

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Evaluation of Change in Serum Potassium Level in Patients Undergoing Lower Third Molar Surgery under Local Anesthesia with and Without Adrenaline.

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### ABSTRACT

This study was undertaken to observe and compare the change in serum potassium levels due to amide linked local anaesthetics with and without adrenaline in minor oral surgical procedure such as lower third molar surgery. Twenty healthy patients requiring surgical removal of bilaterally impacted lower third molar were selected from the Department of Oral and Maxillofacial Surgery. These twenty patients were divided into Group-I, Group-II each group comprising of 20 patients. 2% Lignocaine hydrochloride with 1:2,00,000 adrenaline was used in Group I and 0.5 % Bupivacaine hydrochloride was used in Group II. First sample was taken 30 min after breakfast but before administration of local anesthetic solution. Twenty min later second blood sample was withdrawn. The values were compared and were statistically analyzed by independent sample 't' test. Five minute before administration of local anesthesia, serum potassium level did not differ significantly between two study groups ( $P>0.05$ ). Immediate after administration of local anesthesia, serum potassium level did not differ significantly in both two study groups ( $P>0.05$ ). After 10 minutes administration of local anesthesia, serum potassium level significantly decreased in Group I as compared to Group II ( $P<0.05$ ). After 20 minutes administration of local anesthesia, serum potassium level significantly decreased in Group I as compared to Group II ( $P<0.05$ ). After 30 minutes administration of local anesthesia, serum potassium level did not differ significantly in both study groups ( $P>0.05$ ). As the epinephrine containing local anesthetic solution (xylocaine) causes hypokalemia. The 0.5% Bupivacaine hydrochloride local anesthetic solution is a long acting local anesthetic solution, it is safe to use 0.5% Bupivacaine hydrochloride in the patients suffering from problems or medical conditions like congestive heart failure, hepatic insufficiencies, nephrotic syndrome or the patient on medications like Thiazide diuretics.

**Keywords:** Local anesthesia, Impacted Mandibular third molar, plasma potassium.

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## INTRODUCTION

For thousands of years doctors and researchers have searched for a drug that could eliminate or at least ease the pain of surgery. Carl Koller who was an ophthalmologist, has the credit for the discovery of cocaine as a local anaesthetic. Since then, surgeons from all surgical fields adapted the newly discovered anaesthetic to all sorts of novel and complicated surgical interventions [1].

The term 'local anaesthesia' was used first by James Young Simpson in 1848. Benjamin Ward Richardson in 1858 has contributed for the use of different local anaesthetic agents. Jokichi Takamine discovered the same hormone in 1901 [2]. Adrenaline is a catecholamine secreted by adrenal gland. It was first isolated and identified in 1897 by John Jacob Abel. Lidocaine, the amino amide-category local anaesthetic was first synthesized under the name of Xylocaine by Swedish chemist Nils Lofgren in 1943 [3]. In 1903, adrenaline was first used by Braun in local anaesthetic solutions for intraspinal blocks to prolong the action of cocaine by reducing the local blood supply and delaying its uptake in order to reduce cocaine toxicity with systemic absorption [1].

Adrenaline is used in local anaesthetics, because it's inherent property of vasoconstriction has some distinct advantages like, it promotes longer lasting anaesthesia, diminishes the toxic effects by delaying absorption and reduces blood loss during oral surgical procedures [4,5].

Intravenous infusion of epinephrine has been shown to reduced plasma potassium and magnesium concentration [6]. Epinephrine is one of several circulating hormones that influence plasma potassium concentration. Meechan and Rawline [7] have shown that administration of epinephrine containing dental local anesthetic solution in amounts consistent with normal clinical practice reduced plasma potassium levels in healthy volunteers. Although the cardiovascular responses to intraoral injection of epinephrine containing dental local anesthetic solution have been well documented, the effect on plasma potassium levels has received little attention [8].

Meechan and Rawline [8] investigated the influence of two different dental local anesthetic solutions on plasma potassium level during third molar surgery. They concluded that plasma potassium level reduces significantly in early post injection period in local anesthesia using adrenaline. In various medical conditions like congestive heart failure, hepatic insufficiencies, nephrotic syndrome or the patients who on medications like Thiazide diuretics potassium concentration reduced.

Many studies have been conducted for hemodynamic evaluation in patients undergoing oral surgical procedures under general anesthesia, where parameters such as blood pressure levels, plasma potassium levels, were checked [7-10]. But there is no study to determine the change in serum potassium level due to amide linked local anesthetics containing adrenaline in oral surgical procedures. Therefore, this study was undertaken to observe and compare the change in serum potassium levels due to amide linked local anesthetics with and without adrenaline in minor oral surgical procedures.

## MATERIALS AND METHOD

The study was conducted on 20 patients reporting to the Department of Oral and Maxillofacial Surgery, who were indicated for surgical removal of bilateral impacted mandibular third molars.

### Inclusion Criteria

- Healthy patients in the age group of 18 to 45 yrs.
- Patients with bilaterally impacted third molars.

### Exclusion Criteria

- Female patients who were pregnant or lactating.
- Patients who were suffering from renal disorders

**Methodology**

The present study was randomized, single blind Split Mouth study. The randomization was done on the basis of a coin toss. The study was conducted after obtaining clearance from institutional review board. These twenty patients were divided into:

Group I- 2% Lignocaine hydrochloride with 1:2, 00,000 adrenaline

Group II-0.5% Bupivacaine hydrochloride.

All the patients were examined preoperatively for routine blood examination like haemogram, bleeding time and clotting time. Pre-operative antibiotic, anti-inflammatory and analgesic drugs were prescribed. The informed written consent was taken from each patient. The patients were given appointment for the surgical removal of impacted third molar between 10 am and 12noon. They were asked to report to the department without having any food. The patients were advised a potassium restricted diet 24 hours prior to the procedure.

Each patient was scheduled for the surgery on two occasions at the same time of the day. A 21 gauge cannula was introduced in the median cubital vein for withdrawing blood. The blood withdrawal was done preoperatively five minutes before the administration of local anesthetic and time recorded. 2ml of blood was withdrawn into the glass bulb. The local anesthetic blocks pterygomandibular and long buccal nerve blocks were given. On one schedule, 2% Lignocaine hydrochloride with 1:2,00,000 adrenaline was used as local anesthetic. In the other schedule, after 4 weeks 0.5% Bupivacaine hydrochloride was used. The order of injections was randomized, and was given by same operator. 2mL blood was withdrawn for estimation of serum potassium level immediately after the administration of local anesthetic. After blood withdrawal, surgery was conducted after the confirmation of effect of local anesthetic action. Depending on the type of tooth either Ward’s incision or Modified Ward’s incision was taken. Mucoperiosteal flap was reflected. The buccal bone guttering was done with no -8 round carbide bur and sectioning of tooth was done with 703 straight fissure bur. Tooth was elevated and removed from the socket. The bony socket was irrigated with normal saline and checked for any remaining tooth or bone. After ensuring hemostasis, wound was closed with 3-0 black silk interrupted sutures. The withdrawal of blood for serum potassium estimation was repeated after 10, 20, and 30 minutes after the end of local anesthetic administration.

All blood samples were examined for serum potassium at the biochemistry laboratory. The patients were given post-operative instructions. The patients were recalled after 24 hr. and checked for swelling, trismus and intraoral wound healing. The patients were recalled after 7 days for suture removal.

**RESULTS**

The mean and standard deviation between the groups were calculated (Table 1)

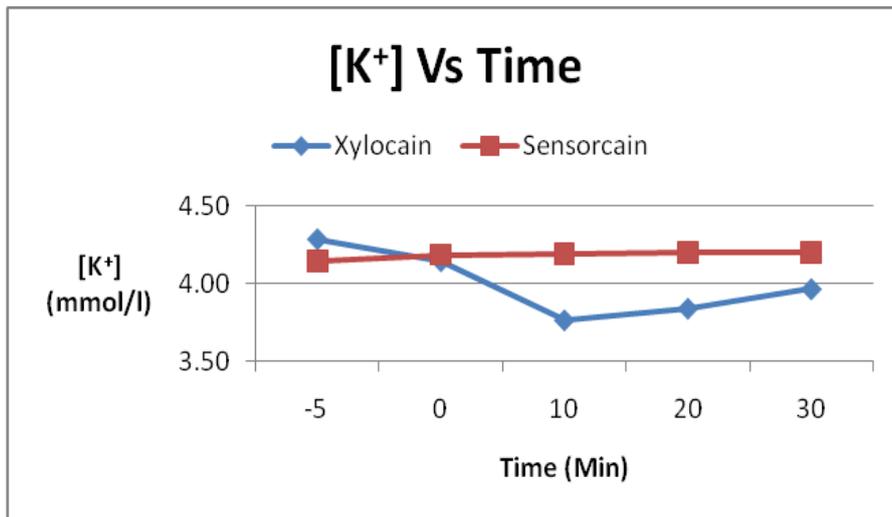
**Table 1: Mean and standard deviation values for both the groups.**

	Group	N	Mean	Std. Deviation	Std. Error
five_Min_Before	1	20	4.2850	.58063	.12983
	2	20	4.1450	.43344	.09692
Immediate_after_LA	1	20	4.1450	.63947	.14299
	2	20	4.1900	.41663	.09316
After_10min	1	20	3.7650	.45685	.10215
	2	20	4.1950	.47292	.10575
After_20min	1	20	3.8400	.55193	.12342
	2	20	4.2050	.46507	.10399
After_30min	1	20	3.9650	.67845	.15171
	2	20	4.2050	.48826	.10918

The serum potassium levels were evaluated between the levels with P-values were obtained using independent sample ‘t’ test. P-value<0.05 was considered to be statistically significant.

- 1) Five minute before administration of local anesthesia, serum potassium level did not differ significantly between two study groups ( $P>0.05$ ).
- 2) Immediate after administration of local anesthesia, serum potassium level did not differ significantly in both two study groups ( $P>0.05$ ).
- 3) After 10 minutes administration of local anesthesia, serum potassium level significantly decreased in Group I as compared to Group II ( $P<0.05$ ).
- 4) After 20 minutes administration of local anesthesia, serum potassium level significantly decreased in Group I as compared to Group II ( $P<0.05$ ).
- 5) After 30 minutes administration of local anesthesia, serum potassium level did not differ significantly in both study groups ( $P>0.05$ ).

Figure 1: Between Group distribution of serum potassium levels



**Comment**

Pooled values of serum potassium concentration against time for both treatments, showing significant differences between treatments at -5, 0, 10, 20, 30 minutes following injection of local anesthetic.

Figure 2: Change in serum potassium levels Five minute before.

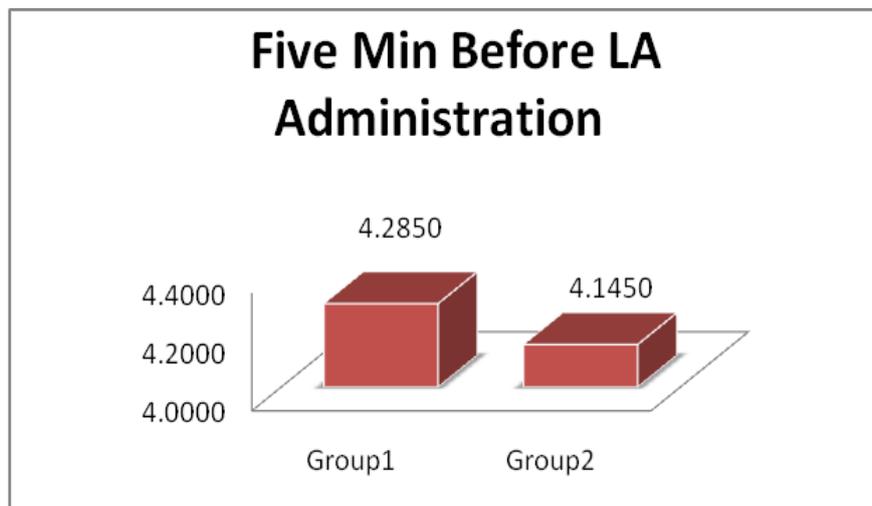


Figure 3: Change in serum potassium levels immediately After LA Administration

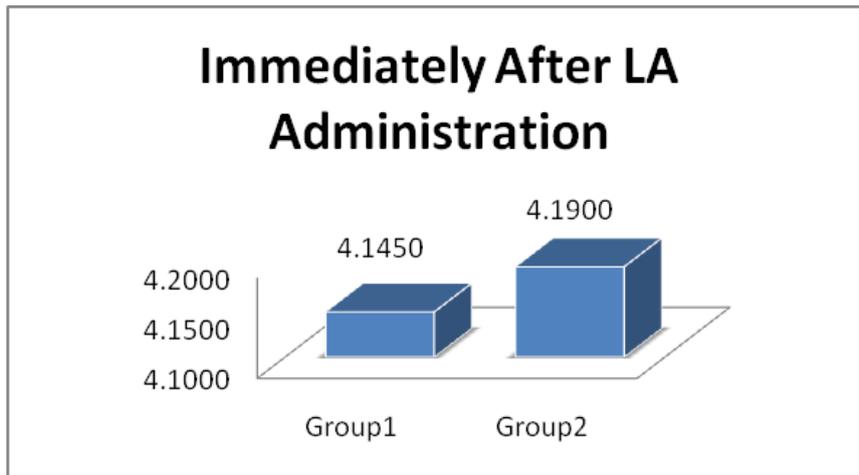


Figure 4: Change in serum potassium levels Ten minutes after LA administration

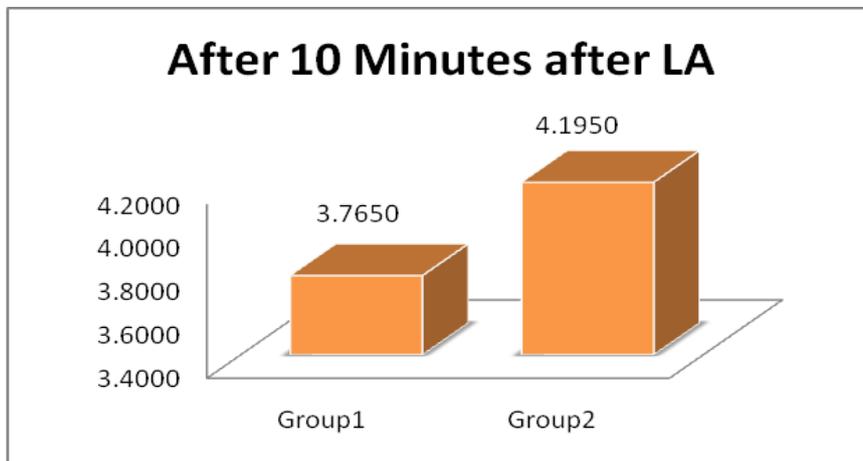


Figure 5: Change in serum potassium levels Twenty minutes after LA administration

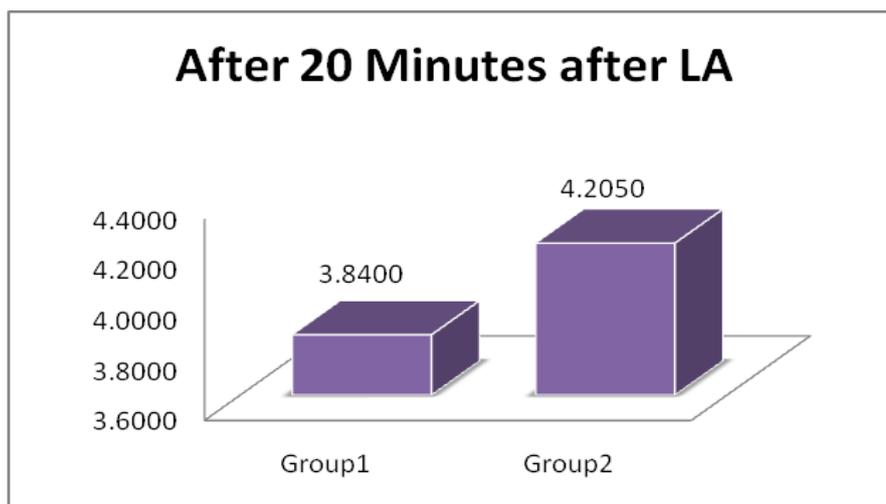
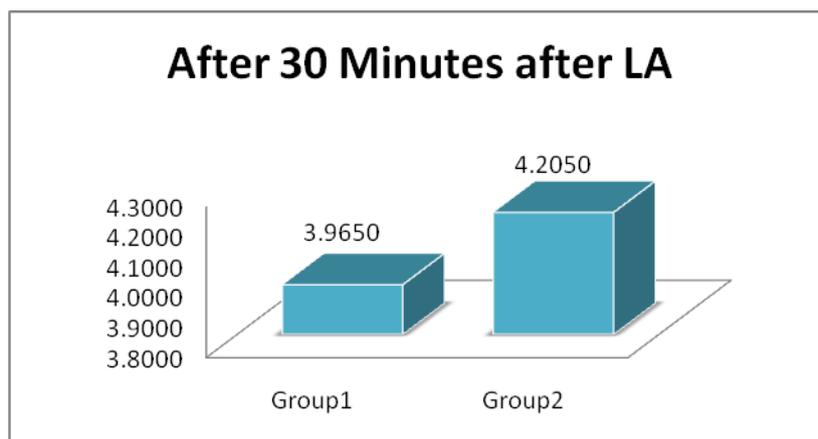


Figure 6: Change in serum potassium levels Thirty minutes after LA administration



### DISCUSSION

For any oral surgical procedure the most important aspect is to take a detailed case history. In this, the oral surgeon needs to evaluate the patients medically especially suffering from various medical conditions like congestive heart failure, hepatic insufficiencies, nephrotic syndrome or the patient on medications like Thiazide diuretics. Meechan JG (1997)[11] studied the plasma potassium changes in hypertensive patients undergoing oral surgery with local anesthetic containing epinephrine and concluded that ten min following the injection of the local anesthetic, plasma potassium concentration was significantly raised in patients who received treatment with non-potassium sparing diuretics than on patients treated with nonselective beta-adrenergic blocking drug therapy. These conditions cause hypokalemia which can be serious problem for oral surgical procedures [12].

In oral surgery procedures, local anesthesia with epinephrine is commonly used and the concentration of anesthesia varies from 1: 50,000, 1: 80,000, 1: 1, 00,000 to 1: 2, 00,000[3]. Epinephrine is a vasoconstrictor that is used in local anesthesia to retard the systemic absorption of the local anesthetic agent. By the virtue of this property of epinephrine, it prolongs the duration of anesthesia and decreases the possibility of systemic toxicity. It also helps in controlling the bleeding because of the hemostatic effect that it provides [8].

Lofgren A, Hahn RG [13] studied the effect of adding epinephrine to the local anesthetic solution and of upper abdominal surgery on the hypokalemia following intercostal nerve block. Intercostal block was induced with bupivacaine 0.5 % and 1:20000 adrenaline and hypokalemia doubled on its usage. Hahn RG, Lofgren A [14] in another study concluded the relation between electrocardiogram and the plasma epinephrine and serum potassium. The results show hypokalemic effect of epinephrine was reduced when the plasma epinephrine concentration exceeded 3nmol/ L. A multiple regression analysis demonstrated that the ST level and the T- wave amplitude were most consistently affected by a low serum potassium level, while a high plasma epinephrine level correlated only to a depression in the T-wave amplitude.

Durbar [15] et al studied epinephrine – induced changes in serum potassium and cardiac repolarization and effects of pretreatment with propranolol and diltiazem. The major ECG effect of epinephrine infusion was dose related increase in Etc. At an epinephrine dose of 40ng/kg/min, QTc prolongation persisted and was inhibited by diltiazem. These suggest that the major electrocardiographic effect of epinephrine infusion is mediated by increase in calcium content. At dose >80 ng/kg/min, plasma epinephrine concentrations are comparable to those observed with severe stress, and hypokalemia is common. The use of epinephrine as an electrophysiological provoker at dosage >80ng/kg/min results in both direct and indirect effect due to hypokalemia.

Rainer [16] et al undertaken the study to determine the dose- response effects of systemic epinephrine infusion on the relationship of Plasma renin activity (PRA) and plasma aldosterone concentration

Circulating epinephrine induces both stimulation PRA and a decrease in serum potassium concentration. These above study show the hypokalemic affects seen similar in our study.

Dury A, Holler JW, Smith C [17] studied the changes in plasma potassium level after epinephrine in normal human beings and in persons with epilepsy, normal human and patients with idiopathic epilepsy and found that the main plasma potassium was found to be depressed from initial levels at 4 minutes after the epinephrine and persisted for a relatively prolonged time compared to the changes found in the normal group.

However, Struthers et al showed that epinephrine could precipitate a significant hypokalemia in healthy young adults [6]. This is because of increased circulating adrenaline that produces fall in potassium concentration i.e. hypokalemia; which is mediated by a beta-2 adrenergic agonist mechanism where a membrane bound Na/K – ATPase dependent pump pushes potassium into the cell [23].

Two percent Lignocaine hydrochloride and 0.5% Bupivacaine hydrochloride are amide linked local anesthetic agents. As stated earlier, in two percent Lignocaine hydrochloride with adrenaline because of its vasoconstriction effect thereby prolonging the anesthetic effect, while 0.5% Bupivacaine hydrochloride has inherent long acting effect [3].

In our study, an attempt was made to evaluate the change in serum potassium levels in healthy patients undergoing oral surgical procedure under amide linked local anesthetics with and without adrenaline using either 2% Lignocaine hydrochloride with 1:2, 00,000 adrenaline (Xylocaine) or 0.5 % Bupivacaine hydrochloride (Sensorcaine).

In the present study 20 patients with bilaterally impacted mandibular third molars indicated for surgical removal were divided into two equal groups, Group I (2% Lignocaine hydrochloride with 1:2, 00,000 adrenaline) and Group II (0.5% Bupivacaine hydrochloride).

All the patients were given appointment for surgical removal of third molar in between 10am and 12 noon. They were asked to report to the department without having any food. Each patient on arrival was given same breakfast. Since we have subjected the patients under the same set of circumstances, time, nutrition and environment to injections of either 2% Lignocaine hydrochloride with 1:2, 00,000 adrenaline (Group I) or 0.5% Bupivacaine hydrochloride (Group II), the settings can be considered to be standardized.

In the present study, blood samples were collected five times for estimation of serum potassium level. The time intervals were as follows-

- 5 minutes before administration of local anesthetics,
- Immediately after administration,
- 10 minutes, 20 minutes and 30 minutes after administration of local anesthetics.

In Group I, no significant change in serum potassium level was seen at 5 minutes before administration, immediately after the administration and 30 minutes after administration of local anesthetics. However, significant decrease in the serum potassium levels was seen during 10 and 20 minutes of administration of local anesthesia.

The results of the present study were similar to the studies conducted by Meechan et al and Shannon et al which showed that epinephrine containing dental local anesthetic solutions differ in their effect on plasma potassium concentrations and this effect occurs in the early post injection period [8].

Our results are also concurrent with the study conducted by Dury A et al [17]. He has shown that in epileptic patients plasma potassium levels decrease after administration of local anesthesia containing epinephrine

In Group II, no significant change in serum potassium level was seen at 5 minutes before local anesthesia, immediately after local anesthesia administration and after 10, 20, 30 minutes of administration of local anesthesia.

In the present study, the results of group II were similar to the study conducted by J G Meechan the effect of epinephrine- free solutions on serum potassium levels shows gradual increase and then return to the true baseline state [8]. Sivanmalai S et al [18] studied to investigate the biochemical and hemodynamic effect of adrenaline in lignocaine local anesthetic solutions in patients undergoing third molar surgery under general anesthesia and concluded that exogenous adrenaline administration in clinical doses produces systemic effect even in conditions where the endogenous release of the catecholamine would be expected to be considerable. These were seen in our study too where we claim that long acting anesthetic is better for third molar surgery.

Reid JL, Whyte KF, Struthers AD [19] concluded that Epinephrine induced hypokalemia results from stimulation of a beta- adrenoceptors linked to membrane sodium/ potassium adenosine triphosphates causing potassium influx. Meechan JG [20] et al also stated that there is significant change in plasma potassium concentration before and after administration of local anesthesia containing 2% Lignocaine with 1:80,000 adrenaline. However, Meechan JG, Thomson CW, Blair GS [21] conducted a study for investigating the systemic effect of adrenaline in dental local anesthetic solutions in 20 patients requiring surgical removal of third molar under general anesthesia with Administration of 50ug adrenaline contained in lignocaine local anesthetic solution on hemodynamic and biochemical response were establish by comparing the effect of inferior alveolar block injection of 4ml 2% lignocaine and 4ml 2% lignocaine with 1: 80000 adrenaline in 20 patient having third molar with a standardized general anesthetic regime author in which they concluded that no significant changes in hemodynamic responses between the treatment were apparent.

According to Koch RNS [22] et al hypokalemia alters the function of several organs and most prominently affects the cardiovascular system, neurologic system, muscles, and kidneys. These effects ultimately determine the morbidity and mortality related to this condition. Two major side-effects of hypokalemia affect the cardiovascular system are hypokalemia-related hypertension and hypokalemia-induced ventricular arrhythmias. Both contribute to increased morbidity and mortality. Congestive heart failure, hepatic insufficiency, or nephrotic syndrome, may also exhibit hypokalemia. Finally, patients with diseases that alter renal K<sup>+</sup> conservation through increased salt delivery are at high risk for hypokalemia [22].

Hypokalemia contributes to hypertension in many patients but is frequently unrecognized as an important factor that may produce or worsen this serious health problem. Thiazide diuretics are more likely to cause hypokalemia than loop or osmotic diuretics [23].

Thus the patients with congestive heart failure, hypertension hepatic insufficiency, or nephrotic syndrome or the patients on Thiazide diuretics are more prone to hypokalemia. As the results of our study show that there is decrease in serum potassium concentrations after injection of epinephrine containing anesthetics solution, it is advised to take precautions while treating these patients [12]. As the serum potassium concentration decreases in these patients, further decrease in potassium levels may worsen the condition, which may contribute to morbidity and mortality.

In patients with cardiovascular disease, potassium levels are important in precipitating arrhythmias [8]. This could be of particular relevance with kaliuretic diuretics since, in addition to lowered serum potassium level; such patients are more sensitive to the hypokalemic effect of epinephrine [24].

Thus based on the results of our study, it can be suggested that precautions must be taken in patients suffering from hypokalemia, as the further decrease in serum potassium may produce or worsen the health. But epinephrine containing and epinephrine-free anesthetic solutions can be used in healthy and young individuals

## CONCLUSION

The serum potassium concentration does not show any significant change 5 minutes before administration, immediately after administration of epinephrine containing localanesthetic solution.

The serum potassium concentration shows significant decrease after 10 minutes and 20 minutes after administration of epinephrine containing local anesthetic solution. As the epinephrine containing local anesthetic solution (xylocaine) causes hypokalemia.

The 0.5% Bupivacaine hydrochloride local anesthetic solution is a long acting local anesthetic solution, it is safe to use 0.5% Bupivacaine hydrochloride in the patients suffering from problems or medical conditions like congestive heart failure, hepatic insufficiencies, nephrotic syndrome or the patient on medications like Thiazide diuretics.

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