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ORIGINAL ARTICLE

LIVER FUNCTION TESTS AFTER HALOTHANE ANAESTHESIA

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ABSTRACT: BACKGROUND: Halothane anaesthesia is associated with Halothane hepatitis, first reported by Barton[1] in 1959. As Halothane is still extensively used in India and other developing countries, owing to its low cost, this study was conducted to compare liver function tests before and after Halothane anaesthesia. Results - Slight increase in serum bilirubin, SGOT, SGPT, serum calcium and slight rise in eosinophil count was found in both groups post-operatively, which was statistically not significant except the rise in SGPT levels in immediate post-operative period which was significant in both groups. Conclusion – Halothane anaesthesia with 100% or 40 % oxygen in adults does produce a slight alteration in Liver function tests with no correlation with duration of anaesthesia and gender. However, there was significant rise in SGPT in immediate post-operative period.

KEYWORDS: Halothane hepatitis, liver function tests, duration of anaesthesia, percentage of oxygen.

INTRODUCTION: The widespread and extensive use of halothane exposed its drawbacks like halothane hepatitis and toxicity. Although not a frequent occurrence but it aroused a lot of concern, research and debate. The first case of halothane hepatitis was reported by Barton[1] in 1959 in an eleven year old girl. No patient had history of pre - existing liver disease. The reports of use of halothane with 100% O2 are lacking. Most of the workers have used conventional (33 – 40%) percentage of oxygen with halothane; therefore we undertook this study with 100% as well as with 40% oxygen.

METHODS: The study was approved by the institutional review board. The proposed work was carried out on 80 patients of ASA grade I and II of both sexes in adult patients undergoing various routine surgeries where surgery was expected to be of more than one hour duration. Informed consent from the patients was taken before anaesthesia to take blood samples pre and post operatively for this study. Pre anaesthesia check-up was done with special attention to any positive history of liver disease and if present patients were not included in the study.

Patients operated two months back were not included in the study. Patients taking any medication known to cause liver dysfunction were excluded. Routine investigations were done as per the requirement of the patient. Blood samples were taken for liver function tests preoperatively. All patients were pre-medicated with intravenous glycopyrrolate 0.2 mgs.

The patients were divided into two main groups – A and B of 40 patients each. In group A patients halothane was administered with 100% oxygen and in group patients received halothane along with medical air (total oxygen 40%). Group A was further divided into subgroups A1 and A2 of 20 patients each and group B was further divided into B1 and B2 of 20 patients each. In subgroups A1 and B1 the post-operative samples were taken immediately after the end of halothane anaesthesia and in subgroups A2 and B2 post-operative samples were taken 48 hours after halothane anaesthesia.

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Induction of anaesthesia in both groups was carried out with propofol (2.5–3 mgs per kg), Atracurium (0.5mgs per kg) and fentanyl (50–100mcg) given intravenously followed by endotracheal intubation. Maintenance of anaesthesia in group A was done with 100% oxygen with halothane and muscle relaxant (atracurium). In group B maintenance of anaesthesia was done with 40% oxygen (oxygen and medical air) with halothane and muscle relaxant (atracurium) on controlled ventilation. At the end of the procedure patients were reversed with glycopyrrolate 0.5 mgs and neostigmine 2.5 mgs in both groups.

All patients were closely monitored in pre & post-operative period. Blood samples were taken for serum albumin, serum bilirubin, serum calcium, serum Glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and for eosinophil count. The preoperative values of these parameters served as control for comparison with the post-operative sample (immediate post-operative period in subgroups A1 and B1 and after 48 hours in A2 and B2 subgroups

RESULT: Estimation of serum albumin, serum bilirubin, serum calcium, SGOT, SGPT and eosinophil count was done pre operatively and post operatively after halothane anesthesia and compared in both the groups and sub groups. Comparison of these parameters was also done between subgroups and also in relation to the duration of anesthesia and gender of the patients.

Estimation of serum albumin levels in the immediate post-operative period and after 48 hours in post-operative period did not reveal any significant alteration in both the groups, when compared with the pre-operative values. Similarly there was no significant change in the levels of serum albumin when compared with duration of anesthesia and gender and also no significant difference in per and post-operative values of serum albumin.

There was a slight increase in serum bilirubin levels in immediate post-operative period and also after 48 hours post-operative period in both the groups. There was no significant difference in rise of serum bilirubin levels as regards to the duration and gender of the patient, however, this rise was found to be statistically insignificant ($p > 0.05$).

Similarly, there was a slight rise in serum calcium levels in both groups which was again statistically insignificant ($p > 0.05$). It had again no correlation with either duration of anesthesia or gender of the patients.

The estimation of SGOT levels in post-operative period revealed that there was a slight increase in the levels of SGOT in immediate post-operative period as compared to per operative values. This was again found to be statistically insignificant ($p > 0.05$).

The levels of SGPT in post-operative period also showed a slight increase in all patients. This rise was again found to be statistically insignificant ($p > 0.05$). In relation to the duration of anesthesia, it was interesting to note that there was a moderate rise in SGPT levels when the duration of anesthesia was either 2 – 3 hours or more than 3 hours in immediate post-operative period in both the subgroups (A1 and B1) which was found to be statistically significant ($p < 0.05$). However, after 48 hours in the postoperative period the rise in SGPT was not significant ($p > 0.05$.}

DISCUSSION: The present study was done on 80 adult patients belonging to ASA grade I or II, who underwent various types of surgical procedures of more than one hour duration.

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In both the groups the technique of anesthesia was identical except the percentage of oxygen which was 100% in group A patients and overall 40% in group B patients. Patients of both the groups initially received 2% halothane there after all the patients were maintained on 1.5% halothane.

There was not much change in serum albumin levels after halothane anesthesia in all the sub groups. Though there had been a slight decrease in the serum albumin in sub group A1 patients arid a slight increase in the serum albumin levels in sub groups Al, B1 and B2 but, on statistical analysis this alteration in serum albumin levels was found to be not significant (P>O.O5).

Other workers[2,3,4] have reported a slight decrease in serum albumin levels and alteration in the albumin/globulin ratio, after repeated exposures with halothane anesthesia. In the present study there was no significant change in the serum albumin levels, though our patients were subjected to single exposure of halothane.

The estimation of serum bilirubin level in pre-operative and post, operative period revealed a slight increase in serum bilirubin levels in the post-operative period in all the sub groups. In sub group A1 the mean serum bilirubin levels rose from 0.1mg %> 0.13 to 0.29mg% + 0.22. Similarly in sub group A2 from 0.33mg% ± 0.16, it went to 0.40mg% ±0.19. In sub group B1 and B2 also there was a slight rise in serum bilirubin from 0.23mg% ± 0.07 to 0.28mg% ± 0.24 and from 0.25mg% ± 0.09% to 0.26mg% ± 0.09 respectively. However, on statistical analysis this slight elevation in serum bilirubin levels was found to be insignificant (P>0.05). Our findings are in agreement with Trowel[5] and Fee[6] who have also found that there is not much change in serum bilirubin levels after halothane anesthesia.

The estimation of serum calcium in pre and post-operative periods in all the sub groups revealed a slight increase in serum calcium levels in the post-operative period. However, on statistical analysis this rise in serum calcium in post-operative period was found to be insignificant (P>0.05).

The reports on levels of serum calcium after halothane exposure are lacking but Zucker[7] studied the effects of halothane on calcium transport by microsomes prepared from rat liver and reported that halothane irreversibly inactivated. They have also proposed this mechanism to be responsible for triggering malignant hyperthermia in certain individuals.

The estimation of SGOT levels in pre and post-operative period revealed that there was a slight increase in the levels of SGOT in the post-operative period in sub group A1, B1 and B2 whereas surprisingly in sub group A2 there was a decrease in levels of SGOT in post-operative period. The details have been shown in table-1. However, on statistical analysis this difference in the pre and post- operative mean values of SGOT was found to be not significant (P>0.05).

Other workers [2,8, 9, 10, 11] have also reported an increase in the levels of SGOT specially after repeated exposures. Similarly the levels of SGPT showed a slight increase in the post-operative period as compared to preoperative value. In sub group Al the levels of SGPT raised from49.7U/L ±7. So to 33.30 U/L +7.07 where as in sub group A2 it went up from 45.5U/L +.6.1 to 31.3U/L +6.55. Similarly in subgroup B1 and B2 the levels of SGPT increased from 48.60U/L ±8.48 to 48.60U/L ±6.16 and 49.50U/L + 5.17 to 52.3U/L ±5.03 respectively.

The other workers[2,8, 10, 12] have also reported a rise in SGPT levels especially after repeated exposures of halothane. In our series this rise in SGPT levels in post-operative period in all the sub groups was found to be statistically insignificant (P>0.05). McEwan[13] found a slight elevation in the

levels of SGOT and SGPT on repeated exposures with halothane, this rise which he found was statistically just significant (P=0.05).

The pre and post-operative count of eosinophils in all the sub groups was done, the details of which have been shown in table-4. Though there was a slight increase in the eosinophil count in post-operative period in all the sub groups as compared to pre-operative values. However, again on statistical analysis this rise in eosinophil count was found to be insignificant (P>0.05).

Some workers,[8, 12] reported no change in the eosinophil count in post-operative period after halothane anaesthesia whereas other workers[2, 5, 14, 15] have reported from mild to moderate rise in eosinophil count after repeated halothane exposures.

Similarly there was no correlation between the exposure of halothane and post-operative values of serum bilirubin, though there was a slight rise in serum bilirubin in all the sub groups in post-operative; period, but on statistical analysis this rise was found to be insignificant (P>0.05).

The rise in serum bilirubin was almost identical in the patients who received anesthesia for either 1-2 hours duration or for duration of more than 3 hours and there was not much difference whether the patient received 100% oxygen or they received 40% oxygen. The blood samples collected soon after operation in sub group (A1 and B1) or 48 hours after operation in sub group (A2 and B2) when compared did not reveal any difference.

The estimation of levels of SGPT in post-operative period showed a slight increase in all the sub groups. It was interesting to note that the rise in SGPT was much more when the duration of exposure was either 2-3 hours or more than 3 hours specially when blood samples were collected in immediate post-operative period. In sub group A1 (received 100% oxygen) the pre-operative SGPT mean levels were 33U/L which increased to a mean level of 54U/L in patients who received anesthesia for more than 3 hours.

This difference was statistically significant (P<0.05). Similarly in sub group B1 the patients received anesthesia for a period of 2-3 hours, their mean pre-operative SGPT levels were 3SU/L which increased to 56U/L in immediate post-operative period. This difference was again found to be statistically significant (P<0.05).

When comparison of eosinophil count in post-operative period was done with regards to the duration of halothane exposure, there was not much difference in the eosinophil count in patients who received anesthesia for either a period of 1-2 hours or more than 3 hours. The statistically insignificant identical rise (P>0.05) was seen in all the patients.

The reports of use of halothane anesthesia with 100% oxygen in human beings are lacking. More so it was initially thought that the reductive metabolites of halothane are mainly responsible for hepatic injury[3] and high percentage of oxygen inhibits this reductive pathways of halothane metabolism but Neuberger[14] is of the opinion that metabolites of oxidative pathways which are increased with higher percentage of oxygen are equally dangerous because these can lead to immunological response by sensitizing the hepatocyte membrane components.

In present the study we did not find any alteration (which was statistically significant) in the liver function tests in patients of both the groups who either received halothane anesthesia with 100% oxygen or who received conventional percentage <40%) of oxygen.

The slight increase in serum bilirubin, SGOT, SGPT, serum calcium and a slight rise in eosinophil count was found in both the groups in the post-operative periods. However, this rise was

found to be statistically insignificant (P>0.05) except the rise in SGPT soon after-operation which was found to be statistically significant in both the groups.

Strunin[16] has pointed out that such minor alterations in liver function tests can occur after any type of anesthesia. McEwan[13] has also reported a slight or minor alteration in various liver function tests after halothane and non-halothane anesthesia.

CONCLUSIONS: From the present study it is concluded that halothane anesthesia with either 100 % oxygen or with 40 % oxygen in adult patients does produce a slight alterations in liver function tests, however it was found to be statistically insignificant.

There had been no difference in liver function tests when compared between male and female patients. A larger series is needed to substantiate this conclusion.

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		A1		A2		B1		B2	
		Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Serum Albumin (in gm%)	Pre-op	3.53	0.62	3.5	0.93	3.25	0.51	3.64	0.49
	Post-op	3.46	1.02	3.92	0.47	3.51	0.46	3.69	1.01
Serum Bilirubin (in mg%)	Pre-op	0.12	0.13	0.33	0.16	0.23	0.07	0.25	0.09
	Post-op	0.29	0.22	0.40	0.19	0.28	0.24	0.26	0.09
Serum Calcium (in mg%)	Pre-op	10.33	0.75	9.20	2.56	9.90	2.08	10.65	0.85
	Post-op	10.63	0.75	10.31	1.09	10.86	0.78	11.00	0.76
SGOT (in U/L)	Pre-op	31.50	5.58	45.50	6.12	28.10	3.49	29.90	4.07
	Post-op	33.40	5.83	31.12	2.32	29.50	3.21	31.30	5.45
SGPT (in U/L)	Pre-op	49.7	7.80	45.5	6.12	42.60	8.48	48.6	6.13
	Post-op	53.30	7.07	51.3	6.55	49.50	5.17	52.3	5.03
Eosinophil Count (in %)	Pre-op	1.75	1.42	1.76	1.50	1.285	1.21	1.25	1.29
	Post-op	1.90	1.14	2.47	2.05	1.70	1.48	1.45	1.03

TABLE 1: SHOWS MEAN VALUES OF PRE AND POST OPERATIVE IN ALL SUBGROUPS

		1-2		2-3		Above 3	
		A1 (n=13)	**A2 (n=9)**	**A1 (n=5)**	**A2 (n=6)**	**A1 (n=2)**	**A2 (n=5)**
Serum Albumin (in gm%)	Pre-op	3.42	3.37	3.62	3.46	4.0	3.76
	Post-op	3.19	4.11	3.88	3.43	4.2	4.18
Serum Bilirubin (in mg%)	Pre-op	0.25	0.32	0.02	0.32	0.22	0.36
	Post-op	0.28	0.34	0.36	0.47	0.22	0.41
Serum Calcium (in mg%)	Pre-op	10.22	10.04	10.60	9.38	10.4	9.92
	Post-op	10.6	10.8	10.66	9.76	10.75	10.08
SGOT (in U/L)	Pre-op	31.07	45.70	30.44	28.68	28.0	29.62
	Post-op	32.9	31.11	34.4	31.66	34.00	30.4
SGPT (in U/L)	Pre-op	48.60	45.70	55.20	43.00	33.00	48.00
	Post-op	52.40	52.40	55.20	52.00	54.00	48.40
Eosinophil Count (in %)	Pre-op	1.80	1.66	1.20	1.66	1.50	2.06
	Post-op	2.00	2.30	1.40	2.33	2.00	2.96

TABLE 2: SHOWS RELATIONSHIP OF HALOTHANE EXPOSURE WITH PRE AND POST OPERATIVE MEAN VALUES IN SUB GROUPS

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		1-2		2-3		Above 3	
		B1 (n=17)	B2 (n=15)	B1 (n=1)	B2 (n=3)	B1 (n=2)	B2 (n=2)
Serum Albumin (in gm%)	Pre-op	3.20	3.54	3.60	4.10	3.50	3.75
	Post-op	3.40	3.52	3.90	4.40	4.05	3.90
Serum Bilirubin (in mg%)	Pre-op	0.22	0.25	0.15	0.24	0.32	0.30
	Post-op	0.28	0.26	0.15	0.24	0.35	0.30
Serum Calcium (in mg%)	Pre-op	9.7	10.60	10.50	10.80	10.75	10.75
	Post-op	10.80	10.88	11.00	11.40	11.10	11.25
SGOT (in U/L)	Pre-op	28.10	30.40	28.00	26.60	28.00	31.00
	Post-op	29.05	31.70	32.00	28.60	32.00	32.00
SGPT (in U/L)	Pre-op	43.2	49.0	32.0	48.0	42.0	46.0
	Post-op	49.6	51.4	56.0	55.3	45.0	54.0
Eosinophil Count (in %)	Pre-op	1.05	1.00	3.00	1.00	2.00	3.50
	Post-op	1.64	1.40	3.00	1.00	1.50	2.50

TABLE 3: SHOWS RELATIONSHIP OF HALOTHANE EXPOSURE WITH PRE AND POST OPERATIVE MEAN VALUES IN SUB GROUPS

		1-2		2-3		Above 3	
		A1 (n=13)	B1 (n=17)	A1 (n=5)	B1 (n=1)	A1 (n=2)	B1 (n=2)
Serum Albumin (in gm%)	Pre-op	3.42	3.20	3.62	3.60	4.40	3.50
	Post-op	3.19	3.40	3.88	3.90	4.20	4.05
Serum Bilirubin (in mg%)	Pre-op	0.25	0.22	0.02	0.15	0.22	0.32
	Post-op	0.28	0.28	0.36	0.15	0.22	0.35
Serum Calcium (in mg%)	Pre-op	10.22	9.70	10.60	10.50	10.40	10.75
	Post-op	10.60	10.80	10.66	11.00	10.75	11.10
SGOT (in U/L)	Pre-op	31.07	28.10	34.00	28.00	28.00	28.00
	Post-op	32.90	29.05	34.40	32.00	34.00	32.00
SGPT (in U/L)	Pre-op	48.60	43.20	55.20	42.00	48.00	42.00
	Post-op	52.40	49.60	55.20	50.00	54.00	45.00
Eosinophil Count (in %)	Pre-op	1.80	1.05	1.20	3.00	1.50	2.00
	Post-op	2.00	1.64	1.40	3.00	2.00	1.50

TABLE 4: SHOWS RELATIONSHIP OF HALOTHANE EXPOSURE WITH PRE AND POST OPERATIVE MEAN VALUES IN SUB GROUPS

		1-2		2-3		Above 3	
		A2 (n=9)	B2 (n=13)	A2 (n=6)	B2 (n=3)	A2 (n=5)	B2 (n=2)
Serum Albumin (in gm%)	Pre-op	3.37	3.54	3.46	4.10	3.76	3.75
	Post-op	4.11	3.52	3.43	4.40	4.18	3.90
Serum Bilirubin (in mg%)	Pre-op	0.32	0.25	0.632	0.24	0.36	0.30
	Post-op	0.34	0.26	0.47	0.27	0.41	0.30

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Serum Calcium (in mg%)	Pre-op	10.04	10.60	9.38	10.80	9.92	10.75
	Post-op	10.80	10.88	9.76	11.40	10.08	11.25
SGOT (in U/L)	Pre-op	45.70	30.40	28.60	26.60	29.60	31.00
	Post-op	31.11	31.70	31.60	28.60	30.40	32.00
SGPT (in U/L)	Pre-op	45.77	49.00	43.00	48.00	48.00	46.00
	Post-op	52.40	57.40	52.00	55.30	48.40	54.00
Eosinophil Count (in %)	Pre-op	1.66	1.00	1.66	1.00	2.06	3.50
	Post-op	2.30	1.40	2.33	1.00	2.96	2.50

TABLE 5: SHOWS RELATIONSHIP OF HALOTHANE EXPOSURE WITH PRE AND POST OPERATIVE MEAN VALUES IN SUB GROUPS

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