Does Cementing Influence CRP and ESR Levels after Total Hip Replacement in Early Postoperative Period? A Prospective Interventional Study

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ABSTRACT

Orthopaedics Section

Introduction: The role of C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) in diagnosing delayed (>6 weeks) periprosthetic joint infection prior to performing a revision joint arthroplasty is well established.

Aim: To evaluate the effect of bone cement on C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) in the first 3 weeks after Total Hip Replacement (THR).

Materials and Methods: This prospective interventional study was conducted in Department of Orthopaedics at Government Medical College, Chandigarh, India, between June 2014 to December 2017. Sixteen patients who underwent an uncemented THR and 15 patients who underwent a hybrid THR were included in the study. Serum CRP and ESR were measured on the day before surgery and postoperatively on days 1, 2, 3, 7, 12, and at 3 weeks. Comparison of ESR and CRP values between the

groups were performed using a Student's t-test. A p-value <0.05 was considered statistically significant.

Results: There was no significant difference between the two groups with respect to age, gender, indication of surgery, comorbidities, operative time and blood loss. CRP showed a peak at day two with a mean value of 203.74±46.15 mg/L in the uncemented group and a mean of 206.10±46.78 mg/L in the hybrid group, with normalisation by 3 weeks. ESR values showed a peak on day three with a mean of 94.28±5.97 mm/hour in the uncemented group and 92.15±6.86 mm/hour in the hybrid group and remained elevated even at 3 weeks. Statistically, no significant difference was observed in CRP and ESR values after the usage of cement in total hip arthroplasty (p-value >0.05 in all cases).

Conclusion: Bone cement does not affect CRP or ESR values significantly in the early phase after uncomplicated total hip arthroplasty.

Keywords: Bone cement, C-reactive protein, Erythrocyte sedimentation rate, Total hip arthroplasty

INTRODUCTION

Serological inflammatory makers specifically C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) are often used as initial preliminary diagnostic as well as follow-up tools to rule out a suspicion of infection in joint arthroplasty [1]. Factors that make ESR and CRP the markers of choice in monitoring the acute phase following surgery are that their values increase exponentially as compared to basal concentrations, have a relatively short lag time from the moment of stimulus, are inexpensive, non invasive and are widely and easily available tests [1-4].

The role of CRP and ESR in diagnosing delayed (>6 weeks) periprosthetic joint infection prior to performing a revision joint arthroplasty is well established [5-13]. But their role in diagnosing infection in the immediate postoperative period is still controversial and inconclusive. This is because CRP and ESR being acute phase reactants, show a normal physiological response curve in the immediate postoperative period due to surgery induced tissue damage, which in turn causes an elevation of these markers in the acute phase following surgery [14-19]. Therefore, before CRP and ESR could be used as effective markers of infection, it is essential to establish their baseline values in uncomplicated surgeries.

It is important to realise that a single reading holds very limited value and that a trend must be established in order to effectively diagnose joint infection. It is imperative that baseline values of CRP and ESR be established before diagnosing prosthetic joint infection. Identifying other factors that can alter the values of these markers hence becomes important. There are several known factors that can affect CRP and ESR values in arthroplasty. These factors can be divided

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into patient dependent and procedure dependent [20-25]. Some patient dependent factors include the Body Mass Index (BMI) of the patient, gender of the patient (females are known to have a higher baseline values of ESR), age of the patient and the presence of any pre-existing inflammatory pathologies such as rheumatoid arthritis [20-22]. Procedure dependent factors that can affect CRP and ESR values include the amount of surgical dissection performed, and the duration of surgery [23-25].

Bone cement is commonly used in arthroplasty procedures and cementing during arthroplasty is known to have systemic effects [26,27]. However, it's role as a variable that can affect the local inflammatory response, is a topic, still untouched by current literature so far. Therefore, it is possible that cemented and uncemented arthroplasties have varying natural response curves of ESR and CRP levels. The present study was conducted to compare the early postoperative trend of ESR and CRP in uncemented and hybrid Total Hip Replacement (THR) patients. The present work was done as a pilot study, as to the best of author's knowledge, there is no similar study in the literature evaluating the role of cement on CRP and ESR in Total Hip Replacement (THR) surgeries. It was hypothesised that hybrid THR patients (uncemented cup and a cemented femoral stem) will have higher postoperative values of ESR and CRP as compared to uncemented THR patients.

MATERIALS AND METHODS

This prospective interventional study was conducted in Department of Orthopaedics at Government Medical College, Chandigarh, India, between June 2014 to December 2017. The ethical approval was obtained from Institutional Ethical Committee approval (Ref No.5680). All investigations were conducted in conformity with ethical principles of research and an informed written consent was obtained from each patient.

A total of 31 patients who were matched in terms of their comorbidities (using the Charlson Co-morbidity Index) were enrolled for this study and evaluated preoperatively and postoperatively. Charlson Co-morbidity Index is a tool used to measure the 1 year mortality risk and burden of disease. The index has been extensively used in clinical research and practice to address the confounding influence of co-morbidities and predict outcomes [28].

Inclusion criteria: All patients undergoing hip replacement surgery during the study period, who met the inclusion criteria were enrolled for the study. The patients who had a wide femoral canal (Dorr type C) were selected for the hybrid group and others were included in the uncemented group. The study included patients who presented with primary or secondary osteoarthritis of the hip.

Exclusion criteria: Patients presenting with symptoms of rheumatoid arthritis viz pain in small joints of hand, morning stiffness for more than 30 minutes with deformities of hand and wrist along with elevated levels of ESR and CRP were excluded from the study. Similarly patients presenting with back pain, reduced chest expansion of less than 2.5 cm, a positive Schobers test and elevated inflammatory markers pointing towards ankylosing spondylitis were also excluded from the study. Patients previously operated on the hip for any pathology and those with abnormal baseline value of ESR (>30 mm/hour) and CRP (>5 mg/L) also fell into the exclusion criterion of our study.

Out of the 31 patients,

- Uncemented THR: This group included 16 patients
- Hybrid THR: This group included 15 patients

Thus a total of five patients, of which one patient with symptoms of rheumatoid arthritis, one patient with ankylosing spondylitis and three patients with abnormal preoperative values of CRP and ESR were excluded from the present study. Initially 36 patients were recruited out of which five patients were excluded due to the above mentioned criteria. All uncemented and hybrid THR surgeries were performed using a modified Gibson posterior approach to hip by two separate senior Orthopaedic Surgeons [29].

Data collection: Blood samples for CRP and ESR were obtained one day before the surgery and on 1st, 2nd, 3rd, and 7th postoperative day. Further samples were drawn at the time of suture removal on the 12th day and the time of first follow-up after 3 weeks from the day of surgery. A 2 mL of blood sample for CRP analysis and 2 mL for ESR analysis were collected in plain and Ethylenediaminetetraacetic Acid (EDTA) vials respectively and sent for analysis. Quantitative CRP analysis was done by employing a testing kit which was based on the principle of immunoassay with a normal reference range of 5 mg/L. The ESR was estimated using the Wintrobes method with a normal reference range of 30 mm/hour. A complete haemogram renal and liver function tests, urine routine microscopy and chest X-ray were sent before the surgery and 3 days after the surgery for all postoperative cases to make sure the surgeries were uncomplicated.

Surgical Technique

In both groups, a modified Gibson's approach to hip was followed. Patients were positioned laterally and a straight incision measuring 10-15 cms in length beginning in the mid-lateral thigh was made. The incision was then extended toward the tip of the greater trochanter and then proximally to the level of the iliac crest. After superficial dissection, the plane between the posterior border of gluteus medius and anterior border of gluteus maximus was identified and subsequent deep dissection was followed as per the Kocher-Langenback approach [29]. In the uncemented THR group, a polar stem with R 3 cup (Smith and Nephew) was used, whereas for hybrid THR group, a CPT stem with multi hole Triology cup (Zimmer Biomet) was employed. A 3rd generation cementing technique with vacuum mixing of a Simplex P bone cement (Stryker) was done and used for fixing of the cup in hybrid THR. The average operating time was 1.5 hour and on an average a single unit of blood transfusion was required in the postoperative period for patients in both these groups. Prophylactic antibiotic therapy (3rd generation cephalosporin) was instituted on the morning of surgery and continued 72 hour after surgery. Aspirin 150 mg OD was started from day 1 of the surgery and continued till 6 weeks postoperatively. Patients were mobilised with full weight bearing 24 hour after the surgery with the help of walker. Because of the author's aggressive postoperative physiotherapy regimen and the judicious use of chemical thrombopropholaxis, authors did not encounter any case of deep vein thrombosis in any of the operated patients.

STATISTICAL ANALYSIS

Data was tabulated on an excel spreadsheet and mean and standard deviation were calculated for normally distributed continuous variables. Comparison of ESR and CRP between uncemented and hybrid groups were done using the Student's t-test. A p-value <0.05 was considered statistically significant. The data was tabulated in excel sheets and statistical analyses were conducted using Statistical Package for Social Sciences (SPSS) version 20.0 software.

RESULTS

The study consisted of 22 (71%) male patients and 9 (29%) females patients. The average age of patients undergoing THR was 41.5 years. The comparison between the uncemented and hybrid THR groups is represented in [Table/Fig-1]. There was no significant difference between the two groups with respect to age, gender, indication of surgery, co-morbidities, operative time and blood loss (p-value >0.05 for all comparisons).

Parameters	Uncemented THR	Hybrid THR	p-value (Student's t-test)	
Age (years)*	43.93±10.81	39.26±9.15	0.11	
Gender				
Male	11	11	0.31	
Female	5	4		
Indication				
Avascular necrosis	7	10	0.71	
Primary osteoarthritis	4	2		
Inflammatory arthritis	4	3		
Others	1	0		
Charlson co-morbidity index*	0.63±0.62	0.33±0.49	0.08	
Operative time (minutes)*	76.63±6.70	80.6±7.52	0.13	
Operative blood loss (mL)*	598.1±98.1	573.3±123.9	0.27	
Preoperative haemoglobin (gm/dL)*	11.9±1.6	12.5±1.3	0.18	
Postoperative haemoglobin (gm/dL)*	9.9±1.4	10.5±1.1	0.09	

[Iable/Fig-1]: Comparison of general characteristics and operative details of patients between uncemented and hybrid total hip replacement group. *the values are represented as Mean±Standard deviation

The CRP values in both the uncemented and hybrid groups followed a parallel curve with peak values seen at day two and normalisation at three weeks. The CRP curve showed a peak at day two with a mean of 203.74±46.15 mg/L in uncemented group and a mean of 206.10±46.78 mg/L in the hybrid group. The decreasing trend started after day 3 of surgery. Though the absolute and peak values of mean CRP (mg/L) in the hybrid group were more than that of the uncemented group on days 1, 2 and 3, no statistically significant differences were found between these two groups [Table/Fig-2].

	C-reactive protein (mg/L)				
Day	Uncemented THR (Mean±SD)	Hybrid THR (Mean±SD)	p-value (Student's t-test)		
Preoperative	3.90±0.54	4.31±1.38	0.447		
1	104.27±25.51	110.67±31.96	0.541		
2	203.74±46.15	206.10±46.78	0.888		
3	136.20±61.87	149.94±74.16	0.579		
7	64.51±14.34	63.75±12.66	0.876		
12	11.61±2.61	11.64±2.70	0.982		
21	5.32±1.77	4.91±2.36	0.586		
[Table/Fig-2]: Comparison of C-Reactive Protein (mg/L) values between Uncemented and Hybrid THR groups in preoperative and postoperative periods.					

The ESR pattern in the uncemented and hybrid groups also followed a parallel curve with mean peak values at day three which continued to remain elevated at three weeks. ESR reached a peak at day three with a mean of 94.28±5.97 mm/hour in the uncemented group and 92.15±6.86 mm/hour in the hybrid group. Though a decreasing trend in ESR values were observed after day three the value of ESR remained elevated at three weeks [Table/Fig-3]. Although mean ESR values (mm/hour) in the uncemented group were marginally higher than hybrid group, no statistically significant difference was found between these two, suggesting that the use of cement had no impact on CRP and ESR levels, post total hip arthroplasty in the acute phase.

	Erythrocyte sedimentation rate (ESR) (mm/hr)			
Day	Uncemented THR (Mean±SD)	Hybrid THR (Mean±SD)	p-value (Student's t-test)	
Preoperative	18.50±3.32	19.53±3.81	0.427	
1	50.45±5.06	48.51±6.66	0.368	
2	80.77±6.52	76.52±5.69	0.064	
3	94.28±5.97	92.15±6.86	0.364	
7	70.89±4.49	66.19±4.03	0.071	
12	55.65±5.02	52.39±5.28	0.089	
21	41.80±4.00	41.14±4.17	0.654	
[Table/Fig-3]: Comparison of erythrocyte sedimentation rate (ESR) (mm/hr) values between uncemented and hybrid THR groups in preoperative and postoperative				

between uncemented and hybrid THR groups in preoperative and postoperative periods.

DISCUSSION

Erythrocyte sedimentation rate and C-reactive protein levels are commonly used postoperatively by arthroplasty surgeons for diagnosing prosthetic joint infection. However, the purpose of the present study was not to establish the threshold of CRP or ESR levels to determine Prosthetic Joint Infection (PJI) but to study the natural kinetics and establish baseline values of CRP and ESR in uncemented and cemented hip arthroplasty patients. The authors through this study have attempted to establish the normal baseline levels and kinetics of ESR and CRP after a normal uncomplicated hip arthroplasty, so that it may be used by surgeons as a guide to determine whether subclinical infection is developing or not. This could help alert the surgeon to warrant additional blood investigations and other laboratory tests to rule out infection or could help decide the duration of prophylactic antibiotics at the time of discharge.

The other purpose of the present study was to analyse the effect of cement on the local inflammatory response after a total hip arthroplasty. Cementing is known to have many systemic effects in joint replacement surgery [26,27]. However, its role as a variable that can have a bearing on the local inflammatory response (as measured by postoperative CRP and ESR values) is still debatable. In the study by Szypuła J et al., done on a Caucasian subpopulation, comparison of biocompatibility of cemented vs uncemented hip joint endoprosthesis based on postoperative evaluation of proinflammatory cytokine levels were performed. The study showed a higher CRP and Interleukin-6 (IL-6) levels in cemented hip endoprosthesis as compared to uncemented, a finding that stands in contrast to the results of the present study [30]. The contrasting results could be due to the different demographic and geographic factors of the present study as they are known to affect the baseline levels of the inflammatory markers [31,32].

The present study was conducted to compare the early postoperative trends of ESR and CRP in uncemented and hybrid THR patients. The authors hypothesised that a cemented hip arthroplasty could induce a significantly raised inflammatory response and would thereby result in higher mean values of CRP and ESR in the postoperative period. This stemmed primarily from the notion that the heat of polymerisation of cement would have a bearing on the inflammatory process after a hip replacement surgery. However, the results of the study were contrary to our hypothesis, and a similar and comparable postoperative trend of CRP and ESR were observed after uncemented and hybrid THR, thus highlighting the fact that cementing does not seem to have any significant effect on the local inflammatory process after an arthroplasty procedure.

The current study also confirms and highlights the facts previously recorded in literature [1-7], that CRP correlates with higher degree of inflammatory activity with a more rapid increase and a faster return to normal than ESR at three weeks postoperatively. Serum CRP and ESR differ in their normal temporal patterns of postoperative levels after THR. The temporal changes of CRP values were faster and greater than those of ESR. CRP levels rapidly reached a peak at day two and thereafter the levels decreased in a biphasic pattern. The first phase occurred after day three when CRP levels decreased rapidly and the second phase came after day seven with a gradual decrease until normalisation at three weeks. In contrast, the ESR levels peaked on the third day after surgery and gradually decreased and remained elevated above the normal reference level (30 mm/ hour) at three weeks postoperative. CRP shows a more predictable response with less atypical patterns and appears to be a better indicator of acute-phase response than ESR. Further elaborative studies in this regard would conclusively substantiate the evidence highlighted in this study.

Limitation(s)

This was a single-institution study done on a subset of the Asian population. The sample size of the study population was small with a short follow-up period of three weeks. However, it must be noted that period of 3 weeks was kept to take into account only the acute phase response of CRP and ESR. Though CRP normalised by three weeks, ESR did not. However, it was not followed longer than 3 weeks to see when it was normalised. Only uncomplicated cases were included in the present study to establish the baseline value of ESR and CRP in the Asian population.

CONCLUSION(S)

Bone cement does not affect CRP or ESR values significantly in early postoperative phase after uncomplicated total hip arthroplasty. Hence, it may be used as a reliable marker of infection, both in cemented and uncemented hip arthroplasty. However, further research is required in this field to conclusively provide evidence regarding this.

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