COMPARATIVE STUDY OF CRP AND SERUM ALBUMIN AS STRESS RESPONSE MARKERS IN LAPAROSCOPIC VERSUS OPEN CHOLECYSTECTOMY

Manisha Srivastava[1], Brijendra Nigam[2], Ajay Bhagoliwal[3]

[1]Associate Professor, Department of General Surgery, Rama Medical College Hospital and Research Centre, Kanpur, Uttar Pradesh, India.
[2]Associate Professor, Department of General Surgery, Rama Medical College Hospital and Research Centre, Kanpur, Uttar Pradesh, India.
[3]Professor, Department of Preventive and Social Medicine, Rama Medical College Hospital and Research Centre, Kanpur, Uttar Pradesh, India.

ABSTRACT

BACKGROUND

Body responds to any trauma and surgery with 'stress response' in the form of metabolic and hormonal changes. Change in 'Acute Phase Proteins' (APP) like C-Reactive Proteins and Albumin occurs after surgery. Less injury induces less 'acute stress response' and good surgical outcome. Laparoscopic surgery produces less operative stress as compared to open laparotomy. Changes in albumin levels starts appearing much earlier than changes in levels of CRP. This study was conducted with an aim to compare the response kinetics & levels of acute phase proteins (APP) like C-reactive Proteins and Albumin and asses the accurate predictability of these makers in surgical outcome to the extent of surgical trauma.

Aims & Objectives- To understand the behavior of stress response markers CRP and Serum Albumin in minimally invasive procedure lap-cholecystectomy versus open cholecystectomy and their predictability in clinical outcome.

MATERIALS AND METHODS

Settings & Design- This prospective randomized study was conducted on patients admitted in the Department of Surgery, Rama Medical College, Kanpur during May 2016 to April 2018. 80 Patients with diagnosis of chronic cholelithiasis were included and randomly divided in two groups, open-cholecystectomy (Group A) and lap-cholecystectomy (Group B) each having 40 patients. The levels of C-reactive Proteins (CRP) and serum albumin (S. Alb) were measured 12 hrs. pre-operatively, then post-operatively at 6 Hrs., 12 Hrs., 24 hrs. 2nd, 3rd and 4th day and data analyzed. Sample size was taken for convenience.

Statistical Analysis- Data was analyzed by statistical software package SPSS version 21.0 (SPSS Inc. Chicago, IL, USA). The average (Mean) value of CRP and Albumin in the two groups have been compared using independent sample 't' test. The levels of both CRP and Albumin at different sampling time have been compared by using Repeated Measure ANOVA and individual comparison between individual groups were done using Post-Hoc test (Bonferroni Test. 'p' value < 0.05 is considered significant. 'p' value <0.05 is considered significant.

RESULTS

80 patients were divided into two groups (Open and Laproscopic) randomly. Pre-operative CRP levels are almost equal in both the groups, while there is a sharp rise of CRP levels in both groups from 2nd post-operative day to 3rd post-operative day and then there is slow decline of levels from 4th post-operative day. The rise of CRP level was more in open group as compared to Lap group indicative of extent of trauma in more in open group. The decline in Albumin levels is significant only up to first 24 hrs. and after 24 hrs., decline of Albumin is statistically not significant. This shows that measurement of Albumin level can be used as early predictor of stress response in early post-operative period as compared to CRP levels.

CONCLUSION

Laparoscopic cholecystectomy is less traumatizing as compared to open cholecystectomy. Post-operative albumin drops can be measured as early as 4–6 hours after surgery as compared to rise of CRP levels which occurs in late post-operative period. Hence early measures can be taken to prevent further complications by measuring Albumin levels.

KEY WORDS

CRP, Albumin, Acute Phase Proteins, Stress Response Markers.

HOW TO CITE THIS ARTICLE: Srivastava M, Nigam B, Bhagoliwal A. Comparative study of CRP and serum albumin as stress response markers in laparoscopic versus open cholecystectomy. J. Evolution Med. Dent. Sci. 2019;8(01):47-52, DOI: 10.14260/jemds/2019/11

'Financial or Other Competing Interest': None.
Submission 18-11-2018, Peer Review 25-12-2018,
Acceptance 31-12-2018, Published 07-01-2019.
Corresponding Author:
Dr. Brijendra Nigam,
#13, Hemant Vihar, Sector 3,
Barra 2, Kanpur-208027, Uttar Pradesh, India.
E-mail: brijendramanisha@yahoo.com
DOI: 10.14260/jemds/2019/11

BACKGROUND

Sir David Cuthbertson in 1942 gave the theory of metabolic responses of injuries in his 'ebb' and 'flow' theory.[1,2] After his treatise, the interaction between the immuno-hematological and neuro-endocrine systems and role of cytokines in the response to surgery, has furthered developed in the understanding of 'stress response' to surgery. A number of changes occur following tissue injury whether trauma or surgery. Cytokines, particularly IL-6 is released. This IL-6 stimulates the 'acute phase response' in liver. Liver starts

producing acute phase proteins (APP) like C-Reactive protein instead of production of its usual proteins e.g. Albumin and transferrin. Production of Albumin and transferrin, decreases during 'acute phase response' while there is increase in production of C-reactive protein (CRP), fibrinogen, α_2-macroglobulin and other anti-proteinases.[3] Concentrations of circulating cations such as zinc and iron decrease partly as a consequence of the changes in the production of the transport proteins.[4]

Extent of surgical interventions trigger proportionate 'metabolic stress response' magnitude, which contribute to increased complication rates, delayed recovery, length of hospital stays. More trauma initiates more Stress response. Recent improvements in operative techniques, peri-operative care aiming to modulate and minimize trauma and thereby minimal stress response have been proven to be effective.[5-9] Application of enhanced recovery pathways (ERAS) has shown a decreasing effect on surgical stress and subsequently reducing complications, morbidity and hospital stay.[10-12] A strict peri-operative nutritional support and the use of immune-modulating formulas proved to reduce complications after major surgery. Similarly, the peri-operative use of corticosteroids has been advocated recently. Preliminary results for these simple interventions are promising with regard to postoperative outcomes.[13,14]

Laparoscopic surgery causes less tissue injury than conventional procedures, so the increase in concentrations of biochemical markers of inflammation, such as IL-6 and the acute phase proteins CRP is not as high, while drop in albumin levels are also not so low.[15] Post-operative serum C-reactive protein (CRP) levels are ideally used in clinical practice to assess the extent of post-operative inflammation. A major drawback of CRP as predictor for stress-related complications is its slow kinetics.[6,9,16] Peak values are measured only at postoperative day 2 or 3, which may be too late for early preventive interventions. Albumin is the most abundant protein in humans and widely used as nutritional marker and predictor for outcomes in stress response. In addition, albumin shows an immediate response to 'surgical stress' within 12 hrs. After surgery, hence can be used to measure surgical stress and to predict a complicated post-operative course.[17,18] The aim of the present study was therefore to understand the comparative kinetics of stress response makers to the extent of surgical trauma and assess the comparative predictability of CRP and of serum albumin levels in surgical outcome.

MATERIALS AND METHODS

Present prospective randomized study was conducted at Rama Medical College Hospital and Research Centre, Kanpur, Uttar Pradesh during May 2015 to April 2018. 80 Patients with diagnosis of chronic cholelithiasis were included and randomly divided in two groups, open-cholecystectomy (Group A) and Lap-cholecystectomy (Group B) each having 40 patients. The levels of C-reactive Proteins (CRP) and serum albumin (S. Alb) were measured 12 hrs. Pre-operatively, then post-operatively at 6 Hrs., 12 Hrs., 24 hrs. 2nd, 3rd and 4th day and data analyzed. Sample size was taken for convenience.

Inclusion Criteria

All patients between 20 years to 65 years age of both genders presenting with diagnosis of Chronic cholecystitis with cholelithiasis (Symptomatic Gallstone Disease) were included with Ultrasound proved diagnosis.

Exclusion Criteria

Patients with jaundice, severe infections, other metabolic diseases, neurological or psychiatric diseases, bleeding disorders, hypertension, pregnancy, and those who have not given consent were excluded. CT scans and MRI was done to assist and exclude any associated complications. Patients whose baseline CRP and Serum Albumin was found away from normal limit were also excluded. Patients in whom any need for conversion from lap to open operation, pre-operative cholangiography, CBD exploration or surgery extending beyond 100 minutes were abandoned from study.

Randomization

Randomization was done using computer software, according to a standardized previously reported protocol.[19] A set of random number was generated and sealed numbered envelopes were made with the serial number mentioned on the outside and intervention mentioned inside by a non-participating individual. Once a participating subject gave valid consent, the pre-determined procedure was carried out as follows:

The open cholecystectomy was carried on Group A (n=40) and laparoscopic procedure was done on group assigned as Group B (n=40). According to the principles of the declaration of Helsinki 1975 revised in the year 2000, written, informed consent was obtained from all participants. Ethical clearance was taken from ethics Committee of the institute.

Standard operative procedures were adopted both for open and laparoscopic techniques, clips were used in both procedures for ligating cystic artery/duct and sub-hepatic drain was used in all patients.

In both groups Pre, intra, and post-operative medication, type of anaesthesia and anaesthetic medications used almost consistently in every patient. Pre-operative sample 12 hrs. Before surgery for CRP and Albumin was taken. Similarly, Post-operatively blood sample at 6 hrs, 12 Hrs., 24 hrs, and on 2nd day, 3rd day and 4th day taken to measure the levels of C-reactive Proteins (CRP) and serum albumin levels in both groups. Pertinent demographics, surgical parameters, and clinical outcome measures were prospectively recorded in predesigned format in a computerized database.

Total operation time (OT) was measured by the anesthetist from incision to skin closure.

Statistical Analysis

Data was analysed by statistical software package SPSS version 21.0 (SPSS Inc. Chicago, IL, USA) Continuous variable like patient's age, CRP, Albumin and duration of surgery were expressed as mean ± SD. Qualitative variables were expressed as frequencies and percentages. The average (Mean) value of CRP and Albumin in the two groups have been compared using independent sample 't' test. The levels of both CRP and Albumin at different sampling time have been compared by using Repeated measure ANOVA and individual comparison between individual groups were done using Post-Hoc test (Bonferroni Test. 'p' value < 0.05 is considered significant.

(Since we had to compare the levels in 7 groups (Pre-operative, post-operative at 6 hrs. 12 hrs. 24 Hrs. 2nd, 3rd and 4th post operative day, which are related observations on

the same set of patients, therefore Repeated Measure ANOVA has been used.)

RESULTS

Demographic and surgical details of the study displayed by type of surgery in Table 1. Out of 80 patients enrolled as a case of cholelithiasis the mean age of patients was 42.037 with standard deviation of ±8.947. The mean age of patients in group A was 42 ± 9.07 and in group B was 40.62 ± 11.6. The mean Body mass index (BMI) for group A 28 ± 3 and for group B was 27 ± 6. The mean operating time for group A 65 ± 21 and for group B was 80 ± 20 minutes. The male: female ratio in group A was 15:25 and in group B was 17:23. Figure 1.

The Metabolic Stress Response

CRP Levels

For group A (Open), the mean CRP levels 12 hrs. Pre-operatively was 4.59±0.58 mg/dl. The mean CRP levels post-operatively after 6-hour was 12.83 ± 1.54 mg/dl, after 12 hrs. 21.17 ± 3.47 mg/dl, after 24 hrs. 42.70 ± 8.12 mg/dl. On 2nd post-Op. day was 161.49 ± 24.79 mg/dl, on 3rd post op day was 213 ± 25.15 mg/dl and on 4th post-Op. day it was 186 ± 22.55 mg/dl.

For Group B (Lap), the mean CRP levels 12 hr. pre-operatively was 4.45±0.39 mg/dl. Post-operatively at 6 hrs. Was 7.24 ± 1.79 mg/dl, at 12 hrs. Was 13.40 ± 1.69 mg/dl, at 24 hrs. Was 38.15±9.79 mg/dl, at 2nd post-Op. day 90.83±10.12 mg/dl, at 3rd post-Op. day was 88.76 ± 10.62 mg/dl and at 4th post-Op. day it was 72.95±10.32 mg/dl. (Table 2).

These results clearly show that pre-operative CRP levels are almost equal in both the groups, while there is a sharp rise of CRP levels in both groups from 2nd post-operative day to 3rd post-operative day and then there is slow decline of levels from 4th post-operative day. Table 2 shows the statistical analysis of this rise in CRP levels.

Albumin Levels

For group A (Open) the mean Albumin level 12 hrs. Pre-operatively was found 4.46±0.40 g/dl). Post-operatively at 6 hrs. Was 3.76 ± 0.33 g/dl, at 12 Hrs. Was 3.08 ± 0.41 g/dl, at 24 Hrs. Was 3.07 ± 0.38 g/dl. Mean albumin level on 2nd post-Op. day was 3.05 ± 0.35 g/dl, on 3rd post-Op. day was 3.08±0.38 g/dl and on 4th day it was 3.15±0.35 g/dl.

For Group B (Lap) Albumin levels 12 hrs. Pre-operatively was 4.41 ± 0.38 g/dl and post-operatively at 6 hrs. It was 3.91 ± 0.32 g/dl, at 12 hrs. 3.91 ± 0.32 g/dl, at 24 hrs. 3.86 ± 0.32 g/dl. On 2nd post-Op. day it was 3.86 ± 0.33 g/dl, on 3rd day it was 4.08 ± 0.26 g/dl and on 4th post-Op. day it was 4.23±0.26 g/dl.

For albumin there is significant fall of levels in first 12 hrs. In both the groups, but open group shows more decline as compared to Group B (Lap group). The kinetic pattern of fall in Albumin levels in both the groups found same. (Table 3)

CRP/ albumin relationship examined simultaneously, and it was observed that maximal amplitude of fall of Albumin levels reached within 6 to 12 hrs. But later on fall was not significant. While maximal rise of CRP levels observed after 2nd to 3rd post-operative day and there after slow decline observed. Therefore, it was observed that decline in albumin levels and rise in CRP levels were more in open cholecystectomy as compared to laparoscopic cholecystectomy suggesting lap-cholecystectomy is less stressful procedure.

Table 4 & 5 show the results of the Repeated Measure ANOVA for CRP levels. Table No. 4 is showing results for open Group, while Table No. 5 shows results for Lap group. The rise of CRP is statistically significant in all post-operative levels. Table No. 6 & 7 show the results of the Repeated Measure ANOVA for albumin levels. Table 6 shows levels for open group and Table 7 for Lap group. The decline in Albumin levels is significant only up to first 24 hrs. And after 24 hrs. Decline of Albumin is statistically not significant. This shows that measurement of Albumin level can be used as a predictor of stress response in early post-operative period as compared to CRP levels. Hence this information in early post-operative period can be utilized to take timely measures to prevent untoward outcome.

	Group A	**Group B**
	(Operative)	(Laparoscopic)
	Mean ± Standard Deviation	Mean ± Standard Deviation
Age*	42 ± 9.07	40.62 ± 11.62
BMI †	28 ± 3	27 ± 6
OT Time ‡	65 ± 21	80 ± 20
Table 1. Demographic Characteristics of Sample		
*Values are expressed as Mean ± SD, †BMI=Body Mass Index, ‡OT time= Operation Theatre Time;		

Sample Time	**Group A (Operative)**	**Group B (Lap)**	**t**	**p-Value**
	Mean ± Standard Dev	**Mean ± Standard Dev**		
Pre-Op	4.59 ± 0.58	4.45 ± 0.39	1.225	0.224
6 Hrs.	12.83 ± 1.54	7.24 ± 1.79	15.011	0.000*
12 Hrs.	21.17 ± 3.47	13.40 ± 1.69	12.65	0.000*
24 Hrs.	42.70 ± 8.12	38.15 ± 9.79	2.266	0.026
2nd Post op. day	161.49 ± 24.79	90.83 ± 10.12	16.716	0.000*
3rd Post op. day	213 ± 25.15	88.76 ± 10.62	28.967	0.000*
4th Post op. day	186 ± 22.55	72.95±10.32	28.907	0.000*
Table 2. Mean CRP Levels in Both Groups at Different Stages				
(*) Shows significant difference				

Sample Time	**Group A (Operative)**	**Group B (Lap)**		
	Mean ± Standard Dev	**Mean ± Standard Dev**	**t**	**'p' Value**
Pre-Op	4.41 ± 0.38	4.46 ± 0. 40	0.543	0.589
6 Hrs.	3.76 ± 0.33	3.91± 0.32	2.09	0.040*
12 Hrs.	3.08 ± 0.41	3.91 ± 0.32	9.859	0.000*
24 Hrs.	3.07± 0.38	3.86 ± 0.32	10.001	0.000*
2nd Post - Op. Day	3.05 ± 0.35	3.86 ± 0.33	10.652	0.000*
3rd Post-Op. Day	3.08 ± 0.38	4.08 ± 0.26	13.571	0.000*
4th Post-Op. Day	3.15 ± 0.35	4.23 ± 0.26	15.662	0.999
Table 3. Mean Albumin Levels in Both Groups at Different Sample Time				
(*) Shows significant difference				

Sampling Time vs Comparison	p-Value
Pre-Op vs Post-Op. 6 Hrs.	0.000*
Post-Op. 6 Hrs. vs Post-Op. 12 Hrs.	0.000*
Post-Op. 12 Hrs. vs Post-Op. 24 Hrs.	0.000*
Post-Op. 24 Hrs. vs Post-Op. 2nd Day	0.000*
Post-Op. 2nd Day vs Post-Op. 3rd day.	0.000*
Post-Op. 3rd Day vs Post-Op. 4th Day	0.000*

Table 4. Paired Comparison Results CRP-Open Group (Repeated Measure ANOVA)

(*) Shows significant difference

Sampling Time vs Comparison	p-Value
Pre-Op. vs post-Op. 6 Hrs.	0.000*
Post-Op. 6 Hrs. vs Post-Op. 12 Hrs.	0.000*
Post-Op. 12 Hrs. vs Post-Op. 24 Hrs.	0.000*
Post-Op. 24 Hrs. vs Post-Op. 2nd Day	0.000*
Post-Op. 2nd Day vs Post-Op. 3rd day.	0.430
Post-Op. 3rd Day vs Post-Op. 4th Day	0.000*

Table 5. Paired Comparisons Results CRP-Lap Group (Repeated Measure ANOVA)

(*) Shows significant difference

Sampling Time vs Comparison	p-Value
Pre-Op. vs post-Op. 6 Hrs.	0.000*
Post-Op. 6 Hrs. vs Post-Op. 12 Hrs.	0.000*
Post-Op. 12 Hrs. vs Post-Op. 24 Hrs.	1.000
Post-Op. 24 Hrs. vs Post-Op. 2nd day	1.000
Post-Op. 2nd Day vs Post-Op. 3rd day.	1.000
Post-Op. 3rd Day vs Post-Op. 4th day	1.000

Table 6. Paired Comparisons Results ALBUMIN-Open Group (Repeated Measure ANOVA)

(*) Shows significant difference

Sampling Time vs Comparison	p-Value
Pre-Op vs Post-Op. 6 Hrs.	0.000*
Post-Op. 6 Hrs. vs Post-Op. 12 Hrs.	1.000
Post-Op. 12 Hrs. vs Post-Op. 24 Hrs.	1.000
Post-Op. 24 Hrs. vs Post-Op. 2nd day	1.000
Post-Op. 2nd Day vs Post-Op. 3rd day.	0.000*
Post-Op. 3rd Day vs Post-Op. 4th day	0.022*

Table 7. Paired Comparisons Results ALBUMIN- Lap Group (Repeated Measure ANOVA)

(*) Shows significant difference

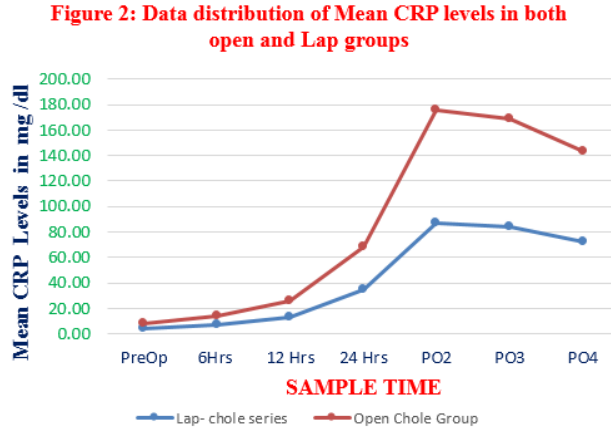

Figure 2. Comparative Graph Showing Mean CRP Levels in Both Open and Lap Group

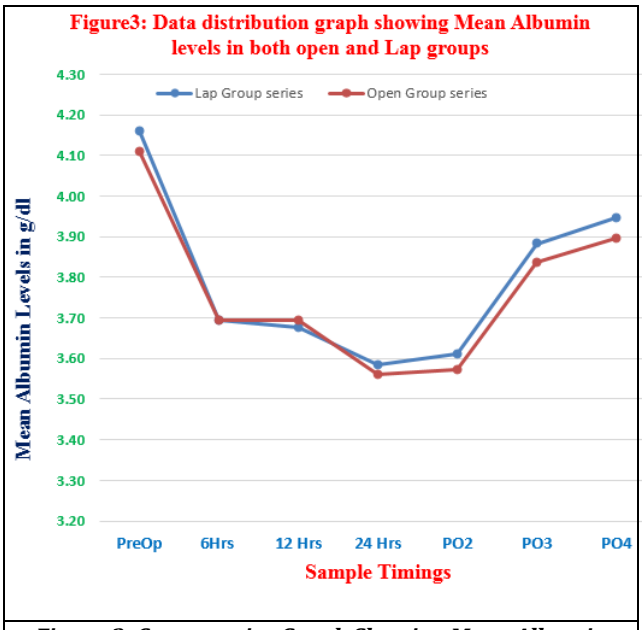

Figure 3. Comparative Graph Showing Mean Albumin Levels in Both Open and Lap Groups

DISCUSSION

Surgical trauma initiates an important metabolic stress response which can be measured by various stress markers in blood. Extent of trauma in surgical interventions trigger proportionate 'metabolic stress response' magnitude, which contribute to complication rate, delayed recovery, and length of hospital stay. Cuthbertson described in 1942 the metabolic responses of injuries in his 'ebb' and 'flow' theory. The interaction between the immuno-haematological and neuroendocrine systems and role of cytokines in the response to surgery, has furthered developed the understanding of stress response to surgery. This phenomenon is known as the 'acute phase response'; one of its features is the production in the liver of 'acute phase proteins (APP)'. IL-6 is a pro-inflammatory cytokine that is released after trauma and surgery and correlates with post-operative insulin resistance.[20,21] The release of IL-6 occurs within few hours after the surgical trauma.[8,22,23,24] This cytokinin IL6 causes decreased production of usual proteins like albumin and transferrin, while there is increase production of C-reactive protein (CRP), fibrinogen, α_2-macroglobulin and other anti-proteinases by liver.[3] Concentrations of circulating cations such as zinc and iron also decreases, partly as a consequence of the changes in the production of the transport proteins.[4] The extent and timing of release of acute phase proteins was investigated in this study by means of rise in CRP levels and the decrease of serum albumin in relation to magnitude of trauma. Laparoscopic cholecystectomy is frequently performed procedures these days. Laparoscopic cholecystectomy when compared with open cholecystectomy is the preferred surgical procedure since 1991 because of less morbidity, mortality and early return to work.[15] The artificial pneumoperitoneum created in laparoscopic procedures induce acidemia and pulmonary hypo-perfusion. In our study we compared the "stress response" in patients undergoing laparoscopic Cholecystectomy and open cholecystectomy by measuring levels of CRP and Albumin 12 hrs. Pre-operatively and at 6 hrs., 12 hrs., 24 hrs., 2nd day, 3rd day, 4th day post-operatively. The mean CRP levels was found high in Group A

(open) at different times post operatively when compared to Group B (Lap) and found statistically significant p = 0.000.

On analysis of levels of "Albumin" we found that there is decline in the mean Albumin levels in early post-operative period in both open and Lap group. The decline in Albumin levels was more in the open cholecystectomy group as compared to Lap cholecystectomy group and statistically significant (p = 0.000).

Skin incision size, intra-operative fiddling of the tissues is responsible for rise of acute phase proteins CRP and decline in Albumin levels. In Lap Cholecystectomy there is minimal skin incision and less tissue handling, which eventually results in decreased morbidity, decreased hospital stays.[25] Pneumo-peritoneum created in Lap procedures does not add to operative stress.[20] so, it can be related with lesser rise of CRP levels and lesser decline of Albumin levels post-operatively in Lap group as compared to open cholecystectomy group.

In another observation in this study it was found that CRP levels starts rising sharply only after 2nd post-operative day till up to 3rd post-operative day and after thereafter it starts declining from 4th post-operative if there is no other added post-operative complication occurs. This kinetics remains same in both open and Lap groups Whereas Albumin levels starts declining as early as after 6 hrs. And keeps on declining up to 24 hrs. Post-operatively and thereafter it remains stationary till 3rd post-operative day and starts recovering after 4th post-operative day if no other added post-operative complication occurs. The kinetics of Albumin also remains same in both Open and Lap groups.

The use of CRP levels on or after 2nd post-operative day has also been advocated as predictor for (Infectious) complications.[26] Kinetics of CRP is rather slow, and plasma peaks are only reached after 2nd and 3rd post-operative day.[27] This leads to predictive delay in taking decisive actions in time. We need a marker which can forecast ensuing complications of surgery and that too at an early initial phase after surgery, so that preventive measures can be taken at early stage in post-operative period. There has been a concern that this stress marker should be easy to measure and should be inexpensive and easily available. It should strongly correlate with the extent of surgical trauma and can be a reliable predictor of complications of surgery thereby prevents prolonged morbidity, prolonged hospital stay and more expenses. So far, no such marker is available.[8,9,26] Since CRP levels starts rising only after 2nd post-operative day, it has less predictive value for post-operative complications.[28] To act early in peri-operative period role of CRP seems limited. Serum albumin is widely used as reliable indicator for nutritional status. Protein metabolism is significantly disturbed after any kind of traumatic event, for example surgery, sepsis, and burn injuries. Albumin protein has been identified as a reliable indicator of this process.[29,30,31,32] Plasma concentrations of albumin reveal an important decrease as early as a few hours after the trauma.[29,31,33] So Albumin which has been studied in this study has been found to have an early predictive value of outcome of surgery and forthcoming complications because decline in Albumin levels starts as early as 4-6 hrs. After surgery.

The present study is done to ascertain the role of stress markers in deciding operative technique and their potential value to predict the related adverse outcomes. Albumin levels as compared to CRP levels is available earlier in the postoperative course to predict complicated outcome and is related to extent of trauma during surgery (Operative time, blood loss). The early decline during the first 24 hrs. And slow recovery of serum albumin during late post-operative days confirms previously published findings of Rittler et al. Furthermore, albumin drop can already be measured just after few hrs. Of surgery. Our study confirms previously published study of Martin Huber et al.[34]

Lastly in practical terms, serum albumin is part of the routine workup before major surgery and inexpensive and seems to reflect metabolic stress.[16,26]

CONCLUSION

Minimal invasive laparoscopic cholecystectomy is less traumatizing as compared to open cholecystectomy. Post-operative albumin drops can be measured as early as 4–6 hours after surgery as compared to rise of CRP levels which can only be measured in late post-operative period. Hence early measures can be taken to prevent further complications by estimation of serum albumin level in early post-operative period. Estimation of Albumin levels though routinely not in clinical vogue at present can be studied further to establish its predictability as surgical outcome as compared to CRP.

ACKNOWLEDGMENTS

The authors would like to thank all colleagues in the departments of General Surgery, Clinical Pathology and Biochemistry for their kind collaboration as well as the nursing staff of General Surgery department, for their invaluable help in timely blood sample collections.

REFERENCES

[1] Cuthbertson DP. Post Shock metabolic response. Lancet 1942;1:343-7.
[2] Cuthbertson DP. The metabolic response to injury and other related explorations in the field of protein metabolism: an autobiographical account. Scott Med J 1982;27(2):158-71.
[3] Castell JV, Gomez-Lechon MJ, David M, et al. Interleukin-6 is the major regulator of acute phase protein synthesis in adult human hepatocytes. FEBS Lett 1989;242(2):237-9.
[4] Wang BH, Yu XJ, Wang D, et al. Alteration of trace elements (Zn, Se, Cu, Fe,) and related metaloenzymes in rabbit blood after severe trauma. J Trace Elem Med Biol 2007;21(2):102-7.
[5] Buunen M, Gholghesaei M, Veldkamp R, et al. Stress response to laparoscopic surgery: a review. Surgical Endoscopy and Other Interventional Techniques 2004;18(7):1022-8.
[6] Desborough JP. The stress response to trauma and surgery. British Journal of Anesthesia 2000;85(1):109-17.
[7] Haga Y, Beppu T, Doi K, et al. Systemic inflammatory response syndrome and organ dysfunction following gastro-intestinal surgery. Critical Care Medicine 1997;25(12):1994-2000.

[8] Hall R. Identification of inflammatory mediators and their modulation by strategies for the management of the systemic inflammatory response during cardiac surgery. Journal of Cardiothoracic and Vascular Anesthesia 2013;27(5):983-1033.
[9] Lin E, Calvano SE, Lowry SF. Inflammatory cytokines and cell response in surgery. Surgery 2000;127(2):117-26.
[10] Coolsen MME, van Dam RM, van der Wilt AA, et al. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. World Journal of Surgery 2013;37(8):1909-18.
[11] Greco M, Capretti G, Beretta L, et al. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. World Journal of Surgery 2014;38(6):1531-41.
[12] Muller S, Zalunardo MP, Hubner M, et al. A fast-track program reduces complications and length of hospital stay after open colonic surgery. Gastroenterology 2009;136(3):842-7.
[13] Karaman K, Bostanci EB, Aksoy E, et al. Effects of dexamethasone and pheniramine hydrogen maleate on stress response in patients undergoing elective laparoscopic cholecystectomy. American Journal of Surgery 2013;205(2):213-9.
[14] Kilger E, Heyn J, Beiras-Fernandez A, et al. Stress doses of hydrocortisone reduce systemic inflammatory response in patients undergoing cardiac surgery without cardiopulmonary bypass. Minerva Anestesiologica 2011;77(3):268-74.
[15] Luo K, Li JS, Li LT, et al. Operative stress response and energy metabolism after laparoscopic cholecystectomy compared to open surgery. World Journal of Gastroenterology 2003;9(4):847-50.
[16] Easton R, Balogh ZJ. Peri-operative changes in serum immune markers after trauma: a systematic review. Injury 2014;45(6):934-41.
[17] Fleck A, Raines G, Hawker F, et al. Increased vascular permeability: a major cause of hypo-albuminemia in disease and injury. The Lancet 1985;325(8432):781-4.
[18] Smeets HJ, Kievit J, Dulfer FT, et al. Analysis of post-operative hypalbuminemia: a clinical study. International Surgery 1994;79(2):152-7.
[19] Urbaniak GC, Plous S. Research randomizer (version 3.0) [Computer software]. 2007. http://www.randomizer.org.
[20] Janicki K, Bicki J, Radzikowska E, et al. C-reactive protein (CRP) as a response to postoperative stress in laparoscopic cholecystectomy using the abdominal wall lift, with performed pneumoperitoneum (CO2), and in open cholecystectomy. Ann Univ Marie Curie Sklodowska Med 2001;56:397-402.
[21] Vozarova B, Weyer C, Hanson K, et al. Circulating interleukin-6 in relation to adiposity, insulin action and insulin secretion. Obesity Research 2001;9(7):414-7.
[22] Glund S, Krook A. Role of interleukin-6 signaling in glucose and lipid metabolism. Acta Physiologica (Oxf) 2008;192(1):37-48.
[23] Van Hall G, Steensberg A, Sacchetti M, et al. Interleukin-6 stimulates lipolysis and fat oxidation in humans. The Journal of Clinical Endocrinology & Metabolism 2003;88(7):3005-10.
[24] Hill AG, Hill GL. Metabolic response to severe injury. British Journal of Surgery 1998;85(7):884-90.
[25] Naz A, Junaid T. Estimation of CRP levels on a measure of stress response after laparoscopic and open cholecystectomy. Pak J Surg 2017;33(1):4-8.
[26] Buganda D, Allegri M, Lavand'homme P, et al. Inflammation-based scores: a new method for patient-targeted strategies and improved perioperative outcome in cancer patients. Article ID 142425, BioMed Research International 2014;(2014): p.11.
[27] Rittler P, Jacobs R, Demmelmair H, et al. Dynamics of albumin synthesis after major rectal operation. Surgery 2007;141(5):660-6.
[28] Ishizuka M, Nagata H, Takagi K. Clinical significance of the C-reactive protein to albumin ratio for survival after surgery for colorectal cancer. Annals of Surgical Oncology 2015: p. 1-8.
[29] Ryan AM, Hearty A, Prichard RS, et al. Reynolds, Association of hypoalbuminemia on the first postoperative day and complications following esophagectomy. Journal of Gastrointestinal Surgery 2007;11(10):1355-60.
[30] Hart DW, Wolf SE, Mlcak R, et al. Persistence of muscle catabolism after severe burn. Surgery 2000;128(2):312-9.
[31] McMillan DC. The systemic inflammation-based Glasgow Prognostic Score: a decade of experience in patients with cancer. Cancer Treatment Reviews 2013;39(5):534-40.
[32] Fleck A, Colley CM, Myers A. Liver export proteins and trauma. British Medical Bulletin 1985;41(3):265-73.
[33] Hulshoff A, Schricker T, Elgendy H, et al. Albumin synthesis in surgical patients. Nutrition 2013;29(5):703-7.
[34] Hübner M, Mantziari S, Demartines N, et al. Postoperative albumin drop is a marker for surgical stress and a predictor for clinical outcome: a pilot study. Article ID 8743187, Gastroenterology Research and Practice 2016;(2016): p. 8.