

# Effects of Combination Anaesthesia on Bio-Chemical Profile and GSH of Cancer Patients at AHRCC, Cuttack

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## ABSTRACT

### OBJECTIVE:

- 1) Estimation of blood glutathione levels of pre and post operative blood samples obtained from patients undergoing cancer surgeries, administered with halothane and thiopental sodium.
- 2) Effect of general anaesthetics on varied biochemical parameters and their subsequent effects on body physiology of cancer patients' post surgery.

### METHODS:

- 1) Estimation of GSH content of pre and post operative blood samples was done according to Ellman's procedure (Ellman, 1959).
- 2) Estimation of serum total protein was done according to Reinhold's method (Reinhold 1953).
- 3) Estimation of serum urea was carried out according to the enzymatic process designed by Seaton and Ali (Seaton and Ali 1954).
- 4) Estimation of serum uric acid was done basing on the principle designed by Fossati and co-workers (Fossati et al 1980).
- 5) Estimation of serum bilirubin was done according to Jendrassik and Groff's method (Jendrassik and Groff 1981).
- 6) Estimation of SGOT and SGPT was done basing on the principle designed by Reitman and Frankel (Reitman and Frankel 1957).

All procedures were carried out using kits from Crest Biosystems, Goa and Accurex Biomedical Private Limited, Thane, Maharashtra.

### RESULTS:

- 1) Serum albumin content in pre and post operative cancer patients analyzed were  $3.42 \pm 0.45$  and  $3.48 \pm 0.45$  mg/dl respectively.
- 2) Serum total protein estimated in pre and post operative serum samples were  $7.06 \pm 0.65$  and  $7.15 \pm 0.67$  mg/dl respectively.
- 3) The serum urea level for both pre and post operative cancer patients were  $27.27 \pm 6.72$  and  $28.16 \pm 6.7$  mg/dl respectively.
- 4) The liver transaminase SGOT tested for both pre and post operative cancer patients were  $29.81 \pm 2.63$  and  $31.0 \pm 2.56$  Unit/litre respectively. SGPT estimates were found to be  $30.27 \pm 5.13$  and  $31.45 \pm 4.74$  Unit/litre for pre and post operative patients respectively.
- 5) The serum bilirubin values in pre and post operative patients were found to be  $1.05 \pm 0.22$  and  $1.05 \pm 0.20$  mg/dl respectively.
- 6) The serum creatinine values in pre and post operative cancer patients was found to be  $1.11 \pm 0.10$  and  $1.20 \pm 1.20 \pm 0.16$  mg/dl respectively.
- 7) The value for GSH level in case of pre and post operative cancer patients administered with halothane and thiopental was estimated to be  $335.92 \pm 5.23$  nmoles/ml and  $301.29 \pm 49.61$  nmoles/ml respectively.

### CONCLUSION:

The investigation showed that the combination anaesthesia of halothane and thiopental sodium has almost no effect on serum biochemical parameters and minimal effects on blood glutathione levels of cancer patients undergoing surgery being administered with the combinational general anaesthetics in question, hence anticipating its routine clinical use.

**BACKGROUND:**

Cancer has been more than a menace in society at present. Every one of us is aware of at least one individual who is suffering from cancer. This dreaded disease otherwise termed as malignant neoplasm, occurs when a number of cells proliferate by themselves without control and reach other parts of the body through blood stream and the lymphatic system.

Cancer is triggered by different factors like heredity, physical agents, environmental factors, chemicals and so on. Recently studies have discovered oxidative stress cancer and this type of stress is believed to either initiate or worsen the progression of the carcinoma. Research has also revealed the oncological implication of surgery induced oxidative stress. Apart from various oxidative stresses, reactive oxygen species (ROS) mediates various cell signalling pathways. Traditionally ROS was believed to be associated with cell death whereas emerging evidence clearly demonstrates that ROS signalling acts as a key regulator in tumour cell survival and in the cellular processes required for tumour cells to successfully metastasize and proliferate. Clinical studies have proved that administration of general anaesthetics especially barbiturates like thiopental may have protective effects against bowel ischemia, but on the other hand can contribute to minimal oxidative stress during or after cancer surgery. Slight accelerations in oxidative stress status of surgical patients administered with thiopental have been observed in certain cases.

Surgical trauma has been associated with pre-anaesthesia fasting, anaesthetic toxicity, hypovolaemic shock and other pathological phenomena. Tissue glutathione, thiobarbituric

reacting substances, and radical trapping activity have been reported at various times to test for generation of free radicals. (Hanley et al 2003). GSH concentrations showed a significant decline, in cases of post cancer surgery, where the combined anaesthetics had been administered (i.e. Halothane and thiopental). The decrease in GSH is assumed to have resulted from rapid reaction with lipid peroxidation products generated during the metabolism of these anaesthetics which might be consumed by glutathione peroxidase activity (GSH-Px). It is a known fact that GSH-Px detoxifies hydrogen peroxide and converts lipid hydroperoxides into non toxic alcohols (Halliwell et al 1996). The decrease in plasma GSH in the present study may be due to inactivation of enzymes by hydrogen peroxide.

**OBJECTIVE OF THE INVESTIGATION:**

After 3 decades of research in various areas of oxidative stress status of cancer patients undergoing surgery, under influence of general anaesthetics (i.e. halothane and thiopental), it has been seen that these anaesthetics contribute to oxidative stress in minimal degree. To gain insight into free radical generation under influence of general anaesthetics, GSH alteration in post operative blood is often analyzed. Despite a significant reduction in GSH of post-operative serum taken during 5-8hrs after surgery (peak effect time) by almost 40% , the mechanisms that substantiate changes in GSH redox status, the enzymatic processes of GSH synthesis and oxidation are unexplained till date.

The present investigation is designed to find out "Effect of thiopental sodium and halothane combination anaesthesia on serum biochemical parameters and glutathione status in patients undergoing cancer surgery at Acharya Harihar Regional Cancer Centre, Cuttack, Odisha.

## **MATERIALS AND METHODS:**

### **Procuring of samples:**

1. Pre and post operative blood samples (3ml each) were obtained from cancer patients undergoing surgery who had been administered with general anaesthetics i.e. thiopental sodium and halothane respectively. Pre operative blood samples were collected during the morning from patients on empty stomach, with help of patholab technicians. Post operative blood samples were collected after surgery from patients under supervision of attending physician. Data on age, physique, health problems and patients own case histories were recorded.

2. Blood samples were drawn from healthy individuals (3ml each) their ages being in the range of those patients from whom post and preoperative samples had been collected previously. These healthy samples served as controls.

### **Procuring of chemicals:**

Reduced and oxidised forms of glutathione were obtained from SISCO Research Laboratory, India. Metaphosphoric acid and DTNB were procured from Sigma-Aldrich Chemical Company, USA. All other laboratory chemicals were of the highest purified grade available.

### **Procuring of kits for biochemical investigations:**

The total protein kit and the albumin kit were procured from Crest Biosystems, Goa, India. The kits for estimation of serum urea, serum uric acid, serum bilirubin and serum creatinine were all procured from Accurex Biomedical Private Limited, Thane, Maharashtra .

### **EXPERIMENTAL DESIGN:**

Pre and post operative blood samples (3ml each) drawn from cancer patients

administered with halothane and thiopental were subjected to the following experimentation and tests:

1. Estimation of glutathione content of pre and post operative blood samples was done according to Ellman's procedure (Ellman 1959).

2. Estimation of serum albumin was done according to the principle designed by Spencer and Price, 1977. Estimation was done using kits obtained from Crest Biosystems, Goa, India.

3. Estimation of serum total protein was done according to Reinhold's procedure (Reinhold 1953). Kits for estimation were obtained from Crest Biosystems, Goa, India.

4. Estimation of serum urea was done according to principle designed by Seaton and Ali (1954). The estimation of serum urea was carried out using Auto enzyme urea kit by enzymatic processes obtained from Accurex Biomedical Private Limited, Thane.

5. Estimation of serum uric acid was done according to the principle designed by Fossati and co-workers (1980). The working reagents and kits were obtained from Accurex Biomedical Private Limited, Thane.

6. Estimation of serum bilirubin was done according to the principle designed by Jendrassik and Groff (1981). Working reagents and kits were obtained from Accurex Biomedical Private Limited, Thane, Maharashtra.

7. Estimation of serum creatinine was done according to protocol designed by working laboratories of MCI, India. Kits were obtained from Accurex Biomedical Private Limited, Thane, Maharashtra.

8. Estimation of SGOT and SGPT was done using kits provided by Accurex Biomedical Private Limited, Thane, Maharashtra, based on

the principle designed by Reitman and Frankel (1957).

## RESULTS:

### 1. Changes in serum biochemical parameters :

Serum biochemical parameters were measured to know about the overall health status of the patients undergoing surgery under the influence of halothane and thiopental. Total protein and albumin estimates are indicators of the patient's protein utilization, nutritional and general health status. Serum bilirubin, SGOT and SGPT values are indicators of liver function while serum urea, uric acid and creatinine estimates are indicators of kidney function. The results after estimation of biochemical profiles showed that there exist no statistically significant alterations in serum biochemical parameters in any of the groups studied. Thus the anaesthetics used (i.e. halothane and thiopental) have no adverse effects on patients undergoing surgery under their influence.

Parameters	Control	Pre-operative Cancer Patient	Post-operative Cancer Patient
Total Protein (mg/dl)	7.61 ± 0.50	7.06 ± 0.65	7.15 ± 0.68
Albumin (mg/dl)	3.96 ± 0.29	3.43 ± 0.45	3.48 ± 0.46
Urea (mg/dl)	34.69 ± 2.88	27.27 ± 7.06	28.25 ± 6.97
Uric Acid (mg/dl)	5.94 ± 0.61	5.03 ± 0.70	5.0 ± 0.59
Bilirubin (mg/dl)	1.24 ± 0.23	1.05 ± 0.22	1.05 ± 0.20
Creatinine (mg/dl)	1.25 ± 0.13	1.14 ± 0.10	1.20 ± 0.16
SGOT (IU/L)	34.23 ± 2.73	29.82 ± 2.64	31.27 ± 2.73
SGPT (IU/L)	36.82 ± 1.54	30.27 ± 5.14	31.45 ± 4.74

Serum biochemical parameters of control and cancer patients. Data are expressed in ± sd of 11 observations taken in duplicate.

### 2. Changes in serum GSH levels :

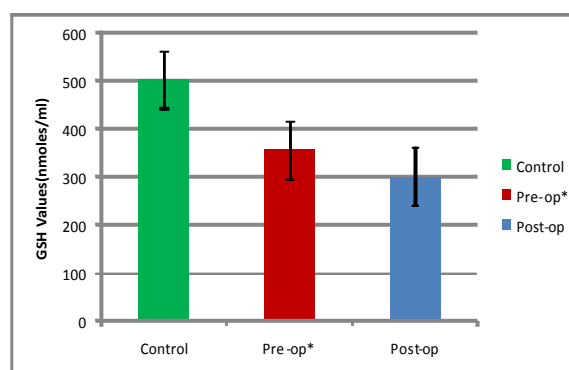
The results showed a significant decline in the level of serum glutathione content (17%), of the patients suffering from cancer in comparison to their age matched healthy counterparts. However surgical intervention with halothane and thiopental sodium anaesthesia failed to alter the serum GSH level significantly. The reduction of 17% in serum GSH levels in cancer patients was indicative of cellular utilization for maintenance of a complex set of oxidation reduction reactions governing the physiological activity of a cell. The reduction in GSH level also has been reported for stomach and colon carcinomas (Siegers et al 1984) in various studies.

Control	Pre-operative	Post-operative
502.09 ± 185.08	357.81 ± 95.23*	301.29 ± 49.61

Serum GSH (nmoles/ml) in control and cancer patients (n = 11)

Data are expressed as mean ± sd

P < 0.05 with respect to control and post operative group.



## DISCUSSION:

The present study on the effect of combination anaesthesia of halothane and thiopental sodium on blood glutathione levels and biochemical parameters of patients undergoing

surgery at AHRCC, Cuttack is summarized as below:

1. The serum albumin content in pre and post operative cancer patients analyzed was  $3.42 \pm 0.45$  and  $3.48 \pm 0.45$  mg/dl respectively. Increase in serum albumin in post operative cancer patients may be due to oxidative stress related exertion in the cellular system.
2. The serum total protein content estimated in pre and post operative serum samples were  $7.06 \pm 0.65$  and  $7.15 \pm 0.67$  mg/dl respectively. These values imply for the persistency of patients' health condition.
3. The serum urea level measured for both pre and post operative serum samples were  $27.27 \pm 6.72$  and  $28.16 \pm 6.97$  mg/dl respectively. Elevated urea levels post cancer surgery may be due to surgery induced stress exhibited by hepatic cells and in turn it is suggestive of the efficiency of protein catabolism.
4. The liver transaminase SGOT tested for both pre and post operative cancer patients administered with the combination of halothane and thiopental were  $29.81 \pm 2.63$  and  $31.0 \pm 2.56$  Unit/litre respectively, whereas SGPT estimates were found out to be  $30.27 \pm 5.13$  and  $31.45 \pm 4.74$  Unit/litre for pre and post operative patients respectively. The increased SGOT and SGPT level in post operative cancer patients is suggestive of normal metabolic function.
5. The serum bilirubin analysed in post operative patients was slightly decreased compared to the preoperative estimates, whereas preoperative values were estimated around  $1.05 \pm 0.22$ mg/dl , post operative values were around  $1.05 \pm 0.20$ mg/dl respectively.
6. The level of serum creatinine values determined in postoperative cancer patients administered with halothane and thiopental during

surgery, was found to be slightly increased as compared to preoperative samples. Pre-op values were around  $1.13 \pm 0.10$  mg/dl where as postoperative values were around  $1.20 \pm 0.15$  mg/dl respectively.

7. The serum GSH level measured for postoperative cancer patients administered with halothane and thiopental sodium during surgery was reduced age by 17% as compared to their age matched healthy counterparts i.e. post operative serum GSH values were around  $301.294 \pm 49.61$  nmoles/ml, while those of controls were around  $502.09 \pm 185.08$  nmoles/ml.

However there was no significant decrease in serum GSH levels of post-operative cancer patients who had undergone surgery under the administration of halothane and thiopental sodium, their values being  $301.29 \pm 49.61$  nmoles/ml as compared to the pre-operative samples whose serum GSH values were around  $335.92 \pm 95.23$  nmoles/ml .

#### CONCLUSION:

Oncoanaesthesiology has gained wide popularization in using various kinds of anaesthetics for treatment of cancer patients be it for treatment for surgical procedures or for pain management techniques. However there are no standard guidelines for the administration procedure of each anaesthetic for different cancer types. The intrinsic defence mechanism of a cell are competent immune cells such as CD4 TH type 1 cells, CD8Tc cells and all natural killer cells , (Welden et al 2009). Surgical intervention using anaesthetics for cancer treatment has been found to suppress the activity of these effector cells. (Duncan et al 1977), including some suppressive immune cells responsible for tumour recurrence and metastasis after surgery.(Kurosawa 2012) Although surgical treatment of cancer is necessary

using anaesthesia, the increasing risk of tumour recurrence. has been widely reported for many perioperative factors such as surgery, stress, inflammation, pain, anaesthetic drugs, blood transfusion etc. (Beloel and Nouette-Gaulain, 2012). The present investigation came to a conclusion that the combination anaesthesia of halothane and thiopental sodium has no significant effect on serum biochemical parameters and minimal effects on glutathione status of cancer patients undergoing surgery under its administration, hence anticipating its routine clinical use.

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