Original Research Article

Change in kidney function following intravenous inducing agents for general anaesthesia: A descriptive study in a teaching hospital of West Bengal

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Abstract

BACKGROUND: The choice of intravenous anaesthetic agents used for induction of general anaesthesia depends upon the hemodynamic status of the patient, presence of co- morbidities and systemic organ dysfunctions. **METHOD:** The study was conducted in a charitable teaching hospital of West Bengal from January to August 2019. Otherwise healthy adult individuals, admitted for minor surgical operations, were selected from both genders and age varying from 20 to 55 years. Minor surgeries with known standard anaesthetic technique with Thiopentone, Ketamine and Propofol which are supposedly innocuous as regards to kidney were taken in the present study. The relevant investigations were studied on the first and fifth post-operative days and the values were compared with that of the pre-operative values and between the first and fifth post-operative days. Furthermore, it was attempted to find out, whether the changes which occurred on the post – operative days were the same for all the groups. **RESULTS:** The investigations were statistically different on different days and in different groups, but it was not clinically significant as all were within the normal range. **CONCLUSION:** The values of the test being within the normal range, there was no real clinical significance. Hence it could be concluded that the three drugs-Thiopentone, Ketamine and Propofol had no deleterious effect per se on the kidney when used as an inducing agent.

KEY WORDS: Kidney function tests, Thiopentone, Ketamine, Propofol

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INTRODUCTION

It is a common knowledge that liver plays the prominent role in the metabolism of the anaesthetic drugs and its metabolites are excreted through kidneys. Most of the anaesthetic drugs are believed to be protoplasmic poisons in greater or lesser degree, hence it is reasonable to presume that vital organs like kidney may be affected under the influence of these drugs and any evidence, clinical or biochemical of kidney dysfunction will prejudice its place in the list of unsafe anaesthetic agents. Thiopentone, Ketamine and Propofol are three of the most commonly used anaesthetic agents used in the operation theatres throughout the country. Amongst the three drugs, Thiopentone is a rapidly acting barbiturate, Ketamine, a dissociative anaesthetic, derivative of phencyclidine series, is a potent analgesic and propofol is a phenol derivative totally metabolized quickly and may have extra-hepatic metabolism. All the three drugs are

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metabolized by the liver and metabolic products are excreted in the urine. All barbiturates are filtered by renal glomeruli, but the high degree of protein binding limits the magnitude of filtration, whereas high lipid solubility favours reabsorption of any filtered drug back into circulation. Less than 1% of administered Thiopentone is excreted unchanged in urine. Volatile anaesthetics produce similar dose related decrease in renal blood flow, glomerular filtration rate, and urine output which can be attenuated by pre- operative hydration. With Thiopentone there is fall in renal blood flow and the degree of depression of flow will depend upon the depth of anaesthesia. Renal function after kidney transplantation is not uniquely influenced by the volatile anaesthetic administered.[1] Prolonged sevoflurane, anaesthesia does not impair renal concentrating function, despite higher peak plasma fluoride concentration compared with enflurane. [2,3] Inhaled anaesthetics such as methoxyflurane and enflurane undergo greater intrarenal metabolism to fluoride than sevoflurane which is more important factor for nephrotoxicity.[4,5] Desflurane administered at 1.25 MAC for 2, 4 or 8 hours and isoflurane using fresh gas flows did not produce any evidence of renal injury.[6,7,8] Many authors have demonstrated that most operative procedures do not produce any change in the renal circulation.[9] Painful stimulation as produced by surgery may evoke the release of ADH. Aggressive and early treatment of perioperative oliguria is most important for those patients at increased risk for developing acute renal failure.[10] The objective of this study was to observe changes of kidney function following Thiopentone, Ketamine and Propofol in inducing doses and their safety in the body with respect to kidneys.

METHODS

The study was conducted in a charitable teaching hospital of the capital city of the state West Bengal of India from January to August 2019. A total number of 30 cases of American Society of Anesthesiologists (ASA) grade I was selected for the purpose of the study. The patients were grouped into 3 categories according to the drug used for induction of anaesthesia. Each drug was administered to a group of 10 patients. Group I, II and III received patients received Thiopentone, Ketamine and Propofol respectively. Operations of lesser magnitude and known standard anaesthetic technique for maintenance which is documented to be innocuous as regards to kidney were employed in the present study. All patients were premedicated with glycopyrrolate (0.2 mg) intramuscularly one hour before anaesthesia. On arrival of the patient in the operation theatre, pulse oximeter, non-invasive blood pressure, ECG, were attached. The patients were pre-oxygenated for 2 to 3 minutes. Anaesthesia was induced with either Thiopentone 5mg/kg, Ketamine 2mg /kg or Propofol 2mg/kg intravenously to the eligible patients. This was followed by Atracurium 0.5mg/kg during which ventilation with 100% oxygen was carried out. Intubation was done with a proper size cuffed endotracheal tube and anaesthesia was maintained with nitrous oxide, and oxygen, using controlled respiration through a Bain's circuit. Reversal of residual curarisation was done at the end of operation by glycopyrrolate followed by neostigmine intravenously in appropriate doses. Meticulous care was taken to prevent hypoxia, hypercarbia and hypotension. All patients were given infusion of 200-500 ml of Ringer Lactate. All patients were supervised carefully for blood pressure, pulse rate, temperature and infection. The following kidney function tests were done before premedication of the patient and following anaesthesia on first and fifth post-operative days: routine urinary examination including 24 hrs urine volume, specific gravity, bile salts and pigments, albumin and microscopical examination and blood urea and creatinine. Sample study of arterial oxygen and carbon dioxide tension were performed before premedication and during anaesthesia following the three studied inducing agents. This was carried out on one patient in each group selected randomly. Mean and standard deviation had been worked out for each group of patients receiving the drug. Comparison of tests done between the basal and post-operative days (1st and 5th post-operative days) and between the 1st and 5th post-operative days were made. To see whether all the three drugs behaved in the same way or differently, with respect to the functions of the kidney, comparisons were also made on the reports of those days for each group. Paired 't' test was used to compare the tests. For multiple comparisons Tukey's procedure, was adopted. Results were considered statistically significant at p value of .05 or less.

RESULTS

The blood investigations were studied on the first and fifth postoperative days and the values were compared with that of pre-operative values (taken as basal value) and between the first and fifth post-operative days. The means (with standard deviation) of the urinary volume in 24 hours and the specific gravity during the pre-operative period and on the first and fifth post-operative days for the three groups is shown in table 1. Figure 1 shows the changes in 24 hours urine volume following three intravenous inducing agents. Figures 2 to 4 shows specific gravity of patients of all groups against urine volume on pre-, first- and fifth- post-operative days.

Table 1: Volume and specific gravity of urine of participants on different days

Group	Period	Urinary volume (ml in 24 hours)		Specific gravity	
		Mean	S.D.	Mean	S.D.
I	Pre – op. (basal)	1590	370.00	1015	3.440
	Post – op. 1st day	705	146.50	1026	4.749
	Post – op. 5th day	1303	296.78	1018	4.784
II	Pre – op. (basal)	1330	208.80	1017	1.612
	Post – op. 1st day	726	117.40	1027	3.878
	Post – op. 5th day	1151	206.60	1019	2.497
III	Pre – op. (basal)	1575	566.67	1014	4.578
	Post – op. 1st day	797	384.29	1026	5.986
	Post – op. 5th day	1308	296.54	1017	1.400

Computed values of 't' statistic for comparing the averages of urinary volume and specific gravity of the three groups on first and fifth post-operative days with that of the average basal value and in between the first and fifth post-operative days is shown in table 2.

Table 2: Urinary volume and specific gravity on 1st and 5th post-operative days in all groups

Group	Degrees Of freedom	Comparison between days	Value of 't' statistic	
			Urinary Volume	Sp. Gr.
I	9	Pre – op. 1st post – op	6.661**	7.799**
		Pre – op. vs. 5th post – op.	4.545**	2.142
		1st post – op. vs 5th post – op.	5.968**	6.875**
II	9	Pre – op. vs. 1st post – op.	9.326**	8.874**
		Pre – op. vs. 5th post – op.	4.609**	3.154*
		1st post – op. vs 5th post – op.	5.434**	5.855**
III	9	Pre – op. vs. 1st post – op.	3.405**	5.208**
		Pre – op. vs. 5th post – op.	1.745	0.758
		1st post – op. vs 5th post – op.	3.353**	4.676**

Computed values of 'w' statistic to note the homogeneity between the groups in respect of urinary volume and specific gravity in between the pre-operative and post-operative days and between the first and fifth post-operative days by Tukey's procedure is shown in table 3.

Table 3: Urinary volume and specific gravity on pre-operative, 1st and 5th post-operative days

Comparison between Groups	Comparison between days	Value of 'w' statistic	
		Urinary volume	Sp. Gr.
Group I and II	Pre – op. vs 1st post – op.	1.788	0.357
	Pre – op. vs 5th post – op.	1.003	0.084
	1st post – op. vs 5th post – op.	1.590	0.463
Group I and III	Pre – op. vs 1st post op.	1.107	0.595
	Pre – op. vs 5th post – op.	0.901	0.336
	1st post – op. vs 5th post – op.	0.747	0.397
Group II and III	Pre – op. vs 1st post – op.	0.681	0.238
	Pre – op. vs 5th post – op.	0.102	0.420
	1st post – op. vs 5th post – op.	0.843	0.066

The means (with standard deviation) of blood urea and creatinine levels during the pre-operative period and on the first and fifth post-operative days for the three groups is shown in table 4.

Table 4: Blood urea and creatinine levels on pre-operative, first and fifth post-operative days

Group	Period	Urea		Creatinine	
		Mean (mg%)	S.D	Mean (mg%)	S.D
I	Pre – op. (basal)	30.6	4.630	0.95	0.585
	Pre – op. 1st day	52.7	16.774	1022	0.692
	Post – op. 5th day	38.0	4.449	1.00	0.550
II	Pre – op. (basal)	33.3	6.915	0.78	0.265
	Pre – op. 1st day	45.5	9.779	0.85	0.574

	Post – op. 5th day	39.0	7.771	1.09	0.641
III	Pre – op. (basal)	32.3	6.325	0.96	0.617
	Pre – op. 1st day	48.3	11.644	1.6	0.685
	Post – op. 5th day	35.6	9.024	1.10	0.663

Figures 5 and 6 shows the changes of blood urea and creatinine levels following the three intravenous inducing agents respectively.

Computed values of 't' statistic for comparing the averages of blood urea and creatinine of the three groups on first and fifth post-operative days with that of the average basal value and in between the first and fifth post-operative days is shown in table 5.

Table 5: Blood urea and creatinine on pre-, first- and fifth- post operative days

Group	Degrees of freedom	Comparison between days	Value of 't' statistic	
			Urea	Creatinine
I	9	Pre – op. vs. 1st post – op.	3.947**	20456*
		Pre – op. vs. 5th post – op.	3.814**	0.318
		1st post – op. vs. 5th post – op.	3.283**	2.057
II	9	Pre – op. vs. 1st post – op.	2.952*	1.283
		Pre – op. vs. 5th post – op.	1.550	2.671*
		1st post – op. vs. 5th post – op.	2.853*	1.661
III	9	Pre – op. vs. 1st post – op.	3.319**	0.795
		Pre – op. vs. 5th post – op.	0.605	3.117*
		1st post – op. vs. 5th post – op.	2.429*	0.313

Computed values of 'w' statistic to note the homogeneity between the groups in respect of blood urea and creatinine in between pre-operative and post-operative days and between the first and fifth post-operative days by Tukey's procedure is shown in table 6.

Table 6: Blood urea and creatinine on pre-operative and post-operative days

Comparison between Groups	Comparison between days	Value of 'w' statistic	
		Urea	Creatinine
Group I and II	Pre – op. vs 1st post – op.	3.509	0.083
	Pre – op. vs 5th post – op.	1.985	3.156
	1st post – op. vs 5th post – op.	2.847	3.508
Group I and III	Pre – op. vs 1st post op.	1.406	1.047
	Pre – op. vs 5th post – op.	0.266	2.655
	1st post – op. vs 5th post – op.	1.585	1.659
Group II and III	Pre – op. vs 1st post – op.	2.182	1.008
	Pre – op. vs 5th post – op.	2.202	0.709
	1st post – op. vs 5th post – op.	0.126	2.020

Table 7 shows the sample studies of oxygen and carbon dioxide tension in arterial blood before and during anaesthesia for the three groups. For this one patient was studied from each group.

Table 7: Oxygen and carbon dioxide tension in arterial blood before and during anaesthesia

	Group I		Group II		Group III	
	Basal value	During anaesthesia	Basal value	During anaesthesia	Basal value	During anaesthesia
PaO_2 (mm of Hg)	98	110	97	108	98	110
PaCo2 (mm of Hg)	38	39	41	39	40	41

DISCUSSION

The functions of the kidneys are complex. Many factors other than the anaesthetic agents per se may adversely affect these functions during anaesthesia and operation. Since age may be a factor in making the kidneys more susceptible to the effects of anaesthetic agents including the inducing drugs, all the patients studied were young otherwise healthy adults. As regards the nature of

operation, severe traction on the large bowel may produce temporary vasoconstriction of the renal vessels and major surgical trauma and stress particularly under very light anaesthesia – may lead to depression of renal blood flow.[11] Thus, this study was carried out in operation of lesser magnitude and no patient undergoing upper abdominal surgery was included in the series. Patients with clinical conditions like chronic sepsis, pulmonary tuberculosis, thyrotoxicosis, intestinal obstruction, advanced carcinoma, severe burn, enlarged prostate, diseases of urinary bladder and ureter were excluded. Certain other factors associated with anaesthesia, like hypoxia, hypercarbia and hypotension have profound effects on kidneys. The technique of controlled respiration during anaesthesia with the help of muscle relaxants, nitrous oxide, oxygen, through Bain circuit system helped to avoid hypoxia and hypercarbia. In the present study, a sample study of PaO2 and PaCO2, before and during anaesthesia, with all the three drugs were found within normal limits. This indicated that with the methodology used in the study no hypoxia occurred. Post-operative complications like infection may be attributable to the dysfunction of the kidneys. Infection or any other complication did not occur in the case under study. The result of various tests used in the present study suggest that renal function was adequate for patients of all the three groups during the post-operative period. Many researchers have observed that nearly all anaesthetic agents stimulate the secretion of antidiuretic hormone and produce oliguria. Muscle relaxants are known to be innocuous to the kidneys. Dundee has shown that there is no relationship between the use of muscle relaxants in anaesthesia and the excretion of urobilinogen in the urine after operation.[12] Deutsch *et al* suggested that thiopentone-nitrous- narcotic-relaxant anaesthetic was a more profound stimulus for ADH secretion.[13] Renal effects of thiopental include, modest decreases in renal blood flow and glomerular filtration rate. The most likely explanation is drug – induced decrease in systemic blood pressure and cardiac output.[14,15.] Histologic evidence of renal damage is not detectable after use of Thiopentone for induction of anaesthesia.[16] Ketamine does not significantly alter laboratory tests that reflect kidney function. Prolonged infusions of propofol may result in excretion of green urine, reflecting the presence of phenols in urine. This discolouration does not alter renal function. Thus, most of the studies by the previous workers are in agreement with the work of the present study.

CONCLUSION

There is no clinically significant difference in the renal function tests following administration of three intravenous anaesthetic agents, Thiopentone, Propofol and Ketamine. The three drugs had no deleterious effect per se on the kidney when used as an inducing agent, although there might have been some transient changes as evidenced by some of the tests of kidney function.

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