

Evaluation of inflammatory markers after orthopedic surgical intervention in children



Ann. Ital. Chir., 2013 84: 117-121
pii: S0003469X13018769

Radivoj Brdar^{*/**}, Bojan Bukva^{*}, Dejan Nikolic^{***}, Ivana Petronic^{**/**}, Zoran Golubovic^{*/**}, Dusan Abramovic^{*}, Marko Vidosavljevic^{*}, Sinisa Ducic^{*/**}, Vladimir Radlovic^{*}, Dragana Cirovic^{**/**}

^{*}Pediatric Surgery Department, University Childrens Hospital, Belgrade, Serbia

^{**}Faculty of Medicine, University of Belgrade, Belgrade, Serbia

^{***}Physical Medicine and Rehabilitation Department, University Childrens Hospital, Belgrade, Serbia

Evaluation of inflammatory markers after orthopedic surgical interbention in children

OBJECTIVE: *The study aim was to evaluate inflammation markers values (C-reactive protein (CRP), Erythrocyte sedimentation (ES), White blood cells count (WBC)) in surgically treated pediatric patients with diagnosed developmental displasia of the hip or Perthes disease before and after operation.*

METHODS: *We have evaluated 43 children (20 patients were with diagnosed unilateral developmental displasia of the hip while 23 had Perthes disease). Blood samples were drawn at the admission and 5 days after admission, and further inflammatory parameters were analyzed: ES (mm/hour), CRP (mg/L) and WBC ($\times 1000/\text{mm}^3$) count.*

RESULTS: *Elevated erythrocyte sedimentation (ESR) was significantly frequent than elevated CRP ($p < 0.01$) and elevated WBC as well ($p < 0.01$). Values of ESR and WBC do not correlate closely with age ($F_{\text{ESR}} = 1.805$; $F_{\text{WBC}} = 0.130$; $p > 0.05$) while CRP values correlate significantly with the age of the patients ($F_{\text{CRP}} = 4.948$; $p < 0.05$). The most frequently isolated marker was ESR (34.88%). The most frequent elevated two markers were ESR and CRP (44.19%).*

CONCLUSION: *Surgical procedure could alter the values of inflammatory markers leading to the increasement even though there is no other clinical signs of infection. For estimation of the possible presence of the infection, clinical signs and patients intensive clinical follow-up after the surgery, should be done along with the evaluation of inflammatory markers.*

KEY WORDS: Children, Inflammatory markers, Surgery.

Introduction

Elevated body temperature could be the sing of infection in the postoperative period, and every infection might significantly impact the course and outcome in surgically treated patients ¹. Surgical intervention is con-

nected with tissue damage that could lead to the syndrome of inflammatory reaction without infection as well to alter the elevation of standard laboratory inflammatory markers: C-reactive protein, erythrocyte sedimentation and leukocyte count ¹⁻³. Evaluation of inflammatory markers is of benefit especially for these orthopaedic patients if treated surgically, since wound infections beside serious complications for the patient itself, increase the cost of therapy as well ⁴. Orthopedic surgery in pediatric population is mainly clean and extensive with great tissue damage ^{5,6}. Currently there are several different techniques for the correction of developmental displasia of the hip (DDH) or Perthes disease in children population, from less invasive to severe invasive ⁷⁻¹⁰. Since

Pervenuto in Redazione Gennaio 2012. Accettato per la pubblicazione Aprile 2012

Correspondence to: Bojan Bukva, MD, Pediatric Surgery Department, University Children's Hospital, Tirsova 10, 11000 Belgrade, Serbia (E-mail: denikol27@yahoo.com)

the trauma of the tissue is not equal, evaluation of inflammation markers could be of great benefit for the monitoring of tissue reaction to the surgery and possible onset of the infection.

Aim of our study was to evaluate inflammation markers values (C-reactive protein, erythrocyte sedimentation and leukocyte count) in surgically treated pediatric patients with diagnosed DDH or Perthes disease before and after operation.

Material and Methods

STUDY GROUP

In our study we have included and evaluated 43 children over 3 years period from 2008-2010 years. From observed population 20 patients were with diagnosed unilateral DDH while 23 had Perthes disease. Patients with DDH and Perthes disease were completely assessed clinically by a pediatric surgeon, physiatrist and radiologist with appropriate diagnostic evaluation in order to confirm the diagnosis. Informed consent from parents or legal guardians was obtained before inclusion in the study. Ultrasonography was performed in young patients since it is the method of choice because of femoral head anatomical determinants and acetabulum accurate visualization. Plane radiography was done in the group of older children, even though it is suggested that ultrasonography can be an alternative imaging method ¹¹. We performed Salter's innominate osteotomy as surgical technique in 40 hips and Chiari innominate osteotomy in 3 hips. We performed Chiari osteotomy in older children with severe dysplasia and/or poor joint congruency ^{12,13}, particularly above 10 years of age due to the high rate of graft resorption ¹⁴. It is proposed that when there is incongruity between the femoral head and acetabulum after adolescence, Chiari osteotomy might improve femoral head coverage and decrease the shear stress ¹⁴. Patients were divided into 3 groups regarding age: first group included those at age between 2-7 years, second group between 8-13 years and third group between 14-18 years of life.

STUDY MATERIAL

Before inclusion in the study, all patients were evaluated for the presence of inflammation. Blood samples were drawn at the admission and further inflammatory parameters were analyzed: erythrocyte sedimentation rate (mm/hour), C reactive protein (CRP) (mg/L) and white blood cells (WBC) ($\times 1000/\text{mm}^3$) count. From the study we have excluded those with confirmed presence of inflammation. Values exceeding 20 mm/hours for sedimentation rate (elevated sedimentation rate (ESR)), 20 mg/L for CRP and $15 \times 1000/\text{mm}^3$ for WBC were considered elevated for observed parameter ¹⁵. In order to evaluate correlation of sedimentation rate, CRP and WBC values before and after surgery, blood samples were

drawn before surgery and 5 days after the surgery. To exclude the possibility of infection, all patients were given the prophylaxis with antibiotics (second generation Cephalosporin's) during the surgery and 3 days after the surgical procedure.

Statistical Analysis

Evaluated parameters were presented as whole numbers, percents and median values (MV) with standard error of mean (SEM) and as range intervals. Chi squared test (χ^2) was used to evaluate presence of significance between proportions of observed elevated inflammation markers after the surgery. Students t test was used to evaluate correlation between ESR, CRP and WBC values before surgery and after the surgery. Unifactorial ANOVA was used to evaluate ESR, CRP and WBC values in different age groups. Statistical significance was set on $p < 0.05$.

Results

We have evaluated 43 children with DDH and Perthes disease that were referred to University Childrens Hospital for diagnosis and treatment. In table I, patients characteristics were presented. Elevated ESR was noticed to be significantly frequent than elevated CRP ($\chi^2_{\text{ESR/CRP}} = 13.03$; $p < 0.01$) and elevated WBC as well ($\chi^2_{\text{ESR/WBC}} = 286.51$; $p < 0.01$).

In table II, mean values of non specific inflammatory markers before and after surgical correction of DDH or Perthes disease were presented. It is noticed that for all evaluated markers (ESR, CRP and WBC) there was significant ($p < 0.01$) increase in values. Mean values for ESR and CRP after surgery were higher than referential values for the define child age ¹, while mean values for

TABLE I - Patients characteristics (N=43)

Parameter	Values	Range
Age (years)	6.84 $\pm$ 0.61	2 - 18 (years)
Elevated ESR after surgery (N%)	88.37%	28 - 110 (mm/hour)
Elevated CRP after surgery (N%)	58.14%	21 - 99 (mg/L)
Elevated WBC after surgery (N%)	11.63%	15.4 - 31.2 ($\times 1000/\text{mm}^3$)

TABLE II - Mean values of inflammation markers

N=43	Before surgery MV $\pm$ SEM	After surgery MV $\pm$ SEM	t values
ESR (mm/hour)	8.84 $\pm$ 0.71	48.40 $\pm$ 3.39	11.42*
CRP (mg/L)	1.50 $\pm$ 0.28	30.00 $\pm$ 3.70	7.68*
WBC ($\times 1000/\text{mm}^3$)	7.44 $\pm$ 0.29	11.24 $\pm$ 0.76	4.67*

* $p < 0.01$

TABLE III - Mean values of inflammation markers after surgery due to age

Parameters after surgery		MV±SEM	ANOVA
ESR (mm/hour)	Age (2-7 years) (N=26)	53.50±4.65	F=1.805; p=0.178
	Age (8-13 years) (N=12)	40.83±5.52	
	Age (14-18 years) (N=5)	40.00±6.89	
CRP (mg/L)	Age (2-7 years) (N=26)	24.62±3.43	F=4.948; p=0.012*
	Age (8-13 years) (N=12)	46.83±9.24	
	Age (14-18 years) (N=5)	17.60±6.90	
WBC (x1000/mm ³)	Age (2-7 years) (N=26)	11.27±1.18	F=0.130; p=0.878
	Age (8-13 years) (N=12)	11.59±0.97	
	Age (14-18 years) (N=5)	10.22±0.51	

*p<0.05

TABLE IV - Proportion of elevated inflammatory markers after surgery (N=43)

Parameters N (%)	Proportion
None	2 (4.65)
ESR	15 (34.88)
CRP	2 (4.65)
WBC	0 (0)
ESR and CRP	19 (44.19)
ESR and WBC	0 (0)
CRP and WBC	1 (2.33)
ESR and CRP and WBC	4 (9.30)

WBC after surgery remained in referential values for the define child age.

In table III, mean values of inflammation markers after the correction of DDH or Perthes disease were analyzed due to age of the patients. ESR and WBC values does not correlate closely with age ($p>0.05$) while CRP values correlate significantly with the age of the patients ($p<0.05$). In table IV, proportions of elevated inflammatory markers after the surgery were analyzed. The most frequently present isolated marker was ESR (34.88%), while there were no patients with elevated WBC only. For those with elevated two evaluated markers, the most frequent was presence of ESR with CRP (44.19%). The presence of elevated all 3 markers is expected in every tenth patient (9.30%) who undergo DDH or Perthes disease correction.

Discussion

It is still not known what is the exact role of CRP in physiological processes as well in pathological conditions¹⁶. Such

statement is mainly due to insufficient knowledge of the structural polymorphism of human CRP and modes that could be implemented for the inhibition or depletion of human CRP in vivo¹⁶. There are studies addressing that CRP is classical marker of inflammation but it cannot with confidence distinct bacterial from other type of infection¹⁷.

In our study we have demonstrated that 9 out of 10 patients that undergo surgical correction had elevated values of ESR, implicating significantly higher proportion of patients with elevated ESR in postoperative period ($p<0.01$). There is as well significantly higher proportion of patients that will present with elevated CRP post-surgery ($p<0.05$). Contrary to these findings, elevation of WBC was seen in 1 out of 10 patients, stressing out significantly higher proportion of those with WBC within physiological range in postoperative period ($p<0.01$). Patients with increased WBC undergone more extensive surgical procedure than the one without elevation in WBC count. Possible elevation in WBC is particularly seen after hip surgery, and is proposed as normal physiological response in the absence of clinical signs and symptoms¹⁸. It is proposed as well that following long bone surgery, increase in WBC could be the result of systemic response¹⁹. Further, our results point out that in the period after surgical correction of DDH and Perthes disease it is expected for ESR to be elevated in majority of patients. Elevation of CRP values is also expected, while elevation in WBC should be considered as marker of the possible systemic response in these patients in absence of the infection. Therefore, significantly increased frequency of elevated ESR and CRP after orthopedic surgery in patients without infection, could bring to the assumption that they are more non specific inflammatory markers than WBC in pediatric population that undergo orthopedic surgery.

We have demonstrated that in different age groups only CRP values are significantly changing after the surgery, pointing out that this inflammatory parameter is age dependent with significant increase in the age group between 8 and 13 years. For the ESR, even though there is no significant difference in values between different age groups, it is noticed that as children are older there is constant decrease in ESR values in the post-surgery period. Therefore it can be assumed that age of patients particularly in pediatric population could influence to the certain degree on the extent of possible elevation of ESR and CRP after orthopedic surgical intervention. The possible explanation could be justified in different systemic responses that are associated with the age especially in the period of growth and development.

The most frequent inflammatory markers that were elevated were ESR alone or ESR and CRP both, composing more than 3/4 (79.07%) of the entire study group. This can lead to the assumption that both ESR and CRP are non specific inflammatory markers and are expected to be elevated in post-surgical period. Since, significant proportion of patients with elevated WBC (80.00%) were with elevated ESR and CRP as well, it is expected that elevation in WBC is not isolated, but with elevation of ESR and CRP. Since, patients with elevated WBC that undergone surgical correction had more extensive procedure, co-joined elevation of ESR and CRP could be as well reaction to extensive tissue damage.

If there is possibility of infection it is recommended as mandatory to analyze evaluated inflammatory markers. Further, if the infection is confirmed these markers (ESR, CRP and WBC) should be routinely drowned for follow-up and their values can be predictors or indicators of the treatment success after surgical intervention. The values of these markers therefore could be used for the treatment duration plan as well.

In the conclusion, ESR, CRP and WBC present standard inflammatory indicators for the estimation of infection presence. Surgical procedure alone could alter the values of these inflammatory markers leading to the increasement even though there is no other clinical signs of infection. Therefore, for the estimation of the possible presence of the infection, clinical signs as well as patients intensive clinical follow-up after the surgery, should be done along with the evaluation of these inflammatory markers.

Riassunto

Lo scopo dello studio è quello di valutare i livelli dei markers di infezione (PCR, VED e conta dei GB - globuli bianchi) nei bambini operati di displasia congenita dell'anca o per malattia di Perthes prima e dopo l'intervento.

Abbiamo studiato 43 bambini (in 20 era stata diagnosticata la displasia congenita monolaterale dell'anca, e in 23 la malattia di Perthes). Campioni di sangue sono stati prelevati al ricovero e cinque giorni dopo l'intervento chirurgico per analizzare i parametri della flogosi: mm/h della VES, mg/L della PCR e conta dei GB ($\times 1000/\text{mm}^3$).

L'aumento della VES è risultata significativamente più presente di quello della PCR ($p < 0.01$) e della conta dei GB ($p < 0.01$). I valori della VES e dei GB non si correlano strettamente con l'età ($F_{\text{ESR}} = 1.805$; $F_{\text{WBC}} = 0.130$; $p > 0.05$), al contrario di quelli della PCR ($F_{\text{CRP}} = 4.948$; $p < 0.05$).

Il marker più frequentemente rilevato è stata la VES (34.88%). I marker più frequentemente aumentati sono stati la VES e la PCR (44.19%).

Si può concludere che la procedura chirurgica potrebbe alterare il valore dei markers dell'infiammazione nel senso dell'aumento anche se risultano assenti altri segni di infezione. Per confermare la possibile presenza di una infezione oltre ai valori dei markers dell'infezione bisogna seguire clinicamente in modo intensivo i pazienti nel postoperatorio.

References

1. Laffely JG, Boylan JF, Cheng DC: *The systemic inflammatory response to cardiac surgery: implications for the anesthesiologist*. Anesthesiology, 2002; 97(1):215-52.
2. Than P, Malovics I: *Significance of postoperative fever after hip prosthesis implantation*. Z Orthop Ihre Grenzgeb, 2000; 138(5):430-35.
3. Gaynes RP, Culver DH, Horn TC, Edwards JR, Richards C, Toison JS: *Surgical site infection (SSI) rates in the United States, 1992-1998: the National Nosocomial Infections Surveillance System basic SSI risk index*. Clin Infect Dis, 2001; 33(Suppl 2):S69-77.
4. Kokavec M, Fristáková M: *Efficacy of antiseptics in the prevention of post-operative infections of the proximal femur, hip and pelvis regions in orthopedic pediatric patients. Analysis of the first results*. Acta Chir Orthop Traumatol Cech, 2008; 75(2):106-9.
5. Bilgen O, Atici T, Durak K, Karacaminogullari, Bilgen MS: *C-reactive protein values and erythrocyte sedimentation rates after total hip and total knee arthroplasty*. J Int Med Res, 2001; 29(1):7-12.
6. Greidanus NV, Masari BA, Garbuz DS, et al.: *Use of erythrocyte sedimentation rate and C-reactive protein level to diagnose infection before revision total knee arthroplasty. A prospective evaluation*. J Bone Joint Surg Am, 2007; 89(7):1409-16.
7. Brdar R, Petronic I, Abramovic D, Nikolic D, Lukac M, Cirovic D: *Double innominate osteotomy and the Smith-Petersen technique in the treatment of developmental hip disorder*. Acta Chir Belg, 2011; 111(1):18-22.
8. Firth GB, Robertson AJ, Schepers A, Fatti L: *Developmental dysplasia of the hip: Open reduction as a risk factor for substantial osteonecrosis*. Clin Orthop Relat Res, 2010; 468(9):2485-94.
9. Kim JR, Shin SJ: *Severe Perthes' disease or late avascular necro-*

sis after successful closed reduction of developmental dysplasia of the hip. *J Pediatr Orthop B*, 2010; 19(2):155-57.

10. Milasinovic S, Brdar R, Petronic I, Nikolic D, Cirovic D: *Developmental dysplasia of the hip: angels trends after operation in different age groups*. *Arch Med Sci*, 2010; 6(5):800-805.

11. Ozçelik A, Akçar N, Inan U, Omeroğlu H: *Assessment of the use of hip ultrasonography by Graf's method between 1 and 6 years of age*. *J Pediatr Orthop B*, 2005; 14(2):97-100.

12. Ito H, Tanino H, Yamanaka Y, Nakamura T, Minami A, Matsuno T: *The Chiari pelvic osteotomy for patients with dysplastic hips and poor joint congruency: long-term follow-up*. *J Bone Joint Surg Br*, 2011; 93(6):726-31.

13. Kotz R, Chiari C, Hofstaetter JG, Lunzer A, Peloschek P: *Long-term experience with Chiari's osteotomy*. *Clin Orthop relat Res*, 2009; 467(9):2215-20.

14. Karami M, Fitoussi F, Ilharreborde B, Pennecot GF, Mazda K, Bensahel H: *The results of Chiari pelvic osteotomy in adolescents with a brief literature review*. *J Clin Orthop*, 2008; 2(1):63-8.

15. Pääkkönen M, Kallio MJ, Kallio PE, Peltola H: *Sensitivity of erythrocyte sedimentation rate and C-reactive protein in childhood bone and joint infections*. *Clin Orthop Relat Res*, 2010; 468(3):861-66.

16. Casas JP, Shah T, Hingorani AD, Danesh J, Pepys MB: *C-reactive protein and coronary heart disease: a critical review*. *J Intern Med*, 2008; 264(4):295-314.

17. Baruti Gafurri Z, Pacarizi H, Zhubi B, Begolli L, Topciu V: *The importance of determining procalcitonin and C reactive protein in different stages of sepsis*. *Bosn J Basic Med Sci*, 2010; 10(1):60-4.

18. Deirmengian GK, Zmistowski B, Jacovides C, O'Neil J, Parvizi J: *Leukocytosis is common after total hip and knee arthroplasty*. *Clin Orthop Relat Res*, 2011; 469(11):3031-36.

19. Hughes SF, Hendricks BD, Edwards DR, Maclean KM, Bastawrous SS, Middleton JF: *Total hip and knee replacement surgery results in changes in leukocyte and endothelial markers*. *J Inflamm (Lond)*, 2010; 7:2.

