0.25±0.46	0,340
	Median (min-max)	0.05 (0.01-0.1)	0.06 (0.01-1.1)	0.08 (0.04-1.55)	0.1 (0.03-5.77)	0.1 (0.03-2.19)	
	P value	reference	0.120	0.167	0.213	0.064	

* C: Celcius, WBC: White Blood Cell, CRP: C-Reactive Protein, PCT: Procalcitonin, min: minimum, max: maximum

DISCUSSION

The most common complications of ventriculostomy (shunt or ventricular drainage) for hydrocephalus treatment are infections (meningitis, surgical wound infection, abscess, subdural empyema), which occur between 1.5% and 38%[8,9]. Factors such as age, diabetes, the presence of systemic diseases, the use of steroids and the ventriculostomy infection history are considered important risk factors. Pediatric patients are more affected by this infection complication. Mortality rate of shunt infections in a large series have been identified as 7.1 % in the literature[10].

Extensive studies have been performed to estimate shunt infection rates. Most of these studies have been obtained through a retrospective review of the records of patients before 1990. One of the greatest of these studies was performed by Reddy et al. and a group of 1015 patients who underwent shunt operation between 1961 and 2010 in a single institution were included in the study[11]. During this time, the infection rate was found to be 10.5, and it was observed that infection rate appeared to have 7.2% frequency when considered per surgical operation. Stone et al. reported 9% infection rate in 64 children to whom shunt was placed in the University of Rochester Medical Center between 1990 and 1996 with 19.9 years mean follow up period[12]. In a study conducted by Pan P. 137 patients included in the study and shunt infection rate was reported as %16.21[13]. Kanangi et al. asserted shunt infection to be 3% in their studies[8]. In the current study, we had only one patient (3,7%), among 27 cases, to have shunt-associated infection within one year follow-up period.

The infections associated with VP shunt and EVD which are accepted to be indispensable instruments in hydrocephalus treatment encourage clinicians to make researches on this matter. WBC, ESR and CRP which are used today for the early diagnosis of infection are not specific to this factor. Furthermore, both surgery and infection type affect these parameters seriously as it was specified by the researchers who previously studied this issue[14-16]. Considering these, we made this research in order to find out whether procalcitonin level in blood highly selective especially against bacterial infections can be availed in the determination of infective complications after ventriculostomy (shunt or ventricular drainage).

In the literature, there are numerous studies to report that PCT has a high diagnostic value for bacterial infections[17-21]. Shimetani et al. published a study which showed CRP, Serum Amiloid A(SAA) protein and PCT levels in serum and CSF in 30 patients with bacterial, viral and mycotic meningitis[22]. They concluded that 10% of the patients with bacterial and viral meningitis had increased CRP levels. They also concluded that SAA level increased in all the patients with bacterial and mycotic meningitis and in 95% of the patients with viral meningitis. Furthermore, PCT levels were found to increase only in serious bacterial infections, and no increase was found to be of great importance as regards to PCT levels in CSF. In a meta-analysis published by Henry et al., the data of 616 patients and 8 studies were analyzed, and it was concluded that PCT was a highly relevant parameter in distinguishing bacterial meningitis from viral meningitis[23] . In the study carried out by Meisner et al., it was found out that PCT was above 1 ng/ml following minor and aseptic surgeries only in less than 8% of the cases[24]. A majority of the patients reached peak values in the postoperative 1st day. In this study, the highest PCT values were observed after intestinal and abdominal surgeries (1,65 ng/ml on average). In the study carried out by Yu et al. to determine the infection developing after craniotomy, it was concluded that PCT increased seriously in patients with postoperative infections and that PCT was an important indicator for the diagnosis of intracranial infection[25]. Therefore, we planned this study on 27 patients in order to research the effect of infection and surgical trauma on PCT, WBC, Body Temperature and CRP and to question the predictability of an infection that may develop. We concluded that the average PCT level of the 27 cases was 0,05 (0,01-0,1) ng/ml. This result was below the normal values (below 0,1). We determined that the inflammatory reaction due to surgery did not cause a substantial increase in PCT values.

The studies carried out on the postoperative course of CRP observed that it increased secondary to surgery. The study of Santonocito et al. established that CRP increased distinctly in blood during the first 4 days in patients who had major surgery and that it may indicate infection only if it takes course above 100 g/ml[15].

Similarly, Scherer et al. specified that peak CRP values were reached in the postoperative 2nd day

and that peak CRP values were affected by the area of trauma[26]. In another study, CRP levels were seen to be very high during postoperative period in patients who had anteromedial temporal lobe resection due to epilepsy surgery but no infection was found in these patients[27]. The preoperative value of our cases was 5,0 (3-140) mg/L on average (Table 3). Such result confirms to other studies that were performed previously. In the light of our results and the previous literature, it is possible to say that trauma due to surgery affects CRP very seriously rather than PCT and that the values can reach up to 10-20 times higher than the normal values regardless of infection.

The other parameters discussed here were WBC and body temperature. The mean preoperative value of WBC of our patients was 8000 (3200-17500). It reached to the highest value in the postoperative 2nd day and, after that, started to decrease. As regards to body temperature, mean preoperative value was 36,4°C. It was affected by the inflammatory response following surgery and started to decrease after the high values in the 1st day.

In this study, 5 cases (18,7%) developed postoperative infection complication. The complications that developed were observed as urinary tract infection in 2 patients (7,4%), pneumonia in 1 patient (3,7%), pneumonia with decubitus ulcer in 1 patient (3,7%) and surgical wound site infection (meningitis) in 1 patient (3,7%). The PCT value of the patient with meningitis increased 200 times (22 ng/ml) in the 1st day and was above much higher than the normal values. On the other hand, CRP had a normal increase and started to decrease after peaking in the 2nd day. However, it made a second peak in the 6th day. Similarly, WBC peaked in the 2nd and 6th days like CRP. Body temperature was found to be high in the 5th and 6th days. Antibiotics regime was initiated in the postoperative 1st day due to high levels of PCT. The PCT level of a patient with urinary tract infection increased in the postoperative 1st day while CRP and WBC values followed a standard course but peaked in the 2nd day. Body temperature was 38°C during the postoperative first 3 days. The clinical table in this patient was managed by providing antibiotics and had favourable response to treatment.

This study conforms to the results of the literature. We found that the PCT values of the cases with systemic complication were above 0,1 ng/ml. According to the results of this study, we inferred that the patients with PCT values above 0,1 ng/ml in the postoperative 1st and 2nd days required more meticulous monitoring for postoperative complications. Besides, we found that the CRP values of a majority of the patients who developed complication were similar to those who did not develop any complication. Also, WBC, another parameter in this study, did not took a standard course like PCT and CRP after the operations but had levels above the normal limit especially in patients who developed complications.

In consideration of the foregoing, it should be said that PCT surpasses WBC in terms of determining complications in advance. We can assert that the disadvantage of WBC is that it follows a standard kinetic subsequent to operation. This makes WBC an unreliable parameter to anticipate the infective complications which may develop after operations.

There are some limitations in our study. One of them is this study was carried out on cranial surgery with a limited group and number of patients. The other limiting issues of the study were the 2 different neurosurgical and anesthesiological intervention applied on patients. This study could be carried out by subdividing into 2 different groups however we assume that with this limited population it would not be appropriate statistically.

The results acquired in this study conform to previous studies, and quite low infection rates were obtained. The current research is an important study in terms of revealing the curve of PCT, a reliable infection parameter, after surgical operations in patients that develop infection following ventriculostomy (patients to whom shunt or ventricular drainage is placed) and in patients that do not and in terms of evaluating the superiority of PCT to other parameters that are routinely used. Upon further comprehensive studies, we believe that PCT will be an important and reliable parameter for monitoring systemic complications that occur after cranial surgeries.

Currently, there is no routinely availed infection parameter specific to bacterial infections which is not influenced by the inflammatory reactions due to surgery. Considering that postoperative infections lead to serious consequences in neurosurgery practice, PCT seems to be a reliable lab indicator which can be used in the early diagnosis and treatment of infections.

Yazar Katkıları: Çalışma konsepti/Tasarımı: Fİ; Veri toplama: VA, AİÖ; Veri analizi ve yorumlama: AİÖ, SKO; Yazı taslağı: SKO, AA; İçeriğin eleştirel incelenmesi: VA, Fİ; Son onay ve sorumluluk: AA, SKO, VA, Fİ, AİÖ; Teknik ve malzeme desteği: AA; Süpervizyon: Fİ; Fon sağlama (mevcut ise): yok.
Bilgilendirilmiş Onam: Katılımcılardan yazılı onam alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : Fİ; Data acquisition: VA, AİÖ; Data analysis and interpretation: AİÖ, SKO; Drafting manuscript: SKO, AA; Critical revision of manuscript: VA, Fİ; Final approval and accountability: AA, SKO, VA, Fİ, AİÖ; Technical or material support: AA; Supervision: Fİ; Securing funding (if available): n/a.
Informed Consent: Written consent was obtained from the participants.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. Balk RA. Systemic inflammatory response syndrome (SIRS). Virulence. 2014;5:20–6.
2. Miglietta F, Faneschi ML, Lobreglio G, Palumbo C, Rizzo A, Cucurachi M et al. Procalcitonin, C-reactive protein and serum lactate dehydrogenase in the diagnosis of bacterial sepsis, SIRS and systemic candidiasis. Infez Med. 2015;23:230–7.
3. Kip MMA, Kusters R, IJzerman MJ, Steuten LMG. A PCT algorithm for discontinuation of antibiotic therapy is a cost-effective way to reduce antibiotic exposure in adult intensive care patients with sepsis. J Med Econ. 2015;18:944–53.
4. Pontrelli G, De Crescenzo F, Buzzetti R, Jenkner A, Balduzzi S, Calò Carducci F et al. Accuracy of serum procalcitonin for the diagnosis of sepsis in neonates and children with systemic inflammatory syndrome: a meta-analysis. BMC Infect Dis. 2017;17:302.
5. Lim J, King N, Low S, Ng W. Serum procalcitonin is a marker for prediction of readmission from an intermediate care to an acute care hospital in neurosurgical patients. Surg Neurol Int. 2015;6:144.
6. Wang XY, Zhang J, Liu L, Ji Z, Chen C, Yang JY et al. The significance of clinical indicators of different Gram-stained bacteria resulted in secondary intracranial infection after craniocerebral operation. Zhonghua Yi Xue Za Zhi. 2018;98:1588–92.
7. Zhu L, Dong L, Li Y, Lu G, Zhang H, Wang X, et al. The diagnostic and antibiotic reference values of procalcitonin for intracranial infection after craniotomy. World Neurosurg. 2019; 126:e1-e7.
8. Kanangi SMR, Balasubramaniam C. Shunt infections: a review and analysis of a personal series. Childs Nerv Syst. 2018;34:1915–24.
9. Caldarelli M, Di Rocco C, La Marca F. Shunt complications in the first postoperative year in children with meningomyelocele. Childs Nerv Syst. 1996;12:748–54.
10. Gathura E, Poenaru D, Bransford R, Albright AL. Outcomes of ventriculoperitoneal shunt insertion in Sub-Saharan Africa. J Neurosurg Pediatr. 2010;6:329–35.
11. Reddy GK, Bollam P, Caldito G. Ventriculoperitoneal shunt surgery and the risk of shunt infection in patients with hydrocephalus: long-term single institution experience. World Neurosurg. 2012;78:155-63.
12. Stone JJ, Walker CT, Jacobson M, Phillips V, Silberstein HJ. Revision rate of pediatric ventriculoperitoneal shunts after 15 years. J Neurosurg Pediatr. 2013;11:15–9.
13. Pan P. Outcome analysis of ventriculoperitoneal shunt surgery in pediatric hydrocephalus. J Pediatr Neurosci. 2019;13:176–81.
14. Bengzon J, Grubb A, Bune A, Hellstrom K, Lindstrom V, Brandt L. C-reactive protein levels following standard neurosurgical procedures. Acta Neurochir (Wien). 2003;145:667–71.
15. Santonocito C, De Loecker I, Donadello K, Moussa MD, Markowicz S, Gullo A et al. C-reactive protein kinetics after major surgery. Anesth Analg. 2014;119:624–9.
16. Jaye DL, Waites KB. Clinical applications of C-reactive protein in pediatrics. Pediatr Infect Dis J. 1997;16:735-46.
17. Omar AS, ElShawarby A, Singh R. Early monitoring of ventriculostomy-related infections with procalcitonin in patients with ventricular drains. J Clin Monit Comput. 2015;29:759–65.
18. Wei TT, Hu ZD, Qin BD, Ma N, Tang QQ, Wang LL et al. Diagnostic accuracy of procalcitonin in bacterial meningitis versus nonbacterial meningitis. Medicine (Baltimore). 2016;95:e3079.
19. Park BS, Kim SE, Park SH, Kim J, Shin KJ, Ha SY et al. Procalcitonin as a potential predicting factor for prognosis in bacterial meningitis. J Clin Neurosci. 2017;36:129–33.
20. Mandell IM, Aghamohammadi S, Deakers T, Khemani RG. Procalcitonin to detect suspected bacterial infections in the PICU. Pediatr Crit Care Med. 2016;17:e4–12.
21. Memar MY, Varshochi M, Shokouhi B, Asgharzadeh M, Kafil HS. Procalcitonin: the marker of pediatric bacterial infection. Biomed Pharmacother. 2017;96:936–43.
22. Shimetani N, Shimetani K, Mori M. Levels of three inflammation markers, C-reactive protein, serum amyloid A protein and procalcitonin, in the serum and cerebrospinal fluid of patients with meningitis. Scand J Clin Lab Invest. 2001;61:567–74.
23. Henry BM, Roy J, Ramakrishnan PK, Vikse J, Tomaszewski KA, Walocha JA. Procalcitonin as a serum biomarker for differentiation of bacterial meningitis from viral meningitis in children. Clin Pediatr (Phila). 2016;55:749–64.
24. Meisner M, Tschaikowsky K, Hutzler A, Schick C, Schüttler J. Postoperative plasma concentrations of

procalcitonin after different types of surgery. Intensive Care Med. 1998;24:680–4.
25. Yu Y, Li HJ. Diagnostic and prognostic value of procalcitonin for early intracranial infection after craniotomy. Braz J Med Biol Res. 2017;50:e6021.
26. Scherer MA, Neumaier M, von Gumppenberg S. C-reactive protein in patients who had operative fracture treatment. Clin Orthop Relat Res. 2001;393:287–93.
27. Woernle CM, Neidert MC, Wulf M-A, Burkhardt J-K, Grunwald T, Bernays RL. Excessively elevated C-reactive protein after surgery for temporal lobe epilepsy. Clin Neurol Neurosurg. 2013;115:1245–9.