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Clinical Article

Sequential Changes of Plasma C-Reactive Protein, Erythrocyte Sedimentation Rate and White Blood Cell Count in Spine Surgery : Comparison between Lumbar Open Discectomy and Posterior Lumbar Interbody Fusion

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Objective : C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are often utilized to evaluate for postoperative infection. Abnormal values may be detected after surgery even in case of non-infection because of muscle injury, transfusion, which disturbed prompt perioperative management. The purpose of this study was to evaluate and compare the perioperative CRP, ESR, and white blood cell (WBC) counts after spine surgery, which was proved to be non-infection.

Methods : Twenty patients of lumbar open discectomy (LOD) and 20 patients of posterior lumbar interbody fusion (PLIF) were enrolled in this study. Preoperative and postoperative prophylactic antibiotics were administered routinely for 7 days. Blood samples were obtained one day before surgery and postoperative day (POD) 1, POD3, and POD7. Using repeated measures ANOVA, changes in effect measures over time and between groups over time were assessed. All data analysis was conducted using SAS v.9.1.

Results : Changes in CRP, within treatment groups over time and between treatment groups over time were both statistically significant $F(3,120)=5.05$, $p=0.003$ and $F(1,39)=7.46$, $p=0.01$, respectively. Most dramatic changes were decreases in the LOD group on POD3 and POD7. Changes in ESR, within treatment groups over time and between treatment groups over time were also found to be statistically significant, $F(3,120)=6.67$, $p=0.0003$ and $F(1,39)=3.99$, $p=0.01$, respectively. Changes in WBC values also were be statistically significant within groups over time, $F(3,120)=40.52$, $p<0.001$, however, no significant difference was found in between groups WBC levels over time, $F(1,39)=0.02$, $p=0.89$.

Conclusion : We found that, dramatic decrease of CRP was detected on POD3 and POD7 in LOD group of non-infection and dramatic increase of ESR on POD3 and POD7 in PLIF group of non-infection. We also assumed that CRP would be more effective and sensitive parameter especially in LOD than PLIF for early detection of infectious complications. Awareness of the typical pattern of CRP, ESR, and WBC may help to evaluate the early postoperative course.

Key Words : Open discectomy · Posterior lumbar interbody fusion · Postoperative infection · C-reactive protein · Erythrocyte sedimentation rate · White blood cell.

INTRODUCTION

The reported incidence of acute postoperative spinal infections ranges from less than 1% to 13%. The type and length of the procedure influences the infection rate. Infection rate of lumbar open discectomies without fusion is known to be 1−2%, microdiscectomy 5%, instrumented posterior lumbar fusions 2−6%, respectively[5,13].

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) have been used to diagnose postoperative infections after spinal surgery. Several studies have reported the usefulness of CRP, ESR, and WBC as a predictor of infection after spine surgery. However, it is difficult to detect infection before day 7 because incubation period where the immune system is activated

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to protect a living body from invading bacteria. The CRP is a too sensitive marker to distinguish the case of early infection from postoperative inflammation.

The purpose of this study was to assess the normal range and pattern of the change in plasma CRP, ESR, and WBC according to operative method and extents of spinal surgery.

MATERIALS AND METHODS

Forty patients in two groups were prospectively enrolled from March of 2006 to June of 2006. Group A included 20 patients who had single level lumbar open discectomy (LOD) and group B consisted of 20 patients who had posterior lumbar interbody fusion (PLIF) with stand-alone cage after decompression. All patients were operated by the same surgeon and all did not have postoperative infection. They did not have any constitutional symptoms of infection with normal surgical wound healing and normal CRP three months after surgery.

Inclusion criteria included those 18 years-old older with surgical indication for elective surgery, either single level discectomy or PLIF and hospital length of stay of 7 days or more after the surgery. We excluded the patients who had previous spinal surgery, transfusion during the surgery, anemia, history of immunodeficiency, autoimmune disease such as rheumatoid arthritis, and any history of infection within 6 months of the surgery.

All patients had blood draws for CRP, ESR, and WBC count 1 day before surgery and postoperative day (POD) 1, POD3, and POD7. The CRP level in serum was determined with the latex agglutination methods. The normal CRP value in the authors' hospital was less than 0.3 mg/dL. ESR is a manual test in which the level of blood collected in a Western sedimentation rate tube is read by a technologist after a specific time period. Normal ESR range is less than 20 mg/dL. The WBC counts were obtained with an automatic cell counter. Preoperative and postoperative prophylactic antibiotics were administered intravenously for 7 days.

Statistical analysis was performed with using repeated measures ANOVA, and changes in effect measures over time and between groups over time were assessed. All data analysis was conducted using SAS v.9.1.

RESULTS

Changes of CRP, ESR, and WBC in lumbar open discectomy group (Group A)

The mean CRP value of preoperative was 0.78 mg/dL (0.5−3 mg/dL), which increased to 1.11 mg/dL (0.2−3.8 mg/dL) at POD1. At POD3 and POD7, it decreased to 0.54 mg/dL (0.1−2.0 mg/dL), 0.4 mg/dL (0.1−2.7 mg/dL) respectively. Change rates of CRP value, comparing with preoperative CRP were 42.3% increase at postoperative first day, 30.7% decrease at postoperative 3rd day and 40.8% decrease at postoperative 7th day.

Preoperative mean ESR value was 4.71 mm/hr (2−43 mm/hr), and postoperative mean ESR value of first, third and seventh day were 2.14 mm/hr (2−27 mm/hr), 6.0 mm/hr (2−31 mm/hr), 6.4 mm/hr (2−43 mm/hr) respectively. Change rates of ESR value, comparing with preoperative ESR were 54.6% decrease at postoperative first day, 27.3% increase at postoperative 3rd day and 35.8% increase at postoperative 7th day.

Preoperative mean WBC values was $9.44\times10^3/mm^3$ ($3.65-17.58\times10^3/mm^3$), and postoperative mean WBC value of first, third and seventh day were $14.6\times10^3/mm^3$ ($7.44-26.75\times10^3/mm^3$), $11.0\times10^3/mm^3$ ($5.44-23.10\times10^3/mm^3$), $7.8\times10^3/mm^3$ ($4.33-16.60\times10^3/mm^3$), respectively. Change rates of WBC value, comparing with preoperative WBC were 54% increase at postoperative first day, 16.5% increase at postoperative 3rd day and 17.3% increase at postoperative 7th day.

Changes of CRP, ESR, and WBC in decompression and posterior lumbar interbody fusion with stand-alone cage group (Group B)

The mean CRP value of preoperative was 0.67 mg/dL (0.5−1.6 mg/dL), which increased to 1.55 mg/dL (0.5−5.1 mg/dL), at postoperative first day. At postoperative third and seventh day, it decreased to 1.52 mg/dL (0.1−7.6 mg/dL), 1.03 mg/dL (0.1−4.2 mg/dL), respectively. Change rates of CRP value, comparing with preoperative CRP, were 131.4% increase at postoperative first day, 126.8% increase at postoperative 3rd day and 53.7% increase at postoperative 7th day.

Preoperative mean ESR value was 6.75 mm/hr (2−33 mm/hr), and postoperative mean ESR value of first, third and seventh day were 5.78 mm/hr (2−26 mm/hr), 15.2 mm/hr (2−22 mm/hr), 17.4 mm/hr (2−24 mm/hr), respectively. Change rates of ESR value, comparing with preoperative ESR were 14.3% decrease at postoperative first day, 131.0% increase at postoperative 3rd day and 157.7% increase at postoperative 7th day.

Preoperative mean WBC value was $8.02\times10^3/mm^3$ ($4.86-11.43\times10^3/mm^3$), and postoperative mean WBC value of first, third and seventh day were $14.60\times10^3/mm^3$ ($8.21-20.59\times10^3/mm^3$), $11.70\times10^3/mm^3$ ($7.70-22.90\times10^3/mm^3$), $9.94\times10^3/mm^3$ ($5.39-16.50\times10^3/mm^3$), respectively. Change rates of WBC value, comparing with preoperative WBC were 82.0% increase at postoperative first day, 31.4% increase at postoperative 3rd day and 23.9% increase at postoperative 7th day.

Overall differences CRP, ESR, and WBC between two groups

Fig. 1 shows the changes of mean CRP, ESR, and WBC on preoperative and postoperative 1, 3, and 7 days comparing between two groups according to the postoperative day.

In open discectomy group (Group A), mean CRP was normalized rapidly at postoperative 3rd day. While mean CRP of Group B showed steady decrease and mean CRP did not normalized to preoperative state even in POD 7th day.

Mean ESR level changes in both group A, B showed decrease on the 1st postoperative day, and then clearly elevated above its preoperative levels on the 3rd postoperative day, showing steady increase until 7th postoperative day. However, mean ESR chang-

es in Group B showed steeper inclination than Group A. Mean ESR value at postoperative third day increase more rapidly in Group B than Group A.

Both group A, B of mean WBC count elevated rapidly on 1st postoperative day, and then decreased to normalize after 3rd postoperative day. Mean WBC changes of group A showed faster normalization than that of group B at POD 7th day.

Fig. 2, 3 show the scattered pattern of CRP, ESR, and WBC.

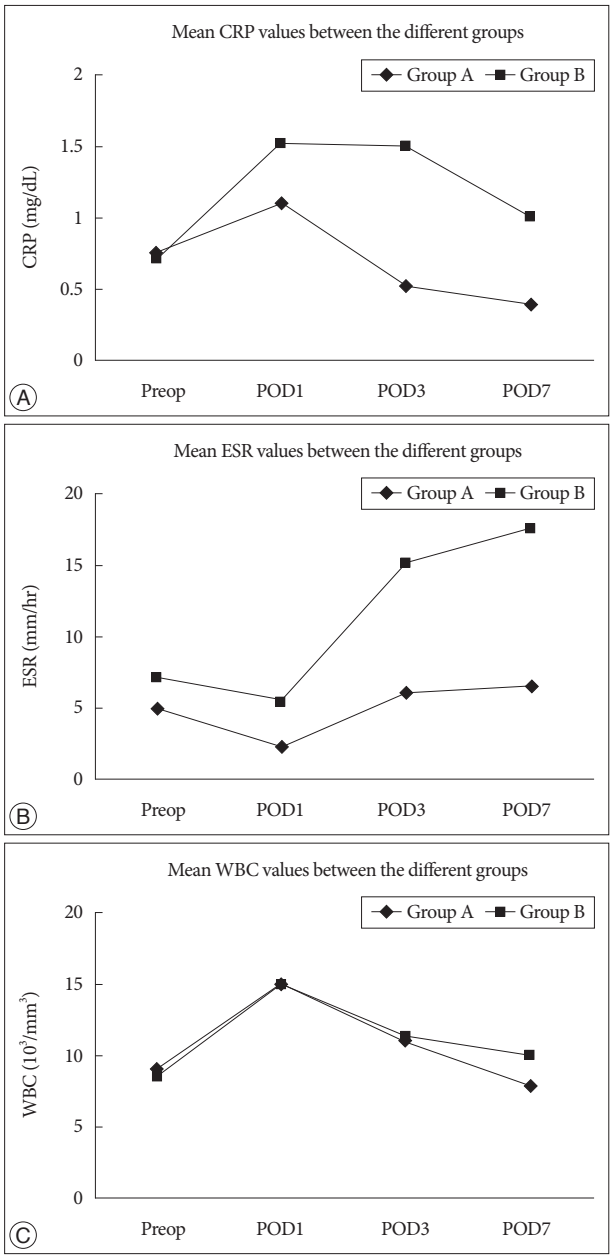

Fig. 1. The changes of mean CRP (A), ESR (B), and WBC (C) on preoperative and postoperative 1, 3, and 7 days comparing between Group A and B according to the postoperative day. Group A : open lumbar discectomy, Group B : posterior lumbar interbody fusion. In group A, mean CRP was normalized rapidly at postoperative 3rd day. While mean CRP of Group B showed steady decrease and mean CRP did not normalized to preoperative state even in POD 7th day (A). Mean ESR level changes in both group A, B showed decrease on the 1st postoperative day, and then clearly elevated above its preoperative levels on the 3rd postoperative day, showing steady increase until 7th postoperative day (B). Both group A, B of mean WBC count elevated rapidly on 1st postoperative day, and then decreased to normalize after 3rd postoperative day (C). CRP : C-reactive protein, ESR : erythrocyte sedimentation rate, WBC : white blood cell, POD : postoperative day.

Statistical analysis

Changes in CRP, within treatment groups over time and between treatment groups over time were both statistically significant $F(3,120)=5.05$, $p=0.003$ and $F(1,39)=7.46$, $p=0.01$, respectively. Most dramatic changes were decreases in the LOD group on POD3 and POD7.

Changes in ESR, within treatment groups over time and between treatment groups over time were also found to be statistically significant, $F(3,120)=6.67$, $p=0.0003$ and $F(1,39)=3.99$, $p=0.01$, respectively. These differences appear to be in part due to

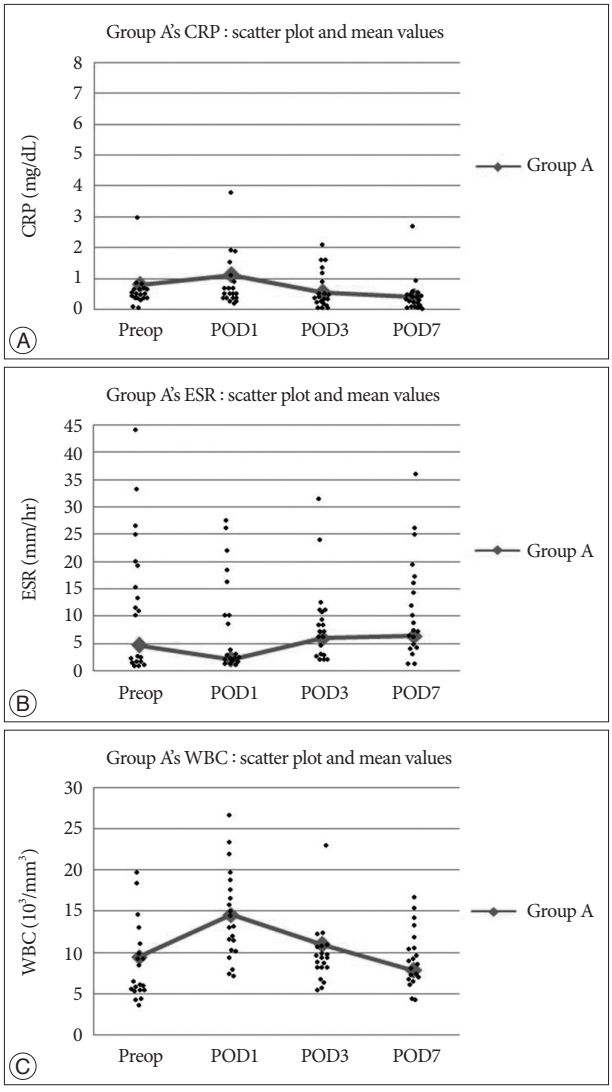

Fig. 2. The scattered pattern of CRP (A), ESR (B), and WBC (C) on preoperative and postoperative 1, 3, and 7 days in Group A according to the postoperative day. Group A : open lumbar discectomy. CRP : C-reactive protein, ESR : erythrocyte sedimentation rate, WBC : white blood cell, POD : postoperative day.

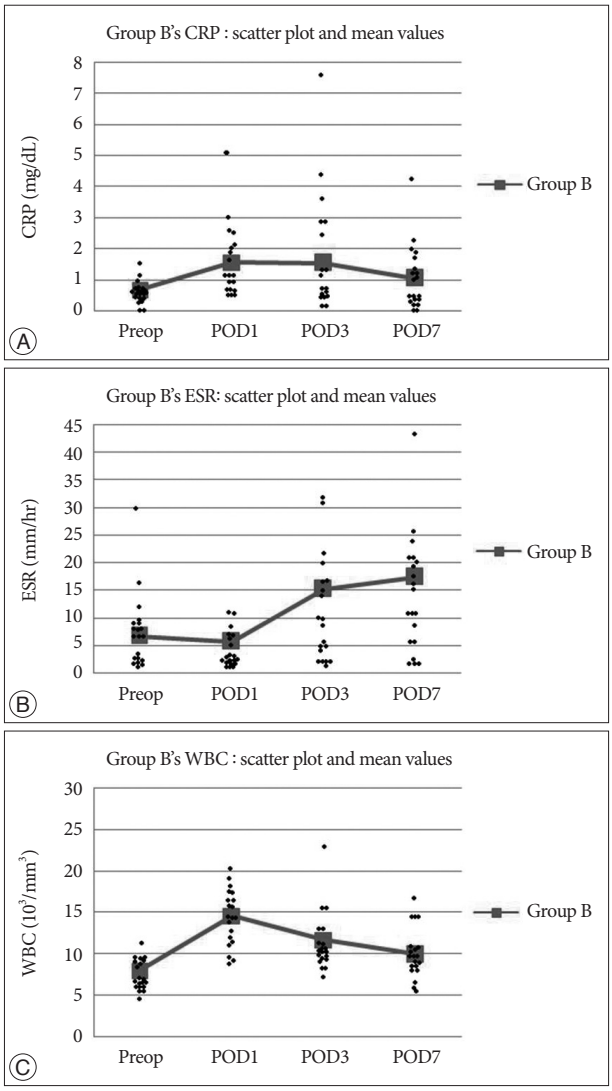

Fig. 3. The scattered pattern of CRP (A), ESR (B), and WBC (C) on preoperative and postoperative 1, 3, and 7 days in Group B according to the postoperative day. Group B : posterior lumbar interbody fusion. CRP : C-reactive protein, ESR : erythrocyte sedimentation rate, WBC : white blood cell, POD : postoperative day.

dramatic increases in ESR in the PLIF group on POD3 and POD7.

Changes in WBC values also were statistically significant within groups over time, $F(3,120)=40.52$, $p<0.001$, however, no significant difference was found in between groups WBC levels over time, $F(1,39)=0.02$, $p=0.89$.

DISCUSSION

CRP, ESR, and WBC have been widely used for estimating the status of infection. Several studies have reported the usefulness of this predictor and mentioned that the combination of normal CRP, ESR, and WBC levels reliably predicts the absence of infection after elective surgery[5,10,12,18].

C-reactive protein was discovered and named for its reactivity to the C polysaccharide in the cell wall of *S. pneumonia*, which is produced by the liver in response to inflammation, infection, malignancy, and tissue damage with relatively high sensitivity, response speed, and range compared to other acute-phase reactants[1]. Normal CRP concentration in healthy human serum is usually lower than 1 mg/dL, increasing slightly with aging. Higher levels are found in late pregnancy, mild inflammation, and viral infections (1–4 mg/dL); active inflammation and bacterial infection (4–20 mg/dL); severe bacterial infections and burns (>20 mg/dL)[3]. CRP levels normally rise within 2 to 6 hours after surgery and then go down by the third day after surgery[2].

The ESR has been the measure of the quantity of RBC that precipitate in a tube in a defined time and is based upon serum protein concentrations and RBC interactions with these proteins. Inflammation causes an increase in the ESR. The ESR increases in pregnancy or rheumatoid arthritis, and decreases in polycythemia, sickle cell anemia, hereditary spherocytosis, and congestive heart failure[2]. Multiple factors such as patient's age, gender, RBC morphology, hemoglobin concentration, and serum levels of immunoglobulin influence the ESR. The sample must be handled appropriately and processed within a few hours to assure test accuracy. While the ESR is not a diagnostic test, it can be used to monitor disease activity and treatment response and signal that inflammatory or infectious stress is present. For example, in rheumatoid arthritis, the ESR correlates well with disease activity; however normalization of ESR often lags behind successful treatment that causes resolution of the inflammatory state.

Immediately after surgery, lymphocytes decrease due to apoptosis but neutrophils increase causing overall rise in WBC count. Therefore, the change in the peripheral WBC count, especially neutrophil count, over time serves as a useful marker of postoperative progress[17].

There have been several studies that compared CRP, ESR and WBC in regards to early detection of infection. CRP has been known to be more reliable than ESR for monitoring the effectiveness of treatment for acute hematogenous osteomyelitis[19], septic arthritis in children[15], infected total joint arthroplasty[6], and spine infection[7]. CRP changes more quickly than ESR and therefore CRP may be a better reflection of current inflammation. Khan et al.[7] also mentioned that serial CRP level measurement may be helpful in monitoring the treatment of postoperative wound infections after spinal surgery. However, ESR does not appear to be as a sensitive marker of infection resolution.

For the explanation of prompt response of CRP, they assumed that CRP, unlike the ESR, is a fairly stable serum protein whose measurement is not time-sensitive and is not affected by other serum components. The magnitude of inflammation directly relates to the concentration of CRP[20].

Numerous studies have described the normal kinetics of CRP as a rapid rise with peak value on POD2 or POD3, followed by an initial sharp fall and then a gradual decrease with normalization by POD14 to POD21[6-8,15]. Larsson et al.[10] analyzed the prospective study of 89 patients who underwent uncomplicated spinal surgery showed that CRP rises within the first two posto-

perative days and then sharply declines. ESR shows more irregular peak at POD5 and then gradually returns to normal after several weeks[5,7,10,18].

Comparing with our analysis, in LOD group, CRP was normalized at postoperative 3rd day, however, in PLIF group, tendency of consistent high CRP with steady declination was detected. However, there literatures did not design the study as limit to the single procedure. In current study, we compared the changes of CRP, ESR, and WBC according to the procedures (LOD and PLIF). It is hard for us to find the literatures asserting about changes of inflammatory markers according to the procedure. For that reason, we assert that our current study is valuable for that point.

Two different surgical procedures have varying inflammatory peak responses. In spinal surgery, maximum postoperative CRP levels depend on the length and type of surgery performed[9,10,14]. In general, the peak response is affected by the amount of iatrogenic tissue injury at surgery. Our study shows that the peak CRP level is low in LOD group than PLIF's one.

There are a few literatures which measures and showed the normal ranges of CRP, ESR, and WBC in uninfected normal cases according to the procedures. Understanding the determinants of peak value is important because values substantially higher than expected may indicate an abnormal inflammatory response due to a complication. Deviations from normal kinetics of ESR and CRP may indicate an infectious complication. For spine surgery, reported peak values vary across studies. Kock-Jensen et al.[8] reported peak CRP of 28.5 mg/L after lumbar disc surgery. Larsson et al. presented peak values for microdiscectomy (46 mg/L), open discectomy (92 mg/L), anterior lumbar fusion (70 mg/L), and posterolateral interbody fusion (173 mg/L)[18]. Takahashi et al.[16] found significantly higher peak values after posterior lumbar instrumented fusion (91.9 mg/L) than decompression (27.8 mg/L). Deviations from normal kinetics of ESR and CRP may indicate an infectious complication.

There have been several reports about value of CRP, ESR, and WBC according to infection. Chung et al.[2] reported that the postoperative ESR in uncomplicated cases remained elevated 1 week after surgery, while the CRP peaked at day 2 and normalized by day 7 after spine surgery. Mun et al.[13] reported that, if there is persistent elevation or second rise around a week after surgery, the wound infection should be considered. Takahashi et al.[16] found that the post-operative CRP reached its peak on day 2 and remained abnormally elevated even after six weeks. And, Mok et al.[12] tried to derive the normal kinetics of CRP, opening the way for recognition of deviations that may indicate a complication. The kinetics seems to be conserved regardless of operation, magnitude, or region. A second rise or failure to decrease as expected has a high sensitivity, indicating that an infection will cause a positive result.

CRP and ESR reflect the degree of the inflammatory and surgical injuries as CRP has shown to have a higher sensitivity and specificity and is more reliable than ESR for detecting postoperative infection[16]. In additions, some literatures asserted that CRP is a predictable and responsive serum parameter in postoperative monitoring of inflammatory responses in patients undergoing spine surgery[9,11].

Knowledge of the postoperative peak value, either by routine measurement on POD2 or 3 or estimation of the peak value based on the analysis above, allows calculation of expected values at subsequent time points because the kinetics are defined. If a patient presents with findings concerning for infection days or even weeks after surgery, CRP can be measured with a simple blood draw at that time and compared with the value expected if the patient adhered to normal kinetics[12].

In current study, we excluded the patients who had transfusion during the surgery. We tried to minimize the influence of blood transfusion to CRP, WBC, ESR changes. Enright et al.[4] mentioned in his prospective study of CRP concentrations pre- and post-transfusion, serum CRP levels were analyzed before and after transfusion, using a fluorescence polarization immunoassay. He found that small rises in CRP concentrations occurred following 55.6% of transfusions, however, there was no statistically significant difference between pre- and post-transfusion CRP values, and these increases also failed to reach clinical significance. He added that CRP post-transfusion of greater than 100 mg/L occurred on only one occasion, and was more likely to be due to underlying infection[4]. However, ESR and WBC may be affected by transfusion. In current case, we excluded the case of spinal surgery which needed transfusion, and that point made more reliable results than other literatures, reporting the CRP, ESR, and WBC with spinal surgery.

We had very critical shortage that we used the average, median value and limitation of statistical analysis due to small number of prospective study cases. However, we tried to enumerate all the measured value of this study in the table.

We presumed our prospective series might be the valuable report of comparison between surgical techniques without influence of transfusion.

We assume that normalization of CRP at postoperative 3rd day of LOD may give us relief that surgery is not infected and checking and worrying about non-normalization of CRP at postoperative 7th day of PLIF with stand-alone cage might be the unnecessary work.

For ESR, only the thing that we could find is both procedures showed steady increase until 7th postoperative day except steepness of inclination, which might mean that ESR does not help for monitoring the infection after surgery.

For WBC, we presumed that normalization of WBC at postoperative 3rd day of LOD may provide us the non-infected state of surgery, and normalization of WBC at postoperative 7th day of PLIF with stand-alone cage probably may assure of non-infection.

CONCLUSION

We tried to aware the typical pattern of CRP, ESR, and WBC

in non-infected postsurgical patients and knowing the pattern may help to evaluate the early postoperative course. We found that in LOD group of non-infection, dramatic decrease of CRP was detected on POD3 and POD7 and dramatic increase of ESR on POD3 and POD7 in PLIF group of non-infection.

Both group's ESR level showed typical kinetics, not decreased until POD7 and WBC level maintain nearly equal to POD7. However, the CRP level was sharply decreased at POD3 in LOD group that of PLIF. So, we assumed that CRP would be more effective and sensitive parameter than ESR, WBC for early detection of infectious complications, especially in LOD than PLIF.

References

1. Black S, Kushner I, Samols D : C-reactive Protein. **J Biol Chem 279** : 48487-48490, 2004
2. Chung YG, Won YS, Kwon YJ, Shin HC, Choi CS, Yeom JS : Comparison of serum CRP and procalcitonin in patients after spine surgery. **J Korean Neurosurg Soc 49** : 43-48, 2011
3. Clyne B, Olshaker JS : The C-reactive protein. **J Emerg Med 17** : 1019-1025, 1999
4. Enright H, Coyle M, O'Connell LG : C-reactive protein concentrations pre- and post-transfusion. **Clin Lab Haematol 12** : 25-29, 1990
5. Gelalis ID, Arnaoutoglou CM, Politis AN, Batzaleksis NA, Katonis PG, Xenakis TA : Bacterial wound contamination during simple and complex spinal procedures. A prospective clinical study. **Spine J 11** : 1042-1048, 2011
6. Houshian S, Zawadski AS, Riegels-Nielsen P : Duration of postoperative antibiotic therapy following revision for infected knee and hip arthroplasties. **Scand J Infect Dis 32** : 685-488, 2000
7. Khan MH, Smith PN, Rao N, Donaldson WF : Serum C-reactive protein levels correlate with clinical response in patients treated with antibiotics for wound infections after spinal surgery. **Spine J 6** : 311-315, 2006
8. Kock-Jensen C, Brandslund I, Søgaard I : Lumbar disc surgery and variations in C-reactive protein, erythrocyte sedimentation rate and the complement split product C 3 d. **Acta Neurochir (Wien) 90** : 42-44, 1988
9. Kraft CN, Krüger T, Westhoff J, Lüring C, Weber O, Wirtz DC, et al. : CRP and leukocyte-count after lumbar spine surgery : fusion vs. nucleotomy. **Acta Orthop 82** : 489-493, 2011
10. Larsson S, Thelander U, Friberg S : C-reactive protein (CRP) levels after elective orthopedic surgery. **Clin Orthop Relat Res (275)** : 237-242, 1992
11. Meyer B, Schaller K, Rohde V, Hassler W : The C-reactive protein for detection of early infections after lumbar microdiscectomy. **Acta Neurochir (Wien) 136** : 145-150, 1995
12. Mok JM, Pekmezci M, Piper SL, Boyd E, Berven SH, Burch S, et al. : Use of C-reactive protein after spinal surgery : comparison with erythrocyte sedimentation rate as predictor of early postoperative infectious complications. **Spine (Phila Pa 1976) 33** : 415-421, 2008
13. Mun JH, Kim DH, Ryu KS, Park CK, Kim MC : Diagnostic value of early inflammatory reaction in postoperative infection of the lumbar spine. **J Korean Neurosurg Soc 38** : 206-210, 2005
14. Neumaier M, Metak G, Scherer MA : C-reactive protein as a parameter of surgical trauma : CRP response after different types of surgery in 349 hip fractures. **Acta Orthop 77** : 788-790, 2006
15. Peltola H, Vahvanen V, Aalto K : Fever, C-reactive protein, and erythrocyte sedimentation rate in monitoring recovery from septic arthritis : a preliminary study. **J Pediatr Orthop 4** : 170-174, 1984
16. Takahashi J, Ebara S, Kamimura M, Kinoshita T, Itoh H, Yuzawa Y, et al. : Early-phase enhanced inflammatory reaction after spinal instrumentation surgery. **Spine (Phila Pa 1976) 26** : 1698-1704, 2001
17. Takahashi J, Shono Y, Hirabayashi H, Kamimura M, Nakagawa H, Ebara S, et al. : Usefulness of white blood cell differential for early diagnosis of surgical wound infection following spinal instrumentation surgery. **Spine (Phila Pa 1976) 31** : 1020-1025, 2006
18. Thelander U, Larsson S : Quantitation of C-reactive protein levels and erythrocyte sedimentation rate after spinal surgery. **Spine (Phila Pa 1976) 17** : 400-404, 1992
19. Unkila-Kallio L, Kallio MJ, Eskola J, Peltola H : Serum C-reactive protein, erythrocyte sedimentation rate, and white blood cell count in acute hematogenous osteomyelitis of children. **Pediatrics 93** : 59-62, 1994
20. Wener MH : Laboratory Tests for Autoimmune Rheumatologic Disorders in Lahita RG, Weinstein A (eds) : **Educational Review Manual in Rheumatology,** ed 4. New York : Castle Connolly Graduate Medical Publishing, 2007, pp1-42