Annexures

ANNEXURE I : Scientific Publications ... 2
ANNEXURE II: Synopsis and Proforma ... 5
ANNEXURE III: Copy of CASR Approval ... 15
ANNEXURE IV: Curriculum Vitae ... 18
ANNEXURE V: Reprints of Papers ... 45
ANNEXURE VI Master Chart ... 60
ANNEXURE I: SCIENTIFIC PUBLICATIONS

A. Paper Published in part from the Present Thesis Work


B. Previous Personal Publications Relevant to the Present Thesis Work


C. Previous Personal Publications on Coagulation Response during Surgery under Inhalational Anaesthesia (A manifestation of systemic stress response)


D. Personal Previous Masters’ Thesis (Unpublished) WORK for Award of M.D. (Anaesthesiology) in 1988 on coagulation response during surgery under inhalational anaesthesia (A manifestation of systemic stress response)


E. Paper Presented in Conferences Related to Present Thesis

- Presented a paper in International Symposium on predictive, preventive, and mechanistic mutagenesis and XXXIII EMSI Annual Meeting, Jan.1-3, 2008, Department of Agricultural Microbiology, AMU, "Role of TNF-
alpha & CRP as stress marker during open and laparoscopic cholecystectomy in patients fit for laparoscopic cholecystectomy”.


ANNEXURE II: SYNOPSIS AND PROFORMA

**Topic for Ph.D. Thesis:**

"A Prospective Biochemical Study of Systemic Stress Responses during Cholecystectomy and Abdominal Hysterectomy."

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*(Teacher Candidate)*

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Aligarh Muslim University (A.M.U.),

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INTRODUCTION

Injury to human body alters normal physiology across several systems, and these alterations are usually proportional to the extent of injury. Surgery being a form of injury evokes release of various acute phase reactants, along with other circulating factors (1). The capacity to produce circulating factors, the cytokines is central to the regulation of the immuno-inflammatory responses. Acute phase protein response appears to be one example. Cytokines and their inhibitors are thought to be involved in many of the patho-physiological changes associated with trauma and infection. The magnitude of trauma and the degree of tissue damage has an impact on the trauma responses (1). The trauma of surgery evokes metabolic, endocrine, haemodynamic & inflammatory changes in the body. This includes stimulation of pituitary-adrenal axis, activation of sympathetic nervous system, and increase in glucagon secretion, acute phase protein response and release of inflammatory mediators. Stress responses manifested as tachycardia, hyperglycemia, adipose tissue mobilization & activation of coagulation cascade (2). The response of adrenal cortex to this stress during anaesthesia & surgery can affect the whole outcome of the patient. It has detrimental effects in upper abdominal surgery specially the biliary tract surgery as compared to other surgeries. This stress may lead to lethal consequences due to relative or absolute increase in sympathetic tone during elective cholecystectomies results in tachycardia, hypertension, dysrrhythmias, ventricular ectopics, angina or myocardial infarction (3, 5, &7). Even pulmonary edema during intra-operative period is an important cause of postoperative morbidity & mortality. This reflex response is mediated through reflex stimulation of adrenal gland, through coeliac plexus and during surgical manipulation of gall bladder (7, 8).
Various researchers had tried to block these responses by Para vertebral block/Intercostal nerve block/Splanchnic nerve block/Extradural block or even by varying dozes of fentanyl & remifentanyl (4, 10, 11, 12 &15). Knowledge of the above disturbances is of paramount importance to both surgeon & anaesthetist during anaesthesia & surgery to deliver adequate and proper care to the patient during peri-operative period. These changes assume more importance in patients in whom cardiovascular system is the seat of proclaimed or latent disorders, especially in patients undergoing major operations. Recently laparoscopic surgery has gained popularity as day stay stress-free minimally invasive surgery, in comparison to open surgery. Recent developments have allowed most intra abdominal procedures to be performed by the laparoscopic technique. However, a critical assessment of randomized, controlled studies and meta-analysis comprising laparoscopic and open surgery has not convincingly shown that laparoscopic surgery improves the outcome, except in a few operations (16, 17, 18, 19 &20). However, biochemical data to support the safety of this procedure is sparse. Therefore, this study is being undertaken to determine the extent of systemic stress responses in the form of acute phase reactants, hormonal, metabolic and haemodynamic changes during open and laparoscopic abdominal surgery in order to evaluate its implications in relation to safe conduct of anesthesia & post-operative recovery.
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- Murphy, Dermot F. Continuous intercostal nerve block. *Anesthesiology* 1986; 64(5): 669.


• Okajima K. Regulation of inflammatory responses by natural anticoagulants. *Immunol Rev* 2001; 184: 258-274.

• Okajima K. Regulation of inflammatory responses by natural anticoagulants. *Immunol Rev* 2001; 184: 258-274.


• Sherwood ER. Inflammatory response current concepts. In: 57th Annual refresher course lectures and Basic Science Reviews, presented during the annual meeting of American Society of Anaesthesiologists, 2006.


• Tracy RP, et al. Relationship of C-reactive protein to risk of cardiovascular disease in elderly; results from cardiovascular health study and the rural health promotion project. *Arter Thromb Vas Bio* 1997; 17: 1121-1127.


• Wallace LK, Starr NJ, Leventhal MJ, Estafanous FG. Hyperglycemia on ICU admission after CABG is associated with increased risk of mediastinitis or wound infection. *Anaesthesiology* 1996; 85(Suppl): A286.


AIMS AND OBJECTIVES

1. To evaluate hemodynamic changes in normotensive (BP < 130/80 mmHg) and treated hypertensive patients during open abdominal hysterectomy and open & laparoscopic cholecystectomy in terms of clinical parameters.

2. To evaluate hormonal and metabolic disturbances in normotensive & treated hypertensive patients during open abdominal hysterectomy and open & laparoscopic cholecystectomy by determination of plasma cortisol, catecholamines and plasma glucose levels.

3. To evaluate changes in acute phase reactants in normotensive & treated hypertensive patients in terms of cytokines, namely TNF-α as well as expression of serum proteins, during open abdominal hysterectomy and open & laparoscopic cholecystectomy.

MATERIAL & METHOD

The study will be performed after approval through the ethical standard of institutional committee for the procedure. Normotensive (BP < 130/80 mmHg) or treated hypertensive patients (ASA grade I&II) posted for elective open abdominal hysterectomy and open & laparoscopic cholecystectomy will be taken up for the present study. After prior information regarding the nature of the study to the patient, informed consent will be obtained for collection of venous blood. Patients developing hypoxia, hypercarbia and acidosis during anaesthesia or on steroid therapy will be excluded from the study.
The patients will be randomly allocated to open cholecystectomy or laparoscopic cholecystectomy or open abdominal hysterectomy. Following clearance from pre-anaesthetic check-up patient will be received in operation theatre, after preoxygenation for 3 mins. Induction will be done with inj thiopentone sod. (5 mg/kg). Endotracheal intubation will be facilitated with inj succinyl choline (1.5 mg/kg). Anaesthesia will be maintained on nitrous oxide in oxygen along with vecuronium bromide (0.08 mg/kg) and fentanyl (0.002 mg/kg) for surgical procedure. Monitoring will be done peri-operatively with BP, Heart rate, MAP, pulse-oximetry, and electrocardiography. Blood sampling for catecholamine, plasma cortisol, and plasma glucose, TNF-α, and C-reactive proteins will be done in sterilized pre treated vials: a) before induction of anaesthesia b) half an hour following start of operation, c) at the end of operation, d) 24 hours following surgery, and e) 4th postoperative day.

Statistical analysis will be done with standard statistical methods as applicable.

REVIEW OF LITERATURE

Endocrine-metabolic response to surgery anaesthesia has been studied since long (2, 3, 4, 5, 7, 10, 11) with varying results. Initially the concomitant secretion of the peptides as β-endorphin and adrenocorticotrophic hormone (ACTH) from the pituitary in response to acute stress was described in the rat by Guillemin and colleagues (12, 13). Since then an increase in circulating catecholamine, adrenaline, and plasma cortisol concentration has been discussed in a variety of clinical conditions including surgery and anaesthesia. However, the effects of different anaesthetic techniques on
the changes in plasma cortisol, catecholamine concentration associated with surgery have received little attention. Onset of surgery is associated with prompt increase in plasma concentration of noradrenaline & adrenaline. This sympatho-adrenal activation persist into postoperative period (14.)

Kehlet H. 1982(12), had used extensive epidural (up to T 4) anaesthesia to modify the stress induced, adrenocortical responses, but not able to abolish these responses completely. Anaesthetist attempt to modify the endocrine& metabolic responses to surgery have yet to show consistent and worthwhile benefits.

Regional anaesthesia is effective for pelvic and limb surgery only. Even high dose opiates become inefficient in early postoperative period (16). Therefore, this aspect of response has to be investigated thoroughly so that rationale attempt can be made to obtund the diverse metabolic changes to minimize perioperative morbidity and mortality.

REFERENCES


• Kehlet H. The modifying effect of general and regional anesthesia on the endocrine & metabolic response to surgery. *Regional Anaesthesia* 7(s) 1982; 38.


**PROFORMA**

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<th>Control Group/Study Group</th>
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**Particulars Of patients:-**

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<th>Weight</th>
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<td>Ward/Bed</td>
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<tr>
<td>DOA</td>
<td>DOO</td>
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**Chief Complaints:-**

**Detailed History with special emphasis on history of:**
- IHD, HTN, Valvular Heart Disease, Heart Blocks, CHF
- Asthma, COPD, DM, TB, Stroke, chronic medication
- Allergy to any drug, Addictions, Antipsychotic drugs

**General Examination:**

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<td>Clubbing Koilonychias</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
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<td>Edema</td>
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<td>MP Grade-</td>
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**Systemic Examination:-**

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<tr>
<td>CVS</td>
<td>Abdomen</td>
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</table>

**Investigations:-**

1. Hb Gms%
2. Total Leucocytic Count (TLC)
3. Differential Leucocytic Count (DLC)
4. Erythrocyte Sedimentation Rate (ESR)
5. Blood Sugar (BS)
6. Blood Urea (BU)
7. Serum Creatinine (SCr)
8. Chest X-Ray (CXR)
9. Electrocardiogram (ECG)

**American Society of Anesthetists (ASA) Grade:**

1. ASA Grade I
2. ASA Grade II

**Proposed Surgery:**

1. Open Abdominal Hysterectomy
2. Open Cholecystectomy
3. Laparoscopic Cholecystectomy

**Anaesthetic technique:**
**Total Duration of Surgery:**

**Monitoring:**

<table>
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<th>Timings for monitoring &amp; Sampling</th>
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<th>½ hour after incision</th>
<th>End of op.</th>
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<th>4&lt;sup&gt;th&lt;/sup&gt; postop.</th>
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<td>D.B.P. (mmHg)</td>
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<td>M.A.P. (mmHg)</td>
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<td>SpO₂</td>
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<td>E.C.G. changes</td>
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<td>B.Glucose mg/dl</td>
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<td>Adrenaline nmol/L</td>
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<tr>
<td>Noradrenaline nmol/L</td>
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<tr>
<td>C-reactive proteins</td>
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<tr>
<td>TNF-alpha nmol/L</td>
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**Per-operative Complications:**

**Post-operative Complications:**
ANNEXURE III: COPY OF CASR APPROVAL

OFFICE OF THE DEAN, FACULTY OF MEDICINE
JNMC, AMU, ALIGARH

DRAFT MINUTES

of the special meeting of the Committee for Advanced Studies and Research, Faculty of Medicine, AMU, Aligarh held on 21 09 2004 at 12.05 PM in the office of the Vice-Chancellor, following were present:

1. Mr. Naseem Ahmad, Vice-Chancellor (in the chair)
2. Prof. Shamim J. Rizvi, Dean, faculty of Medicine
3. Prof. S.H. Hashmi, Chairman, Dept. of Oral Surgery, Dental College
4. Prof. Javed A. Usmani, Chairman, Dept. of Fore. Medicine
5. Prof. M.K.A. Shereen, Chairman, Dept. of Orth. Surgery
6. Prof. S.C. Sharma, Chairman, Dept. of ENT
7. Dr. D.K. Agrawal, Chairman, Dept. of Physiology
8. Prof. Jamal Ahmad, Chairman, Dept. of Medicine
9. Prof. Ashraf Malik, Chairman, Dept. of Paediatrics
10. Prof. M. Amanullah Khan, Chairman, Dept. of Surgery
11. Prof. Zakia Arshad, Chairman, Dept. of Gynaecology
12. Prof. Mudasir Aziz, Chairman, Dept. of Pathology
13. Prof. Shahzad Bano, Chairman, Dept. of Anaesthesiology
14. Prof. Zulfiqar Khan, Chairman, Dept. of Community Medicine
15. Prof. Abida Fatima, Chairman, Dept. of Microbiology
16. Dr. Gouta Rajput, Chairman, Dept. of Prosthodontics, dental College
17. Dr. S.M. Yunus, Chairman, Dept. of Anatomy
18. Dr. R.A. Khan, Chairman, Dept. of Pharmacology
19. Prof. Rashid Ali, Chairman, Dept. of Biochemistry

Item No.1 Considered and approved the admission of the following candidates in Ph.D. course in the Department of Biochemistry, Faculty of Medicine as recommended by the Special meeting of BOS, Dept. of Biochemistry dated 31 08 2004.

1. Name of the Candidate : Mr. Nadeem Ahmad Ansari
   Supervisor : Prof. Rashid Ali
   Department of Biochemistry, J.N. Medical College
   A.M.U. ALIGARH

2. Name of the Candidate : Mr. Amir Khan
   Supervisor : Prof. Z.H. Beg
   Department of Biochemistry, J.N. Medical College
   A.M.U. ALIGARH

3. Name of the Candidate : Mr. Mudasir Saima Khan
   Supervisor : Prof. Z.H. Beg
   Department of Biochemistry, J.N. Medical College
Considered and approved the protocol for supplication of Ph.D thesis of Dr. Mrs. Shahla Haleem, Reader Dept. of Anaesthesiology, JNMC, AMU, as teacher candidate as recommended in the Special meeting of the BOS held on 26.8.2004.

Name of teacher: Dr. Shahla Haleem, Reader, Dept. of Anaesthesiology, JNMC, AMU

Topic: "A Prospective Biochemical Study if Systemic Stress Responses during Cholecystectomy and Abdominal Hysterectomy"

Considered and approved the protocol for supplication of Ph.D theses of Dr. Seema Hakim, Reader, Dept. of Obst & Gynae, JNMC, AMU, as teacher candidate, as recommended in the Special BOS held on 25.8.2004.

Name of teacher: Dr. Seema Hakim, Reader, Dept. of Obst. & Gynec, JNMC, AMU

Topic: "Expression profiling to identify molecular markers of uterine receptivity and embryo implantation"

Considered and approved the protocol for the supplication of Ph.D theses of Dr. Mohd. Shahid, Lecturer, Dept. of Microbiology, JNMC as teacher candidate, as recommended in the Special meeting of the BOS 31.8.2004.

Name of Teacher: Dr. Mohd. Shahid

Topic: "A clinic-microbiological study on aspergillosis in Patients Bronchogenic carcinoma"

Supervisor: Prof. Abida Malik, Chairman, Dept. of Microbiology, JNMC, AMU

Considered and approved the protocol for the supplication of Ph.D theses of Dr. Mohd. Athar Ansari, Lecturer, Dept. of Community Medicine, JNMC as teacher candidate, as recommended in the special BOS 21.8.2004.

Name of Teacher: Dr. Mohd. Athar Ansari

Topic: "A study of iodine deficiency disorders and the impact of intervention package to improve the consumption of iodised salt"

Supervisor: Prof. Zaffar Khan

Chairman, Dept. of Community Medicine, JNMC, AMU
Item No. 4 Reported the action taken by the BOS of concerned Department regarding rejection of following application forms of the Ph.D candidates:

1. Mr. Deepri Mittal (Dept. of Biochemistry, JNMC) BOS 31.8.2004
2. Prof. Chetali Gupta (Dept. of Biochemistry, JNMC) BOS 31.8.2004
3. Ms. Reena Ahuja (Dept. of Biochemistry, JNMC) BOS 31.8.2004
4. Mr. Shehab Khan (Dept. of Biochemistry, JNMC) BOS 31.8.2004
5. Dr. Neetu Sinha (Dept. of Biochemistry, JNMC) BOS 31.8.2004
6. Ms. Nazira Khan (Dept. of Biochemistry, JNMC) BOS 31.8.2004
7. Ms. Shabana Khan (Dept. of Biochemistry, JNMC) BOS 31.8.2004
8. Mr. Sohail Hussain (Dept. of Biochemistry, JNMC) BOS 31.8.2004
9. Mr. Seeral Zafar Ali (Dept. of Biochemistry, JNMC) BOS 31.8.2004
10. Mr. Hina Ayaz Khan (Dept. of Biochemistry, JNMC) BOS 31.8.2004
11. Ms. Akhlaqul Khatun (Dept. of Biochemistry, JNMC) BOS 31.8.2004
12. Miss. Hina Ayaz Khan (Dept. of Medical, JNMC) BOS 31.8.2004

Item No. 5 Considered and approved the deputation of Ms. Sara Afaq, Ph.D students Dept. of Biochemistry from 8.8.2004 to 14.4.2004 in the laboratory of Prof. Hasan Mukhtar, Dept. of Dermatology, University of Wisconsin, WI, USA, for some thesis related research work.

Item No. 6 Considered and approved the minor change in the thesis topic of Miss Anju Tyagi, a student for Ph.D in Microbiology

Topic (original) "Bacteriological profile and Molecular Characterization of Staphylococcus aureus isolated from clinical specimens and food products"

Topic (after change) "Phenotypic and Molecular characterization of Staphylococcus aureus isolated from clinical specimens and food products of animal origin"

Meeting closed with vote of thanks

(Prof. Shamim J. Rizvi)
Dean

PS Errors omission or any kind of discrepancy in recording the minutes, if found, be informed to this office within a week, if no comments are received in this office with in stipulated time it would be presumed that the minutes are recorded correctly.

Distribution
All members of CASR for Medicine
Controller of Admission & Examination
Registrar (Academic)
PA To VC for information

17
ANNEXURE IV: CURRICULUM VITAE

Dr. (Mrs.) Shahla Haleem

Address for Correspondence:

Department of Anaesthesiology
Jawaharlal Nehru Medical College & Hospital
Aligarh Muslim University, Aligarh 202002, India

Email: shahlahaleem@yahoo.co.in

Phone: +91 9997448172

Professional Qualifications:

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<td>1</td>
<td>M.D. (Anaesthesiology)</td>
<td>1988 July</td>
<td>J. N. Medical College, A.M.U., Aligarh</td>
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<td>(Passed in 1st attempt)</td>
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<tr>
<td>2</td>
<td>D.A. (Anaesthesiology)</td>
<td>1986 July</td>
<td>J. N. Medical College, A.M.U., Aligarh</td>
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<tr>
<td></td>
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<td>(Passed 1st attempt: 60.25%)</td>
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<tr>
<td>3</td>
<td>M.B.B.S</td>
<td>1982 July</td>
<td>G.S.V.M. Medical College, Kanpur</td>
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<td></td>
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<td>(Aggregate 55.6% marks)</td>
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<tr>
<td>4</td>
<td>Internship</td>
<td>1983 July: Compulsory Rotatory Internship in all Clinical Subjects</td>
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Professional Clinical Experience: 25 years (Total)

(22years +4 months) & (2 years +8 months)

(A). After Registrarship (22yrs.4 months):

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<th>TO</th>
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(B). Before Registrarship (2yrs. & 8 months):

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<td>2</td>
<td>Junior Resident in Anaesthesiology</td>
<td>1 yrs. &amp; 3 months</td>
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<td>31.01.85</td>
<td>Sher-e-Kashmir Institute of Medical Sciences, Srinagar</td>
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* Includes E.O.L period from 19.5.1999 to 18.5.2001, worked as specialist in Kingdom of Saudi Arabia, Mecca.

**Permanent Medical Registration No:** 27320, UP Medical Council, Lucknow.

**Publications and Academic Work:**

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<tr>
<td>XII</td>
<td>MEMBERSHIP OF ACADEMIC BODIES</td>
<td>5</td>
</tr>
<tr>
<td>XII</td>
<td>PUBLIC HEALTH FIELD SERVICES</td>
<td>2</td>
</tr>
<tr>
<td>XI</td>
<td>CONTRIBUTION TO KNOWLEDGE IN MEDICAL SCIENCE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A. USED UNUSUAL TERMINOLOGY</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B. DESCRIBED RARE CONDITIONS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C. SUCCESSFUL ATYPICAL TREATMENT USED</td>
<td></td>
</tr>
<tr>
<td>X</td>
<td>INTERNATIONAL RECOGNITION OF ACADEMIC WORK</td>
<td></td>
</tr>
</tbody>
</table>
List of Original Papers Published by Dr. Shahla Haleem:

(A) PAPERS PUBLISHED IN INTERNATIONAL JOURNALS


(B) PAPERS PUBLISHED IN NATIONAL JOURNALS


36. Haleem S, Ansari MM, Shakoor A, Bano S. Prospective Study Of Changes In Serum Calcium After Diethyl-Ether Anaesthesia (Abstract). Indian Journal of Medical Sciences July 1990.


(Including papers related to Ph.D. thesis)
(C) Conferences/Workshops/Symposiums Attended from 1998 (Appointed Reader) to till date


4. **International Anaesthesia Review 06.** Held at Christian Medical College, Ludhiana and jointly organized by CMC and Mayo Clinic College of Medicine (U.S.A.) on 6th to 7th March 06.


7. **Participated in Anaesthesiology & Criticalcare-2003 for World Federation of Societies of Anaesthesiologists & Indian Society of Anaesthesiologists at Himalayan Institute of Medical Sciences, Dehradun on 7th-8th June 2003.**

8. **Participated in Trauma CRITICARE 2003, 7th Conference of “International Trauma Anaesthesia & Critical Care Society”, 26-28th September 2003, New Delhi, INDIA.**

9. **Participated in First International Conference on Trauma and Critical Care at AIMS, New Delhi & Apollo Hospital New Delhi from 22nd-24th November 1996.**

10. **Participated in Workshop on Advanced Intraoperative Monitoring organized by Indraprastha Apollo Hospitals New Delhi on Feb16, 2002.**

11. **Participated CME workshop 98 on “Perioperative Monitoring” 28-29th November 1998 at SGPGI, Lucknow, INDIA.**

12. **Participated in district level training on HIV/AIDS by J. N. Medical College by U.P. State AIDS Control Society, Lucknow from 11th to 13th September 2001.**
13. Participated in prevention of parent to child transmission (PPTCT) programme in Department of Obstetric & Gynaecology at J N Medical College, AMU, Aligarh, Sept.2006

14. Participated in EmOC Training (emergency obstetric course training) in Department of Obstetric & Gynaecology at J N Medical College, AMU, Aligarh, from 16-23rd November 2006.


17. Attended and participated ISACON-2004, 52nd Annual National Conference of Indian Society of Anaesthesiologists, 26th -30th December 2004, Bhopal


20. Participated in 16th Plastic surgery workshop, UP Chapter, as Consultant In charge of anaesthetic team, held on 16th -19th Feb. 08.

21. Participated in 32 Annual conference UP Chapter of Orthopaedic Association, as Consultant In charge of anaesthetic team, for workshop “Spinal Instrumentation and Locked Compression Plating (LCP)” held on 1st-3rd Feb. 08.

22. EmOC training of Gynaecologist in JN Medical College, AMU, Aligarh, from Feb-April(6 weeks) 2008 on Post operative Care and Endotracheal Intubation Delivered Guest Lecture, demonstration & session as long clinic.


24. Attended and Participated in International Symposium on predictive, preventive, and mechanistic mutagenesis and XXXIII EMSI Annual Meeting, Jan.1-3, 2008, Department of Agricultural Microbiology, AMU, presented a paper “role of TNF-
alpha & CRP as stress marker during open and laparoscopic cholecystectomy in patients fit for laparoscopic cholecystectomy.

25. Attended and participated in 1st National conference on obstetric anaesthesia (FNCOA) and 1st International Pre-conference workshop on OBSTETRIC ANAESTHESIA 5th -7th September, 2008 at Chennai. Paper presented was “single shot spinal anaesthesia versus combined spinal epidural anaesthesia for lower segment caesarian section”.

(D). Invited Faculty & Chaired Session at Conferences


5. Critical Care Update-2005, 19-20 November at J N Medical College AMU, Aligarh. Participated by Chairing Session

6. Refresher Course for the Faculty of Medicine 1st -21st Nov 2006. Theme: Recent Advances in Medical Care. Invited Lecture on 18.11.06 “Recent HIV Strategies in Anaesthesia Practice”.

7. EmOC training of Gynaecologist in JN Medical College, AMU, Aligarh from 16-23 November 2006 on Ketamine & Spinal Anaesthesia. Delivered Guest Lecture and taken long clinic.
8. EmOC training of Gynaecologist in JN Medical College, AMU, Aligarh from Feb.-April (6 weeks) 2008 on Post operative Care and Endotracheal Intubation. Delivered Guest Lecture, demonstration and taken long clinic.

9. CONTUING MEDICAL EDUCATION (C.M.E.) organized by Department of Qabalat-wa-amraz-e-niswan, Ajmal Khan Tibbiya College, Faculty of Unani Medicine, AMU, Aligarh, sponsored by Department of AYUSH, Ministry of Health & Family Welfare, Govt. of India, New Delhi. Delivered guest lecture on 3.08.08. Topic: “Pregnancy Induced Hypertension”.

10. PG assembly 2008 october at Maulana Azad Medical College, New Delhi, participated as invited faculty, Topic “Thoracic Anaesthesia”.

(E). Conferences/Workshops/Symposiums Attended From 1985 to 1998:

1. ‘14th Annual Conference of U.P. Chapter of Association of Surgeons of India’ at Jawaharlal Nehru Medical College, A.M.U., Aligarh, on December 3-4, 1988.


6. ‘National Symposium on Pests, Parasites & Environment’, held at Aligarh Muslim University, Aligarh, on December 17-19, 1990.


9. ‘14th Annual Conference of Indian Society of Anaesthesiologists (U.P. Chapter)’. Held at Nainital Club, Nainital, on April 4-5, 1992.

10. Indo-U.S. Workshop on Problem Based Learning and Computer Oriented Teaching in Medical Sciences held at J.N. Medical College, A.M.U., Aligarh, November 11-13, 1997.


(F). Paper Presented/Received at Conferences from October 1998 to till date

(* speaker)


3. MU Zafer*, Shahla Haleem, MR Malik, M Alam. “Effective dose of esmolol required to blunt the circulatory responses to laryngoscopy and tracheal intubation: a comparison of three doses.” UPISACON 2003, 1-2 November 2003 at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, UP.


5. Yasir A Khan*, Shahla Haleem, A.Bhardwaj, Abu Nadeem. “Prospective evaluation of anesthesia for spinal surgeries: The effectiveness of spinal
anesthesia in combination with general anesthesia for controlled hypotension".

6. **Shahla Haleem** Participated and presented poster on “pH adjustment and epidural blockade” in *Anesthesiology & Criticalcare-2003* for World Federation of Societies of Anaesthesiologists & Indian Society of Anaesthesiologists at Himalayan Institute of Medical Sciences, Dehradun on 7th -8th June 2003.


(G). Paper Presented/Received at Conferences from 1988 to before October 1998:

(* speaker)


15. M.M. Ansari*, M.H. Beg, Shahla Haleem. "Early Decortication of Pleural Empyemas". XVII Annual Conference of Association of Surgeons of India with
Annual Conference of International College of Surgeons (Indian Section-North Zone) held at G.S.V.M. Medical College, Kanpur, on 9-10th Nov. 1991.


24. P. Malhotra*, A. Shakoor, Shahla Haleem. "ECG Changes during Induction in Treated Hypertensive Patients Following Different Induction Techniques". XLI Annual National Conference of I.S.A. held on 27\textsuperscript{th} -30\textsuperscript{th} Dec., 1993 at Bangalore.

25. R. Gulati*, Shahla Haleem. "Levels Auto-antibodies in the Cerebro-spinal fluid in the Apparently Healthy Population". Second Asian Pacific Society for Neurochemistry (APSN) Meeting held on 14\textsuperscript{th} -16\textsuperscript{th} April, 1994 at Hyderabad.


29. P. Agarwal*, Shahla Haleem, A. Shakoor, H.K. Garg. “Serum zinc and Copper Levels in Normotensive Hypertensive Patients during Anaesthesia”. XVIII Annual Conference of I.S.A. U.P. Chapter) held on 6\textsuperscript{th}-7\textsuperscript{th} April 1996 at Meerut.

30. Shahla Haleem*, M.M. Ansari, V.K. Srivastava. “Neuro-anaesthesia-7 Years Audit at J.N. Medical College, Aligarh”. Ist International Conference on Trauma & Critical Care, held on 22\textsuperscript{nd} -24\textsuperscript{th} Nov,’ 1996 at AIIMS, New Delhi. Paper Presentation. Paper Presentation


32. Shahla Haleem*. “Anaesthesia for total hip replacement”. XXII annual conference of Indian Orthopaedic association (U.P. Chapter) held on 12-14\textsuperscript{th} February, 1999 at AMU, Aligarh.

(H). Doctoral theses Supervised for M.D. / M.S.

(i). Supervisor for M.D. (Anaesthesia) Theses

1. Effect of PH adjustment of lignocaine and lignocaine bupivacaine solution on onset and duration of epidural analgesia.


3. A comparative study of laryngeal view and pressor response by using three different blades Macintosh, Miller and McCoy blades.
Submitted: 2005 January. Candidate: Dr. Gaurav Dwivedi.

4. Comparison of use of Classic laryngeal mask airway and Proseal laryngeal mask airway in elective surgical cases.
Submitted: 2005 July. Candidate: Dr. Tanu Shree.


6. Identification of epidural space by loss of resistance technique. Comparison of three different approaches.
Submitted: July 2007. Candidate: Dr. Aftab Ahmad.

7. A Comparative study of three different regimes to facilitate LMA insertion in children.

8. Left Lateral Vs. Supine Wedged Position After Spinal Anaesthesia For Caesarian Section: Block Characteristics and Severity of Hypotention.
To be submitted in 2010. Candidate: Shyam Bhandari.

Candidate: Dheeraj Sharma, 2008-2011.

(ii). Co-supervisor for M.D. (Anaesthesia) Theses

1. A clinical comparative study of Vecuronium Bromide and tracurium Besytate.

2. Effects of general anaesthesia on cognitive function.
Submitted: 1993, Candidate: Dr. Zubair Abbas.

3. An evaluation of cardio-vascular effects of intubation under different induction techniques.


5. Chances in arterial oxygen saturation during induction of anaesthesia and intubation.

6. Comparative study of lignocaine (by intravenous, oral viscous or laryngeal routes) on the pressor changes during laryngoscopy and tracheal intubation.

7. An evaluation of peri-anaesthetic changes in trace elements in normotensive and hypertensive patients.
Co-supervisor for M.S. (surgery)

1. Cholecystocardiac link—an intra-operative evaluation during biliary tract surgery.
   Submitted: 1992, Candidate: Dr. Arshad Jamal.

2. Objective assessment of patient’s tolerance to inguinal hernia repair under local anaesthesia: A Prospective study.

Certificate of Honour

1. An special certificate of honour & appreciation from IMPACT INDIA FOUNDATION An International Initiative Against corrective disorders, for voluntary services to Lifeline express 27th January06 –to -27th February 2006 at Babrala (UP).


Certificate of Appreciation

1. From IMPACT INDIA FOUNDATION An International Initiative Against corrective disorders, for voluntary services to Lifeline express 27th January06–to-27th February06 at Babrala (UP) by Tata Chemical Society for rural development.

Specialized Training Courses done:

1. Training Course for Drager equipment and has been instructed for use and application of the following device: Evita 4, place of training Makkah, Hera-Hospital. Date of training 6th February, 2001.
2. Completed National Teachers Training Course at Maulana Azad Medical College, New Delhi in the Department of Medical Education at National Teachers Training Centre in recognition of workshop on “Educational Science Technology for Teachers of Health Professionals” from 19 to 28 November, 2001.

(vii). Individual Research Project


(viii). Contribution to the Department / University

- Worked as coordinator of “Diploma in anesthetic Assistance” Course and actively participated in initiation of course.

(ix). Membership of Academic Bodies

1. Life member of Asian Archives of Anaesthesiology & Resuscitation. And National Association of Critical Care Medicine (INDIA).
2. Life Member of Indian Journal of Anaesthesia, Membership no. S1215.
3. Life Member of Journal of Anaesthesiology & Clinical Pharmacology, Membership no. H007 L.
5. Member of Indian Association of Obstetric Anaesthesiologist. H-5
(x). Public Health Field Services

1. Provided to IMPACT INDIA FOUNDATION An International Initiative Against corrective disorders, for voluntary services to Lifeline express 27th January 06-to-27th February 06 at Babrala (UP) organized by Tata Chemical Society for rural development.

2. Provided to Rotary International, Polio Corrective Surgery & Rehabilitation programme by Rotary Club, Aligarh from Feb 05 to March 05.

(xi). Contribution of knowledge In Medical Science

(a) Unusual Terminology used
- “Cholecystocardiac Link”
- “Vocal Cord Protest”
- “Platelet dysfunction after diethyl ether anaesthesia”
- Haemodynamic Consequences of LMA
- pH Adjustment for Epidural Blockade.

(b) Described Rare Conditions
- Stiff Chest Syndrome & Thyrotoxicosis
- Malignant Tachycardia: A Sole Presentation of Thyroid Crisis
- Tube-in-tube Tracheal Intubation Mimicking Bronchospasm
- Barotrauma to Lung following Endo-tracheal Intubation
- Post extubation pathologic Aerophagy: A sign of progressive airway obstruction
- Survival after Prolonged Failed Resuscitation- a case of “Lazarus Syndrome”
- “Fall in heart rate triggered by the Sellick’s manoeuvre”
- Acute Isoniazid Poisoning with double dose of daily medication
• "Sustained Muscular Spasm" induced by Suxamethonium
• Platelet dysfunction after diethyl ether anaesthesia
• Giant hydatid cyst of lung: a plea for double lumen endobronchial tube
• Low potassium syndrome secondary to third space losses.
• Glycopyrronium Induced "Central Anticholenergic Syndrome".
• Continuous thoracic epidural as sole anaesthesia for upper abdominal surgery
• Barotrauma: An unusual cause of Bilateral Tension Pneumothorax.
• Broken Tracheotomy Tube
• Audiometric changes following Spinal Anaesthesia

(c). Successful Atypical Treatment Used & Published

• Massive Atropinization in Combined Poisoning of Insecticide & Rodenticide.
• Acute propanolol therapy in thyroid surgery
• Epinephrine infusion role in modern CPR
• Continuous Intravenous Thiopentone Drip in Refractory Status Epilepticus.
• Intravenous Vitamin B6 in Suspected Acute Isoniazid Poisoning.
• Double Lumen Endo-bronchial Tube for operation on Giant Hydatid Cyst of Lung
• Continuous Thoracic Epidural As Sole Anaesthesia for upper Abdominal Surgery
• Dramatic Response Of Magnesium in a case of Difficult Weaning From Ventilator.
1. For work titled “Prospective study of changes in serum calcium after diethyl-ether anaesthesia”, published in Indian Journal of Medical Research (B) 1990; 92: 192-194.

   1. Dr. Hellenbrecht ..... (Germany)
   2. Dr. J.P. Layac ..... (France)
   3. Dr. Masuhiko Takaori ..... (Japan)
   4. Dr. Conxi Mora ..... (Spain)
   5. Dr. Danila Pericic ..... (Yugoslavia)
   6. Dr. J.C. Patel ..... (India)
   7. Dr. M. Dyhstra ..... (Netherlands)

2. For work titled “Cholecysto-cardiac Link”, published in Indian Journal of Medical Research (B) 1991; 94: 47-49.

   1. Dr. Armenio A. Santos ..... (Brazil)
ANNEXURE V: REPRINTS OF PAPERS

(RELATED TO PRESENT THESIS WORK)
Cortisol and Glyemic Response to Open and Laparoscopic Cholecystectomy - A Comparative Evaluation


ABSTRACT

Background: Serum cortisol & glucose levels have been monitored as markers of stress response to surgical incision. In this study we compared & validated the levels in patients undergoing cholecystectomy by open & laparoscopic approaches. We also aim to verify the claim that less tissue desolation is the cause of decreased stress levels in laparoscopic surgery.

Patients & Methods: 49 healthy patients with uncomplicated cholelithiasis, undergoing elective cholecystectomy either via open incision (OC24) or laparoscopic approach (LC24), were taken on the basis of power analysis. The anesthetic protocol was standardized and no glucose infusion was given during the peroperative period. Five blood samples were taken from each patient (preoperatively, intraoperative, postoperative - 0th, 24th and 48th). Quantitative assessment of serum cortisol was done by RIA and blood glucose by glucose oxidase method. Data were computed & analyzed with the help of software SPSS V.11, 1.2 two-tailed significance value <.05 considered significant.

Results: Significant (p<0.05) increase in blood glucose and cortisol levels were recorded in both the groups. During surgery greater rise in blood glucose levels were recorded in laparoscopic group (p<0.001), but the increase in blood glucose was continued in perioperative period in open group (p<0.001). Blood cortisol values were revealed more significantly during surgery and in postoperative period in open group as compared to laparoscopic group(p<0.001).

Conclusions: Our study suggests the occurrence of differential hormonal and metabolic response during the perioperative period in both methods of cholecystectomy. The classical stress response in term of blood glucose and cortisol are not changed greatly by reducing surgical trauma, as the stimuli for the stress response arise from visceral and peritoneal adventitious nerve fibres in addition to those from the abdominal wall.

KEY WORDS: Stress evalution, Serum cortisol, Serum Glucose, Laparoscopic cholecystectomy

The cellular or hormonal response against surgical trauma depends upon extent of this controlled deliberate injury. Intra, the normal physiology is altered across several organ systems. These alterations are directly proportional to the extent of injury which is assessed by measuring various acute phase reactants, along with other derailing factors. The capacity to produce circulating factors, especially the cytokines, is also central to the regulation of the immunoinflammatory responses, defense mechanisms and normal cell growth. Reaction of the body to surgical injury evokes endocrine, metabolic & behavioral reactions and trigger reflex responses will consist largely of various interactions between hypothalamic-pituitary-adrenal axis. This has been called "stress response" or "alarm reaction", therefore, hormonal and metabolic response to surgical injury indirectly reflects the alarming or modulation of body to the added stress, which in turn, affects the perioperative outcome.

The host response is graded according to the magnitude of operative procedure. Laparoscopic surgery is steadily gaining popularity over open surgical procedures and one of the purported advantages is the decreased magnitude of stress response as compared to conventional (open) methods. Conclusively, it suggests that the extent of stress due to surgical morbidity, however, still remains elusive. The therapeutic approach is an integral part of modern surgical practice, with the notion of "total or major surgery" evolving to "stress free surgery" on the part of patient as well as surgeon. We wanted to evaluate our anesthetic management in view of this stress. Quantification of the differences of response would enable us to plan a better form of anesthetic management and save help in formulating an effective institutional protocol. The current prospective study was undertaken in patients admitted for gall bladder surgery to evaluate the hypothesis that laparoscopic cholecystectomy produces less of metabolic and hormonal responses than open cholecystectomy using plasma cortisol and glucose levels as "response markers". We aim at evaluation of the extent & risk involved during perioperative period so that a rational anesthetic approach can be applied to abate the diverse metabolic and hormonal changes.

PATIENTS & METHODS

After approval of the University Board of Studies (BOS) and Committee for Advanced Scientific Research (CASR), patients attending the medical college from August 2004 to August 2006 were included in this study after informed consent. Patients with acute cholecystitis, pancreatitis, choledocholithiasis, malignancy, jaundice were excluded from the study.

The anaesthetic techniques and our decision were standardized. Thiopentone sodium (Senglyc), midazolam (Glygep), were used for induction. Tracheal intubation was facilitated with the help of

Drs. Shahia Heeem, Associate Professor, Aftab Ahmed, Registrar, Najmul Islam, Associate Professor, S. Bano, Professor, Deptt. of Anaesthalogy, Maulana Mohd. Ansari, Associate Professor, Deptt. of Surgery, Jawed Mussarat, Chairman and Dean, Braj Rai Singh, Student, Deptt. of Agricultural Microbiology, Faculty of Medicine J.N. Medical College, A.M.U. Aligarh 202002, U.P. INDIA

Correspondence: Dr. Shahia Heeem, Email: shahasheem@yahoo.co.in
HALEEM S; ST AL: PERIO®EVTIVE S'ReSS EVA.JATON WITH SERUV COR-|SCL AND FUSMA GLUCOSE

Vasorumium bromce (0.12nng/kg) where as anesthesia was maintained with 0.2-0.5% halothane with sixty percent nitrous oxide in oxygen. Surgical relaxation was maintained with intermittent repeated doses of hypnotic.

Intensive care unit (ICU) and surgical monitoring included I-1, M, MAP, EKG, pulse oximetry and STCO2. End-tidal carbon dioxide was maintained in the range of 30 to 35 mm Hg. The neuromuscular block was reversed with neostigmine (0.06mg/kg) and glycopyrrolate (0.006 mg/kg) at the end of surgery. All operations were performed after an overnight 8 hr fasting. The coen cholecystectomy was performed through right subcostal incision and laparoscopy by 4-trocar approach with electrocautery dissection. Pre-operative period was adjoined with carbon dioxide insufflation, maintaining intra-abdominal pressure of 12-15 mm Hg.

Pain to the patient was controlled by COX-2 inhibitor, was treated by

Injecting pentazocine (0.6 mg/kg body weight).

Intravenous fluid was drawn and collected in plain, sterile vials. Samples were sent immediately to biochemical laboratory for centrifugation at 3000 rpm for 10 min. for separation of serum. The sera were put in special tubes and transported in ice box for storage in deep freeze at -80° C in the laboratory where the biochemical analyses were done by the competent laboratory personnel based on the study.

Five blood samples were taken from each patient: (preoperatively, intraoperatively, postoperatively - 0hr, 24 hr and 48 hr).

Quantitative assessment of serum cortisol was done by RIA (radio immunoassay) and blood glucose by glucose oxidase method.

Statistical analysis was performed using SPSS v11.0. intra-group & inter-group comparison were done by paired & unpaired t-tests respectively. A 2-tailed p<0.05 was taken as significant.

RESULTS

A total of 42 patients were considered consisting of 21 in each group. O comparison of age, weight and duration of surgery both the groups were similar in age (55±1 and 55±8 years) weight (46±7 and 46±8 kg) and duration of surgery (03±9 and 8±4 minutes) for open and laparoscopic groups respectively (Table-1).

The statistical computations were done by using the software SPSS v11. The independent sample T-test was used for equality of means and Levene's test was used for equality of variances. The 95% confidence interval of mean difference (CII) with lower (L) and upper (U) limits for blood glucose was -7.023 and 7.689 (Lap) & -7.952 and 7.609(open) with 2-tailed significance value of 0.327 indicative of comparable stress involved in both groups in preoperative period. Intraoperative and end of surgery samples had a 2-tailed significance values of 0.34 and <0.001 respectively (Table-1). Conversely the 95% CI was -32.38L and -12.34EU and -10.81L and -6.85EU with 2-tailed significance values of the order of <0.001 on 1st and 2nd postoperative day reflecting differential impact of surgical stress by both types of surgery (kg-1).

The 2-tailed significance value of serum cortisol in preoperative stage and at tail an hour of operation was 0.732 & 0.331, as compared to basal level indicating insignificant differences in the intensity of stress between the two groups respectively. Furthermore, at 1st and end of surgery, 24 hr and postoperative, this 2-tailed significance (p-value) between the two groups became <0.001, indicating a persistent significant stress to the patients in open cholecystectomy as compared to the laparoscopic surgery. Results revealed that the blood cortisol level was altered consistently in open cholecystectomy compared to laparoscopic cholecystectomy and contrary to blood glucose, this rise in plasma cortisol level was continuous and did not return to base line as in the open group (Fig-2).

DISCUSSION

Both anaesthesia & surgery play an important role in triggering stress responses. Magnitude of trauma & degree of tissue damage has a definite impact on 'trauma response'. The role of laparoscopic approach in general surgery is definitely the way forward. Considering the many advantages, I was surprised to learn that the enthusiasm of people on laparoscopic procedure declined in our institution. This study, therefore, was to assess the stress of stress involved to the patients by both techns cases. Blood glucose and serum cortisol are well established markers which have been

Table 1
Demographic profile

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Mean Blood glucose and Blood Cortisol levels following open and laparoscopic cholecystectomy</th>
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<tbody>
<tr>
<td>Sampling</td>
<td>Pre-Op.</td>
</tr>
<tr>
<td>B. Glucose (mg/d)</td>
<td></td>
</tr>
<tr>
<td>Group (open)</td>
<td>96.381±14.45</td>
</tr>
<tr>
<td>Group (Lap)</td>
<td>96.7±12±13.30</td>
</tr>
<tr>
<td>B. Cortisol (ng/ml)</td>
<td></td>
</tr>
<tr>
<td>Group (open)</td>
<td>211.47±19.56</td>
</tr>
<tr>
<td>Group (Lap)</td>
<td>423.30±19.38</td>
</tr>
</tbody>
</table>

47
Comparison of Blood Glucose (OC vs LC)

Figure 1

Showing glucose homeostasis, following laparoscopic (LC) and open cholecystectomy (OC).

The blood glucose level significantly increased following

used previously by several workers to evaluate stress quantification. We have noticed a different pattern in surgical trauma response; in terms of blood glucose and cortisol levels. Serum cortisol levels rise due to surgical stress was ameliorated postoperatively in laparoscopic group but the stress evolved to the patient by open procedure continued even in 1st and 2nd postoperative period (p<0.000). This could be due to lesser inflammatory healing response as significantly lower levels of dissections were done in the laparoscopic group. Blood glucose response was more marked in the laparoscopic group at half an hour and end of surgery but the surgical stress was abolished or minimized in both the groups on 1st and 2nd postoperative day. Differential elevation of plasma glucose during both techniques is also reported by Adrian et al (1996).
of plasma cortisol in both the groups was probably the reflection of additional stress to the patients due to surgical trauma which subsided in due course of time in laparoscopic group but continued in open cholecystectomy group. However, in open cholecystectomy, continued additional stress to patients, could be the interpretation of raised plasma cortisol in postoperative period. The raised blood glucose changes were likely to be induced secondary to hyperperfusion. The influence of soluble carbon dioxide on the corticol and axonal chemoreceptor enhances the sympathetic outflow mediated by different impulses to sub cortical centers. Simulation of sympathetic nervous activity causes elevation of blood glucose primarily by stimulating hepatic glycogenolysis, and suppresses insulin secretion. These accelerated stress responses persisted in intraoperative period only, reverted to normal level within 24 hours in accordance with other investigations. Aono and co-workers have done a comparative analysis, regarding attenuation of stress responses by three different techniques in CO₂ laparoscopic surgery. They observed that the larger dose of fentanyl or even thoracic epidural anaesthesia was unable to block or inhibit the hypothalamic-pituitary-adrenal axis response completely. According to Rademaker et al., peripheral stretching is considered to be an important contributory factor for accelerated metabolic responses in LC and advocated 20 ml of 0.25% bupivacaine to attenuate metabolic hormonal responses to laparoscopic surgery. Kristiansson et al. in 1999, on advanced biochemical study has found similar hormonal responses with varied biochemical, pain and fatigue response. We found cholecystectomy is a stressful surgical procedure, which modifies the stress response significantly, either performed through open incision or laparoscopically. Following laparoscopic surgery the stress hormonal responses were more pronounced during intraoperative period as depicted by serum cortisol levels. However, in the postoperative period catechol hormonal responses were more obvious and continued subsequent to open cholecystectomy. Thus, postoperative morbidity was significantly altered by the technique even as intraoperative parameters were comparable. The lesser dissection was most probably balanced by the stress induced by pneumoperitoneum in laparoscopic surgery.

These hormonal responses are reliable indicators of acute stress. They assume importance at centers with resource constraint where the long term outcome of the patients cannot be effectively evaluated using advanced markers. Current thrust is on advanced biochemical studies like acute phase reactants specialty cytokines, tumour necrosis factor & expression of serum proteins (C-reactive protein) to explore the underlying perceived differences. The analysis of the advanced markers may give greater insight to our effort in quantifying stress response.

However, all these aspects of our study, the direct role of serum cortisol and blood glucose with our observations warrants in-depth investigations and is our target for further investigation. It is hoped that the present study may help in understanding or throwing some light on the cellular mechanisms of patients subjected to stress or trauma.

ACKNOWLEDGEMENT

This research work was supported by grant from Aligarh Muslim University, Aligarh (UP), India and the study was done at Hormonal Laboratory, Dept of Agricultural Microbiology and Dept of Pathology (J.N. Medical College, AMU).

REFERENCES


17. Marek Mgdal Elzbieta Chudzynska- Pomianowska, Elizabeth Vause, Eugenia Henry, Jeffrey Lazar, PEDIATRICS Vol. 115 No. 4 April 2005, 393-398


CORRIGENDUM


Readers are requested to read the blood glucose level at the end of surgery in the OC Group (Open Cholecystectomy) as 146.619±13.249 instead of 138 619±13.249 in the Table 2, with consequently slight change in the Figure 1. These minor changes do not alter the overall results and conclusion.

Corrected Table 2 and Figure 1 are shown as under:

| Table 2 |

<table>
<thead>
<tr>
<th>Sampling</th>
<th>Pre-Op.</th>
<th>12 Hour</th>
<th>End of Op.</th>
<th>24 Hr Post op</th>
<th>48 Hr Post op</th>
</tr>
</thead>
<tbody>
<tr>
<td>B Glucose (mg/dl)</td>
<td>Mean ± S.D.</td>
<td>Mean ± S.D.</td>
<td>Mean ± S.D.</td>
<td>Mean ± S.D.</td>
<td>Mean ± S.D.</td>
</tr>
</tbody>
</table>

Cholecysto-cardiac link

Nabila Haque, M. M. Vasisth, I. Z. Khan & M. H. Bep

Departments of Anaesthesiology & General Surgery, J. N. Medical College
Aligarh Muslim University, Aligarh

Accepted August 8, 1990

Thirty normotensive patients (ASA class I) and 30 treated hypertensives without any cardiac problem (ASA class II) were subjected to elective cholecystectomy under general anesthesia. Patients' age ranged from 25-50 yr. and male:female ratio was 1:1. There were significant increases in heart rate and mean arterial pressure in both the groups (P < 0.05) during surgical manipulations for removal of the diseased gall bladders. The alterations in the untreated hypertensive patients were not only much more than in the normotenives, but also were associated with tachyarrhythmia in 33.3% of hypertensive patients. All changes returned to the pre-induction level at the end of the surgery. Mediation through fifth thoracic spinal segment, a common source of sympathetic supply to heart and gallbladder, explained the observed cholecystocardiac link. Anaesthesists therefore need to be vigilant during cholecystectomies.

It has been postulated that certain autonomic reflexes from diseased gall bladder may bring about circulatory disturbances like decreased coronary blood flow angina and dysrhythmia'. Two workers" had tried to evaluate this phenomenon by paravertebral and intercostal block as well as extradural or even intrapleural nerve block with highly variable results. To the best of our knowledge, the results of a prospective intraoperative study during biliary tract surgery have not been reported in the English literature.

Therefore, a study was designed to assess the possible cholecysto-cardiac link in normotensive and treated hypertensive patients during removal of the diseased gall bladder, a procedure commonly performed in northern India.

Material & Methods

Normotensive patients (ASA class I) and treated hypertensive patients without any cardiac problem (ASA class II) were randomly selected for the study of cardiovascular changes during elective cholecystectomy under general anesthesia.

All patients were premedicated with intramuscular hyoscyamine (0.6 mg kg body weight) and promethazine (0.5 mg kg body weight) 90 min before induction. After pre-oxygenation for 3.5 min. induction of anaesthesia was achieved with a deep dose of intravenous thiopentone sodium (4.7 mg kg body weight) and trachea was intubated under direct vision with well-lubricated orotracheal tube following intravenous succinylcholine chloride (1.5 mg kg body weight). Anaesthesia was maintained with nitrous oxide and oxygen in 66:33 ratio, with fresh gas flow of 8 l min through a semiclosed Mapleson C circuit on controlled ventilation. Muscular relaxation was obtained with pancuronium bromide (80 µg kg body weight). Residual neuromuscular block was antagonised at the end of operation with
neosalicylic (50 mg/kg body weight) plus atropine sulphate (25 mg/kg body weight).

Continuous monitoring of heart rate, rhythm, and systolic as well as diastolic blood pressures was carried out throughout the procedure in all patients, and mean arterial pressure (MAP) was calculated by the method of diastolic pressure plus one third of the pulse pressure. Patients developing any feature suggestive of hypoxia or hypercapnia were excluded from the study. Lightness of anaesthesia was excluded by the normal pupillary size, absence of tears, sweating or hiccup, and absence of skeletal muscle movement. Statistical analysis was done using paired and unpaired t-tests.

Results & Discussion

Thirty hypertensive patients (Group A) and thirty normotensive patients controlled on Dytide+ (benzthiamide + transmethionine diisopropylamine) and nitroprusside (group B), undergoing elective cholecystectomies at J. N. Medical College, Aligarh, from January, 1986 to January, 1990, were studied for perioperative cardiovascular changes. Patients' age ranged from 27-49 yr (mean 36.33) in group A, and from 25-49 yr (mean 35.67) in group B. Male:female ratio was 1:1.4 and 1:1.9 in groups A and B respectively.

Significant changes in heart rate and mean arterial pressure (MAP) were detected during the removal of gall bladder in both the groups (Table). Heart rate increased by 4.63% per cent (group A) and 21.39% per cent (group B), while MAP increased by 7.3% per cent (group 1) and 29.19% per cent (group B). Heart rhythm remained regular throughout cholecystectomy in group A, but 33.33% per cent of the treated hypertensive patients developed tachyarrhythmias (supraventricular tachycardia 9 patients, ventricular tachycardia 1 patient). These alterations in heart rate, rhythm and mean arterial pressure were significantly different between the two groups (P<0.001), and all returned to near normal at the end of operation. Postoperative recovery was uneventful in all patients of the two groups.

Fifth thoracic segment of spinal cord is a common source of sympathetic supply to heart through cardiac plexuses and to biliary tract through coeliac plexus. Moreover, it has been recently observed that the higher branches of greater splanchnic nerves may be traced upwards in the sympathetic trunk as far as second or even first thoracic ganglia. Hence, stretch or distension sensations of biliary tract transmitted through visceral sensory fibres of the splanchnic nerves, may lead to relative or absolute increase in the sympathetic tone, causing tachycardia, hypertension and tachyarrhythmias.

The present observations are in full agreement with those of Mendelson and Monks. 

Table. Changes during elective cholecystectomies seen in normotensive patients (group A) and treated hypertensive patients (group B). (Data are mean ± SD)

<table>
<thead>
<tr>
<th>Type</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>80.60±6.10</td>
<td>81.30±3.40</td>
</tr>
<tr>
<td>Before gall bladder manipulation</td>
<td>80.60±6.10</td>
<td>81.30±3.40</td>
</tr>
<tr>
<td>At the end of operation</td>
<td>80.10±6.00</td>
<td>80.10±6.00</td>
</tr>
<tr>
<td>Mean arterial pressure (MAP)</td>
<td>89.21±6.02</td>
<td>96.26±5.22</td>
</tr>
<tr>
<td>At the end of operation</td>
<td>91.60±5.72</td>
<td>91.60±5.72</td>
</tr>
</tbody>
</table>

MAP mean arterial pressure. *P-values *<0.05, **<0.001, ***<0.001 as compared to preoperative values.
Desborough et al13. However, the reflex stimulation of suprarenal nerve plexuses via the coeliac ganglia may produce adrenal bursts and overall sympathetic over activity. The present study confirmed that the haemodynamic disturbances secondary to the diseased gall bladder and its removal are more marked when cardiovascular system is the seat of proclaimed or latent disorders. Anaesthetists need to be vigilant throughout surgical procedures performed on the biliary tract in order to detect and treat any cardiovascular disturbance, if any.

References
2 Kehlet, H. The modifying effect of general and regional anaesthesia on the endocrine-metabolic response to surgery Regional Anaesth 7 (1982) 18

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Comparative assessment of TNF-α and C-reactive protein in patients subjected to open instead of laparoscopic cholecystectomy


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ABSTRACT

Background: C-reactive protein (CRP) and tumor necrosis factor-α (TNF-α) are specific proteins modulated by the acute stress of surgery. Various retrospective and prospective studies have demonstrated subdued stress responses in laparoscopically operated patients vis-à-vis the conventional (open) method.

Aim: To assess the roles of TNF-α and C-reactive protein levels as tentative stress markers in correlating the extent of perioperative immune modulation during open and laparoscopic cholecystectomy in a subset of an Indian population.

Setting and Design: This study is a prospective study.

Materials and Methods: Forty patients admitted and operated over a period of two years, were assigned to two groups: laparoscopic cholecystectomy (LC) (Group-I) or open cholecystectomy (OC) (Group-II). Selection was based on: patients' preference, patients' insistence, patients' inability to afford the laparoscopic procedure, lack of expertise or lack of facility in the hospital for the laparoscopic procedure. The baseline characteristics in terms of anesthetic protocol, fluid management, postoperative orders and perioperative care were kept similar for both groups.

Statistical Analysis: SPSS v.11 was used for statistical computations. Results: Baseline values of CRP in the OC and LC Groups were 7.9959 ± 5.57837 μg/ml and 11.3948 ± 11.61055 μg/ml respectively. CRP values rose markedly during the intra- as well as the postoperative periods till day 4 (P < 0.001) in both the groups. Intragroup variations were not significantly different from each other (P > 0.05). No such trend was noticed for TNF-α levels under identical conditions. Indeed, the TNF-α levels were 2.0304 ± 5.67384 pg/ml and 11.3406 ± 25.09385 pg/ml in the OC and LC groups respectively. Intragroup changes were not significantly different from each other (P > 0.05). Percentage changes in CRP and TNF-α were higher after OC in comparison to LC. Conclusions: The present study did not record statistical differences in the levels of the two markers (CRP, TNF-α) between the two groups. This reflects the limited tissue trauma due to easy and simple visceral tissue dissection in the two types of nondifficult surgery intraoperatively. However, greater change (P = 0.09) of TNF levels (30% vs. 1.9%) in the OC group on the 4th postoperative day represents the possibility of greater immune modulation in the OC group postoperatively.

Key words: C-reactive protein, laparoscopic cholecystectomy, open cholecystectomy, stress response, TNF-α
Hateem, et al.: Perioperative modulation of CRP and TNF-α

different surgical techniques and emphasis is put mainly on the parietal tissue trauma although it may significantly influence the surgical stress. Laparoscopic cholecystectomy (LC) is usually considered to be a safer procedure than conventional cholecystectomy in terms of metabolic, hormonal and immunological changes.11,12 Although factors like visceral tissue dissection, surgeon’s skills, selection of patients and standardization of the surgical procedure significantly influence the stress response, they have hitherto not been largely considered. We postulated that LC induced lower stress responses than the conventional open cholecystectomy and that comparison of TNF-α and C-reactive protein (CRP) levels would aid in monitoring these stress responses. Therefore, a pilot study was conducted to test the proposed hypothesis in patients of Indian origin with uncomplicated cholelithiasis.

MATERIALS AND METHODS

Subjects

The study was approved by the Board of Studies (BOS) and Committee for Advanced Scientific Research (CASR) of our University. This study was conducted over a period of two years from October 2004 to December 2006. After detailed informed consent, elective cases (American Society of Anesthesiologists (ASA) grades I and II) with symptomatic, uncomplicated cholelithiasis (fit for laparoscopic procedure) were considered for the present study. Forty cases included in the study were divided into two groups-20 patients in each group depending upon the selection criteria. Patients with acute cholecystitis, pancreatitis, cholangolithiasis, malignancy, jaundice, history of allergy, steroid intake, cytotoxic chemotherapy, pregnancy or hypoproteinaemia and patients requiring perioperative blood transfusion were excluded from the study.

Sample size

In consultation with our statistician, the sample size was calculated taking into account the reported prevalence of stress during anesthesia and surgery. Considering the prevalence of stress in surgical patients to be 100% (from previous studies and past records), we took it as 95% and allowed an error of 5% of prevalence of stress on either side so as to correct our estimate in 95 out of 100 patients. Hence, if “p” is the prevalence of stress rate in percentage and “q” is the nonstress rate in percentage and p + q = 100, then the standard error is \( \sqrt{(pq/n)} \) or \( \frac{2}{pq/n} \) = 10% of p where n is the sample size. Putting the value of p = 95% and q = 5% in the equation:

\[
(4 \times 95 \times 5)/n = (10 \times 95/100) \times (10 \times 95/100)
\]

The value of n would be 21.

Following randomization according to patients’ selection criteria, this study included 40 patients.

Reasons for patients undergoing open cholecystectomy (OC)

1. Financial: inability to afford laparoscopic procedure.
2. Patients’ preference: for a specific general surgeon who lacked suitable expertise in the laparoscopic technique.
3. Lack of facilities: de novo absence or malfunctioning of existing gazettes.
4. Patients’ insistence: patients’ phobia of complications after laparoscopic cholecystectomy based on bad experience of kith and kin.

Sample method

Venous blood (5 ml) was withdrawn from the antecubital vein into a plain sterile glass vial. The samples were centrifuged at 3000 g for 10 min for separation of serum. The sera were transferred into plastic tubes and transported in ice boxes for storage at -60°C in the Institute of Microbiology where the biochemical analysis was done by competent laboratory personnel blinded to the study, test serum and surgical intervention given to the patients.

Sample times

Serial measurement of CRP and TNF-α was done by sampling the blood.

1. First baseline sample was collected preoperatively after overnight fasting.
2. Second sample at time of separation of gall bladder from the liver bed.
3. Third sample at the time of completion of surgery.
4. Fourth sample on 1st postoperative day.
5. Fifth sample on 2nd postoperative day.
6. Sixth sample on 4th postoperative day.

Perioperative protocol

All cases were first screened in the preanaesthetic clinic for relevant history and clinical examination. The investigational findings were recorded in the preanaesthetic cards.

All the procedures were explained to the patients who were advised to take tablet diazepam (5 mg) orally the night before the surgery.

Anesthesia

Patients received midazolam (0.04 mg/kg) intravenously in the preoperative room 30 minutes before induction of anesthesia. Subsequently, injection metoclopramide (0.2 mg/kg) and fentanyl (2 µg/kg) bolus were given as preemptive adjuvants to surgical analgesia. Inj. fentanyl was repeated 1 µg/kg/h till the surgery was completed.

All the patients were anesthetized with injection...
The surgical procedures were performed by consultant surgeons. OC was performed through right subcostal incision and laparoscopic by 4-trocar technique with electrocautery dissection. Pneuroperitonum was excluded from the study. Any intraoperative injury to an adjacent organ / structure including bile duct injury led to exclusion of that case from the study.

Immunological assays

The quantitative determination of CRP concentration in plasma was done by a microplate immunoenzymometric assay according to the manufacturer's instructions (Product Code: BC 31109M from CALIBRTECH INC. USA). The absorbance obtained from the microplate enzyme-linked immunosorbent assay (ELISA) reader was plotted in duplicate versus the corresponding CRP concentration in µg/ml with help of "Microbiology-Intoxant" software. The hs-CRP (high-sensitivity CRP) microplate ELISA procedure has a sensitivity of 0.2 µg/ml. The intrasay and interassay coefficients of variation in within-run precision for CRP were 2.3-2.9% and 4.1-2.5% respectively. The expected normal value for hs-CRP was taken as < 3 µg/ml.

Plasma concentration of human TNF-α was determined by ELISA from the kit (BiocauA Immunodiagnostic Systems, USA). The absorbance was read on a spectrophotometer using 450 nm as the primary wave length. Average absorbance was calculated for each set of duplicate standards, samples and controls. The linear standard curve was created by plotting the mean absorbance for each standard concentration on the Y axis against the TNF-α standard concentration on the X axis. The overall intrasay coefficient of variation was calculated to be 2.3%. The interassay coefficient of variation was 9%. Spike recovery ranged from 74-90% and the expected normal serum value was taken as < 8 pg/ml.

Statistical analysis

Data was analyzed with standard computer software (SPSS v11.0). Intragroup and intergroup comparisons were done by paired sample statistics and independent sample T-tests respectively. Values were expressed as means with standard deviation (SD) when normally distributed, or medians with the 25th and 75th percentile interquartile range, when skewed. Nonparametric tests (Mann-Whitney U Test, Wilcoxon signed ranks test) were provided to the patient accordingly and the timing of the injections was noted in the case sheet.

Exclusion criteria

Patients with pre-operative changes in their vital signs > 25% from the basal level and requiring further supplementation in the anesthetic protocol were excluded from the study. Patients developing significant alterations in their baseline preoperative investigations (haemoglobin, total and differential leukocytes count, blood urea, serum creatinine, serum sodium and potassium, platelet count and prothrombin time) were also excluded from the study.

Any intraoperative injury to an adjacent organ / structure including bile duct injury led to exclusion of that case from the study.

Fluid therapy

The intravenous fluid regime consisted of 500 ml of Ringer’s lactate solution and 500 ml of 5% dextrose solution during the intraoperative period. This regime was continued for 6-24 hours at the rate of 80-100 ml/hr depending upon climatic conditions. Usually oral fluid intake was allowed in the same evening in the LC group and in the next morning in the OC group subject to patients' tolerance.

Postoperative care

Deep intramuscular injections of diclofenac sodium 1.5 mg/kg were given together intramuscularly in the night. The intensity of pain was assessed with the help of a visual rating scale (VRS). The amount of pain described by the patient was scored as 0 represented no pain, 1 = mild/slight pain, 2 = moderate pain, 3 = severe pain and 4 = represented very severe or intolerable pain. The cuteral and parenteral analgesics were provided to the patient accordingly and the timing of the injections was noted in the case sheet.
The changes within the groups were evaluated by nonparametric tests. Two-tailed $P$ values were reported and a probability value of $P < 0.05$ was considered statistically significant.

RESULTS

In the study period from October 2004 to December 2006, 406 patients underwent cholecystectomy although only 40 cases could enroll in the study due to the exclusion criteria. Patients included in the study had comparable baseline characteristics (age, sex, weight, height, type and duration of surgery and duration of anesthesia) [Table 1]. The medians of CRP and TNF-α with their 25th and 75th percentile interquartile range were found to be normally distributed and hence, have been documented here. The mean ± SD of CRP and TNF-α were not significantly different ($P > 0.05$) from each other in the peri-operative period (Table 2). Independent sample $T$-test for equality of means by application of Levene’s test for equality of variances and the 95% confidence interval of the mean difference (CID) were comparable in both the groups. When the results were compared between the two groups using the Mann-Whitney U test and the Wilcoxon W test, the two-tailed significance values were $> 0.05$. The response of CRP following surgery was not correlated ($P > 0.05$) to the peri-operative period (Table 3), in both the groups during the intra- as well as postoperative periods till day 4. However, intergroup differences were not significantly different ($P > 0.05$) from each other [Table 2]. In both the groups, the increased serum CRP concentrations reached the maximum level 24-48 hours after surgery and started declining from the 4th day after surgery [Figure 1].

The values of TNF-α in both the groups did not differ significantly ($P > 0.05$) during the intraoperative period. Postoperatively its values rose markedly after the surgery in the OC group from the 2nd to 4th day ($P < 0.01$). However, intergroup changes in TNF-α were not significantly different ($P > 0.05$) from each other in the peri-operative period [Table 3].

Table 1: Comparison of demographic data (mean ± SD) in both the groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Open cholecystectomy</th>
<th>Laparoscopic cholecystectomy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>33 ± 5</td>
<td>31 ± 5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Weight in kg</td>
<td>46 ± 7.4</td>
<td>40 ± 8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>166 ± 4</td>
<td>168 ± 4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>0/21</td>
<td>0/21</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>73 ± 9</td>
<td>71 ± 4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>86 ± 4</td>
<td>83 ± 5</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table 2: C-reactive protein (μg/ml) mean ± SD with $P$ values in patients undergoing laparoscopic cholecystectomy and open cholecystectomy

<table>
<thead>
<tr>
<th>Variables</th>
<th>LC (Mean ± SD)</th>
<th>P value</th>
<th>OC (Mean ± SD)</th>
<th>P value</th>
<th>OC vs. LC P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop</td>
<td>11.3948 ± 11.605</td>
<td>0.862</td>
<td>7.9959 ± 5.7837</td>
<td>0.862</td>
<td></td>
</tr>
<tr>
<td>Dissection of GB</td>
<td>16.8269 ± 12.3920</td>
<td>0.217</td>
<td>9.7660 ± 5.2315</td>
<td>&lt;0.001</td>
<td>0.698</td>
</tr>
<tr>
<td>End of surgery</td>
<td>17.0596 ± 11.9476</td>
<td>0.011</td>
<td>18.3801 ± 11.870</td>
<td>&lt;0.001</td>
<td>0.730</td>
</tr>
<tr>
<td>1st postop day</td>
<td>38.4033 ± 14.82422</td>
<td>&lt;0.001</td>
<td>44.5418 ± 4.9552</td>
<td>&lt;0.001</td>
<td>0.698</td>
</tr>
<tr>
<td>2nd postop day</td>
<td>46.0383 ± 3.27104</td>
<td>&lt;0.001</td>
<td>47.2053 ± 4.7942</td>
<td>&lt;0.001</td>
<td>0.414</td>
</tr>
<tr>
<td>3rd postop day</td>
<td>40.4795 ± 7.90992</td>
<td>&lt;0.001</td>
<td>42.9437 ± 5.70931</td>
<td>&lt;0.001</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Table 3: TNF-α (pg/ml) mean ± SD with $P$ values in patients undergoing laparoscopic cholecystectomy and open cholecystectomy

<table>
<thead>
<tr>
<th>Variables</th>
<th>LC (Mean ± SD)</th>
<th>P value</th>
<th>OC (Mean ± SD)</th>
<th>P value</th>
<th>OC vs. LC P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop</td>
<td>11.3408 ± 25.98285</td>
<td>0.740</td>
<td>2.8034 ± 5.67384</td>
<td>0.740</td>
<td></td>
</tr>
<tr>
<td>Dissection of GB</td>
<td>10.2322 ± 28.90873</td>
<td>0.500</td>
<td>0.3779 ± 0.89007</td>
<td>0.063</td>
<td>0.301</td>
</tr>
<tr>
<td>End of surgery</td>
<td>11.4041 ± 25.06695</td>
<td>0.917</td>
<td>0.6530 ± 2.09292</td>
<td>0.237</td>
<td>0.301</td>
</tr>
<tr>
<td>1st postop day</td>
<td>4.9217 ± 14.03764</td>
<td>0.346</td>
<td>0.7775 ± 3.55977</td>
<td>0.069</td>
<td>0.281</td>
</tr>
<tr>
<td>2nd postop day</td>
<td>19.7909 ± 13.73999</td>
<td>0.589</td>
<td>27.5550 ± 4.09936</td>
<td>0.008</td>
<td>0.074</td>
</tr>
<tr>
<td>3rd postop day</td>
<td>22.7927 ± 70.50003</td>
<td>0.779</td>
<td>59.9436 ± 14.29275</td>
<td>0.008</td>
<td>0.094</td>
</tr>
</tbody>
</table>
DISCUSSION

Surgical intervention, a form of deliberate trauma, is followed by well-documented inflammatory, hormonal and immunological responses that may be the deciding factors for the final outcome of the patient. Laparoscopic surgery is often perceived as minimally invasive surgery with attenuated responses and this perception has been proved in many studies.

However, the majority of these studies fail to specifically address the impact of visceral tissue dissection that may also noticeably affect the neuroendocrine metabolic responses, depending upon whether the cholecystectomy is straightforward easy or difficult.

Our observations on the comparative assessment of TNF-α and CRPs in patients subjected to open instead of LC, \( P > 0.05 \) were consistent with those of McMahon and associates. McMahon et al. evaluated several markers including CRP following LC and mini-laparotomy cholecystectomy. Redmond and colleagues were also unable to detect any significant difference in CRP levels between open and LC. However, they did observe enhanced TNF expression after open cholecystectomy.

These results may imply that the amount of visceral tissue dissection and tissue injury may be an important contributory factor towards systemic immune responses. This aspect may be the true reflection of LC where the patient is invariably selected on the technical feasibility based on preoperative imaging studies. This means that the similar trauma response in both LC and OC groups may be the effect of patient selection criteria. This is because added tissue dissection in complicated cases may enhance the degree of immunological modulation many fold, an observation that was also confirmed by others.

Skin incision is frequently the site of maximum tissue trauma and is accordingly assumed to evoke greater acute phase responses. However, in a prospective randomized study \( n = 34 \), Hill and associates did not find any significant difference in CRP and Interleukin-6 (IL-6) expression following open and laparoscopic inguinal hernia repair that involves only parietal tissue trauma in either approach.

In an animal model study, Douglas et al. and later on, Bossler and associates have observed greater elevations in IL-6 after laparoscopic colectomy in comparison to open colectomy. However, higher percentage increases in TNF levels in the OC group on the 4th postoperative day suggest that LC and OC are equally stressful intraoperatively but subsist less in the...
postoperative period as \( P = 0.094 \).

Therefore, similar acute phase responses are observed intraoperatively in patients fit for LC, when operated on by the open method with easy visceral tissue dissection. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)\(^{2,3}\) Guidelines assume greater significance in the light of the present study as better surgical skills will minimize the visceral tissue dissectional trauma with attenuation of the various acute phase responses that are the deciding factors for the final outcome as evident by peri-operative modulation of TNF-\( \alpha \) and C-reactive proteins. However, this also reflects that these selective stress markers (CRP and TNF-\( \alpha \)) have a limited role in the clinical assessment of immune stress responses and tissue trauma. This finding warrants the search for more sensitive biomarker(s) for peri- and postoperative management of surgical patients.

ACKNOWLEDGMENTS

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REFERENCES
