A comparison of complement C3 and C-Reactive Protein levels in patients treated via open and laparoscopic cholecystectomy.

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Abstract
Background/aims: Surgical trauma has a major impact in patients undergoing surgery. The inflammatory and immune response are the possible predictive factors of patients clinical outcome. The inflammatory response after surgical trauma is mediated by a number of substances which are produced at the site of wounded and manipulated tissues or at more distant places and they can act on local and systemic levels. The potent mediators are cytokines, heat shock proteins, acute phase proteins, eicosanoids and many others. C-reactive protein is a reliable early indicator of inflammation or injury. Serial postoperative CRP levels could predict septic complications before their clinical manifestation. Complement also plays an important role in adaptive immunity involving T and B cells that help in elimination of pathogens and also involved in tissue regeneration. Present study was planned to compare the inflammatory response in open and laparoscopic cholecystectomy. Patients with symptomatic cholelithiasis admitted in Department of General Surgery. A total of 21 patients opted for open cholecystectomy (Group-I) while another 22 patients opted for laparoscopic cholecystectomy (Group-II). Venous blood (5ml) samples from patients before and after operation were collected again at 12 hr, 24 hr and 48 hr., serum separated and stored at -20 ⁰c and send to Microbiology Department for assessment of CRP and C3 levels. In group I CRP mean values at 12hr, 24 hr, 48 hr were 16.08, 34.23, and 44.52 and in group II at same interval were 12.06, 28.96 and 32.23. The means of C3 levels in group I at same intervals were 2.37, 2.67 and 2.57 while in group II the C3 values for the same intervals were 1.96, 2.09 and 1.94 respectively. For the CRP the increase in mean levels was maximum at 48 hrs whereas for C3 the increase was maximum at 24 hrs and thereafter showed a decline. Both CRP as well as complement C3 levels were found to be significantly higher in open as compared to laparoscopic cholecystectomy group at all three follow up intervals. Mean CRP and C3 levels significantly increased in patients who developed infections at all 12 and 24 hrs postoperative intervals and having extended hospital stay. Present study establish the role of CRP and complement C3 as the inflammatory markers and also propose a possible utility for predictive outcome.

Keywords: Inflammatory response, Surgical trauma, Cholelithiasis.
1. Introduction:
Surgical trauma has a major impact in patients undergoing surgery. The inflammatory and immune response are the possible predictive factors of patients clinical outcome. The advantage of laparoscopic techniques with the lesser surgical trauma, the smaller tissue manipulations and the minimal exposure of the viscera to the air may be the cause of a much smaller inflammatory response and a lesser impact in immune response. This is extremely interesting in patients who undergo a surgery for a malignant disease. Where an immune suppression to them may exacerbate their disease. The inflammatory response after surgical trauma is mediated by a number of substances which are produced at the site of wounded and manipulated tissues or at more distant places and they can act on local and systemic levels. The potent mediators are cytokines, heat shock proteins, acute phase proteins, eicosanoids and many others. The most studies in the literature are the cytokines and C-reactive protein and they are studied both in the serum and in the peritoneal fluid. The immune dysfunction is a result of the intense inflammatory response which arises after surgical trauma in order to restore tissue function and to control the infection eradicating the invading microorganisms. The integrity of peritoneal and systemic response also prevents and protects from endoperitoneal or wound site spread and adherence of tumour cells. Major insult, as the big surgical wound in the open colecystectomy and time consuming tumour manipulations are associated with an overwhelming inflammatory response. Elevated level of C-reactive protein (CRP), an acute phase protein, is one of many downstream indicators of inflammation. It is a reliable early indicator of inflammation or injury. Serial postoperative CRP levels could predict septic complications before their clinical manifestation. Complement plays an important role in adaptive immunity involving T and B cells that help in elimination of pathogens and also involved in tissue regeneration. Present study was carried out with an aim to compare the inflammatory response in open and laparoscopic cholecystectomy on the basis of quantitative values in terms of morbidity, mortality, complications and post-operative hospital stay between two groups and to associate the CRP and complement C3 levels with the outcome.

2. Patients and Methodology:
Patients with symptomatic cholelithiasis admitted in Department of General Surgery, KGMU Lucknow UP India from August, 2010 to July, 2011. Randomization was done by computer generated random table. Patients were offered cholecystectomy based on previous documented history of symptomatic cholelithiasis, cholecystitis or pancreatitis and final decision was patient based and was largely influenced by the longer waiting times and increased costs accompanying laparoscopic cholecystectomy. A total of 21 patients opted for open cholecystectomy (Group-I) while another 22 patients opted for laparoscopic cholecystectomy (Group-II). Inclusion criteria were patients of cholelithiasis eligible for elective surgery, with age group 18 to 40 years having no complaints of any metabolic disorder affecting their immunity. Exclusion criteria were acute or emergency cases and patient having history of acute pancreatitis, choledocholithiasis, malignancies, jaundice, allergy, steroid intake, cytotoxic chemotherapy, pregnancy and collagen disorders. Prophylactic antibiotics were administered at induction before open as well as laparoscopic cholecystectomy. Venous blood (5ml) samples from patients before and after operation were collected again at 12 hr, 24 hr and 48 hr, serum separated and stored at -20°C and sent to Microbiology Department of KGMU for assessment of CRP and C3 levels.

3. RESULTS:
The CRP values in group-I preoperatively ranged from 2.7 to 5.2 with a mean of 3.39±0.79mg/100ml whereas in group II 2.0 to 5.4 with a mean of 3.41±0.83mg/100ml. C3 values ranged from 0.6 to 1.7 with a mean of 1.17±0.34mg/100ml in group I and in group II C3 values ranged from 0.7 to 1.4 with a mean of 1.04±0.21 mg/100 ml. In group I CRP mean values at 12hr, 24 hr, 48 hr were 16.08, 34.23, and 44.52 respectively and in group II at same interval were 12.06, 28.96 and 32.23. The means of C3 levels in group I at same intervals were
2.37, 2.67 and 2.57 while in group II the C3 values for the same intervals were 1.96, 2.09 and 1.94 respectively.

Table-1: Correlation between C-reactive protein and Complement C3 levels at different time intervals

<table>
<thead>
<tr>
<th>S.no.</th>
<th>Time interval</th>
<th>Bivariate correlation between C-reactive protein and complement C3 levels (pearson correlation coefficient-r)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Group I (N=21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Group II (N=22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overall (N=43)</td>
</tr>
<tr>
<td>1.</td>
<td>operative</td>
<td>0.195</td>
</tr>
<tr>
<td>2.</td>
<td>At 12 hrs</td>
<td>0.140, 0.239</td>
</tr>
<tr>
<td>3.</td>
<td>At 24 hrs</td>
<td>0.198, -0.264</td>
</tr>
<tr>
<td>4.</td>
<td>At 48 hrs</td>
<td>0.041, 0.051</td>
</tr>
</tbody>
</table>

For individual groups, the correlation between CRP and C3 levels was negligible (r<0.3), however, overall a mild positive correlation was observed between these two variables at 12 and 24 hrs time intervals (r>0.3). At 48 hrs correlation was moderate (r=0.560).

Table-2. Change in CRP & C3 levels of levels of Patients undergoing cholecystectomy (irrespective of group) at different time intervals:

<table>
<thead>
<tr>
<th>Markers</th>
<th>S.no.</th>
<th>Time interval</th>
<th>CRP levels (mg/100ml)</th>
<th>Change from Baseline(mg/ml)</th>
<th>Significance of change from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>1.</td>
<td>Baseline</td>
<td>3.40</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.</td>
<td>At 12 hrs</td>
<td>14.03</td>
<td>3.44</td>
<td>-20.346 &lt;0.001</td>
</tr>
<tr>
<td></td>
<td>3.</td>
<td>At 24 hrs</td>
<td>31.53</td>
<td>5.47</td>
<td>-32.170 &lt;0.001</td>
</tr>
<tr>
<td></td>
<td>4.</td>
<td>At 48 hrs</td>
<td>38.23</td>
<td>7.51</td>
<td>-30.056 &lt;0.001</td>
</tr>
<tr>
<td>C3</td>
<td>5.</td>
<td>Baseline</td>
<td>1.10</td>
<td>0.29</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.</td>
<td>At 12 hrs</td>
<td>2.16</td>
<td>0.45</td>
<td>-20.346 &lt;0.001</td>
</tr>
<tr>
<td></td>
<td>7.</td>
<td>At 24 hrs</td>
<td>2.37</td>
<td>0.52</td>
<td>-32.170 &lt;0.001</td>
</tr>
<tr>
<td></td>
<td>8.</td>
<td>At 48 hrs</td>
<td>2.25</td>
<td>0.48</td>
<td>-30.056 &lt;0.001</td>
</tr>
</tbody>
</table>

4. Discussion:
The present study was carried out to compare the C-reactive proteins and complement C3 levels in patients undergoing open and laparoscopic cholecystectomy before surgery and at different time intervals after surgery. A total of 43 patients fulfilling the inclusion criteria were enrolled in the study. Of these 22 opted for laparoscopic and rest for open surgery. In present study, majority of subjects were in mean age of 33.86±3.83 years for open and 31.41±5.28 years for laparoscopic surgery group. In industrialized countries cholesterol gallstones are very common aminoglycosides\textsuperscript{13, 14}. The traditional risk factors for gallstone disease are the four ‘F’- female, fat, forty and fertile, but age multiparity and cigarette smoking are now additional risk factors in western counties, where cholesterol is the leading component of stones.\textsuperscript{15,16,17} with rapid westernization of diet and environment, cholesterol gallstone disease is no longer rare in younger oriental adults. In present study too, we had a total of 15 (34.9%) patients who were less than 30 years of age. This change in age is reflective of changing lifestyle and dietary pattern. This finding are in agreement with those made by Siddiqui et al(2006)\textsuperscript{18} who had around 20% of their study subjects going for elective cholecystectomy in the age range of 21-30 years. On preoperative assessment the C-reactive protein levels in both the groups were observed to be within normal limit(<6) with similar finding of Bukan et al. (2004)\textsuperscript{19} but with a slightly higher values of C-reactive protein viz. 5.6± 2.7 and 6.2± 2.4mg/100ml. The reason for this difference could be the difference in selection...
criteria for patients who selected the symptomatic patients of cholelithiasis undergoing elective surgery. In both groups levels of CRP as well as C3 postoperatively was statistically significant for both markers. For CRP, the mean levels increased continuously till 48 hours intervals, showing an incremental trend for different follow up periods. Minimum increase from baseline being at 12 hours post operative interval and maximum at the 48 hours. However at all post-operative intervals there was a significant difference in mean CRP levels of both groups with mean value being higher in open cholecystectomy group as compared to laparoscopic group. These observations are in accordance with the finding of Jakeways (1994) who observed the CRP levels of open cholecystectomy group to be significantly higher as compared to those of laparoscopic cholecystectomy group at 24 and 48 hour post-operatively. The trends in present study showed that complement 3 levels were significantly different in open and laparoscopic groups thereby indicating their role as efficient inflammatory markers yet they did not follow a similar path as exhibited by CRP. This indicates a possible different mechanism of action of two markers. The declining C3 levels after 24 hours might indicate its role as an early precursor of decreasing inflammatory activity in a stable condition whereas the response to CRP might be delayed. An attempt was made in present work to explore the role of these markers for predicting an outcome i.e, events of extended hospital stay and infection-for extended hospital stay the mean CRP as well as complement C3 levels were to be significantly higher at all post-operative time intervals. These two markers of inflammation confirm the role by this study while at the same time they propose their utility as predictive markers for an outcome, though this proposition needs a larger study with a larger sample size and with inclusion of more possible outcomes.

5. References:


