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Original Research Article

Sublingual Buprenorphine versus Intravenous Tramadol as Premedicant and Postoperative Analgesic in Head and Neck Surgery under General Anaesthesia

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Abstract:

Background and Aim: The goal of postoperative pain management is to reduce or eliminate pain and discomfort with minimum side effects. Various agents, routes and modes for the treatment of postoperative pain exist. Objective of this study is to find out the efficacy of analgesia in term of intraoperative hemodynamics and postoperative VAS, postoperative requirements of supplemental analgesic, duration of analgesic and side effect of drugs such as sedation, nausea and vomiting.

Material and Methods: The study on sublingual buprenorphine versus intravenous tramadol as premedicant and postoperative analgesic in head and neck surgery under general anaesthesia was carried out in P.D.U. Medical College and hospital, Rajkot during the year September 2019 to September 2021. Patient was randomized in one of the two groups. Group allocation: 50 patients were randomly allocated in 2 groups (n=25) GROUP B: Sublingual buprenorphine 2mg 1 hour before surgery, GROUP T: Inj. Tramadol 1.5mg/kg iv 10 min before induction. Parameters recorded were HR, NIBP- systolic, diastolic and mean, spo2 and ECG were monitored throughout the procedure, time to first analgesic request, postoperative tramadol consumption, pain score at rest, sedation score and complication.

Results: Pulse rate & blood pressure were significantly reduced in group B as compare to group T after 5 minutes. The mean VAS score was consistently low in group B than group T. The mean duration of total analgesia was significantly higher in group B (390± 56.12min) than group T (294 ±22.91 min). Total consumption of tramadol in 24 hours post operatively was less in group B as compared to group T.

Conclusion: sublingual buprenorphine 2 mg can be used as premedicant and analgesic for postoperative pain in head and neck surgery similar to that of injection tramadol 1.5mg/kg. Sublingual buprenorphine improves quality and duration of postoperative analgesia compare to injection tramadol.

Keywords: Buprenorphine, Postoperative Analgesia, Sedation Score, Tramadol.

Introduction

Effective pain management in the early postoperative period is associated with higher levels of patient satisfaction, earlier mobilization, and reduced length of hospital stay. [1] One of the mainstays of early postoperative pain management is the use of i.v. and oral opioids. [2] Use of these agents is not without risk, commonly resulting in adverse effects such as sedation, hypotension, nausea, vomiting, and respiratory depression. [2]

Although pain is a predictable part of the postoperative experience, inadequate management of pain is common and can have profound implications. Unrelieved postoperative pain may result in clinical and psychological changes that increase morbidity and mortality as well as costs and that decrease quality of life. [3]

Negative clinical outcomes resulting from ineffective postoperative pain management include deep vein thrombosis, pulmonary embolism, coronary ischemia, myocardial infarction, pneumonia, poor wound healing, insomnia, and demoralization. [3,4] Associated with these complications are economic and medical implications, such as extended lengths of stay,

readmissions, and patient dissatisfaction with medical care. [5,6] Effective postoperative pain control is an essential component of the care of surgical patient. Inadequate pain control, apart from being in human, may result in increased morbidity or mortality. Evidence suggests that surgery suppresses the immune system and that this suppression is proportionate to the invasiveness of the surgery. Good analgesia can reduce this deleterious effect. The advantages of effective postoperative pain management include patient comfort and therefore satisfaction, earlier mobilization.

The goal of postoperative pain management is to reduce or eliminate pain and discomfort with minimum side effects. Various agents (opioid vs. non-opioid), routes (oral, intravenous, neuraxial, regional) and modes (patients controlled vs. "as needed") for the treatment of postoperative pain exist. Although traditionally the mainstay of postoperative analgesia is opioids based, increasingly more evidence exists to support a multimodal approach with intent to reduce opioid side effect and improve pain scores. Appropriate pain control can lead to improved postoperative outcomes. In addition, uncontrolled acute postoperative pain is associated with longer stay in post-anaesthesia care unit, longer hospital stays, decreased patient satisfaction and quality of life and increased costs.

Buprenorphine is a synthetic opioid analgesic with mixed agonist – antagonist properties. It has been shown to be effective by the sublingual route for pain management and suitability of the drug for this route is suggested by its high lipophilicity, high first pass effect, long duration of action and side effect of the drug such as sedation, nausea and vomiting.

Sublingual route improves patient compliance. It has affinity for mu receptor hence long duration of action. Buprenorphine has low bioavailability (oral form) and thus formulated in sublingual form. Indication of sublingual Buprenorphine are palliation of moderate to severe acute or chronic pain and palliation perioperative analgesia and Advantages are ceiling effect for respiratory depression, Lack of immunosuppressive effect and Low pharmacokinetic interaction. Onset of action of sublingual buprenorphine is 2- 3 min and duration of action is 4-8 hr.

Tramadol is a centrally acting synthetic opioid analgesic and SNRI (Serotonin/norepinephrine reuptake inhibitor). Due to its good tolerability profile and multimodal mechanism of action, tramadol is generally considered a lower risk opioid option for the treatment of moderate to severe pain. Onset of action of tramadol is 1 hour and duration of action is 4-6 hr. [7,8] Pain in Head and Neck surgeries is complex in nature. Primary objective of this study is to find out the efficacy of analgesia in term of intraoperative hemodynamics and postoperative VAS, postoperative requirements of supplemental analgesic, duration of analgesic and side effect of drugs such as sedation, nausea and vomiting.

Material and Methods

The study on sublingual buprenorphine versus intravenous tramadol as premedicant and postoperative analgesic in head and neck surgery under general anaesthesia was carried out in P.D.U. Medical College and hospital, Rajkot during the year September 2019 to september2021 after approval by institutional ethics committee and informed written consent will be obtained from all the patients.

All the cases >18-year, ASA grade 1 ,2 and 3 undergoing head and neck surgery under general anesthesia.

Sample size: We will take total 50 patients in study, 25 in each group.

Sample size: $= 2(Z\alpha+Z\beta)^2*(SD)^2/(d)^2$

d=median range, SD=standard deviation

Inclusion criteria:

- Patients undergoing head and neck surgeries with ASA 1 ,2,3
- Age 18 – 65 years
- Under General Anesthesia

Exclusion criteria:

- Chronic opioids treatment
- Hepatic/Renal /Cardiac failure
- Morbid obesity

For elimination of bias in the treatment assign study to facilitate blinding of identity of treatment from investigators, participants and assessors of the both group study we will do randomization by computer generated sequence numbers; and we will take care in allocation of randomization, we mean that each patient has equal chance.

After assigning eligibility and consent the identically prepare envelop in the sequence will be open. We will take care of envelop sealing, sequence maintenance and opening.

GROUP B: Sublingual buprenorphine 2mg 1 hour before surgery

GROUP T: Inj. Tramadol 1.5mg/kg iv 10 min before induction

Study Protocol: All the patient underwent pre-anaesthetic checkup before surgery and all routine and specific investigations were documented. The patients were nil per oral for 6 hours before

surgery. Prior to operation patients were explained about the procedure and written informed consent were taken. Standard monitors like ECG, NIBP, and pulse oximeter were applied and patient's baseline parameters like pulse, blood pressure, respiratory rate, spO2 were recorded.

Intravenous line secured and Patient was premedicated with:

- Inj. Glycopyrrolate (0.2mg) I.V.
- Inj. Ranitidine (50 mg) I.V.
- Inj. Palonosetron (20 microgm/kg) I.V.

Anesthesia Technique:

Sublingual Buprenorphine was given to patient 1 hour before surgery OR intravenous Tramadol was given to patient 10 min before surgery.

All patients were preoxygenated with 100% oxygen for 3 min. General Anaesthesia was induced with inj Propofol 2-2.5mg/kg and inj Succinylcholine 1.5 mg/kg by intravenous route.

Anaesthesia was maintained using with O_2, N_2O, ISOFLURANE. Neuromuscular blockade was achieved with Inj vecuronium.

Intraoperatively patient was on volume-controlled ventilation and normocapnia was maintained. Intraoperative hemodynamic changes were continuously monitored including HR, NIBP – systolic, diastolic and mean, ETCO2, SpO2 and ECG.

Post-operative hemodynamic changes were continuously monitored including: HR, NIBP, and Spo2. Intensity of post-operative pain was evaluated using VAS (VISUAL ANALOUGE SCORE) with grade 0 (no pain) to grade 9 (worst pain). Pain score were noted every 10 min, if analgesia was unsatisfactory and VAS more than or equal to 4 then rescue analgesia were given and time for rescue analgesia were noted.

Sedation score is assessed by THE RAMSAY SEDATION SCORE

Ramsay Sedation score

1. Anxious, agitated, restless
2. Co-operative, oriented, tranquilated
3. Responds to commands only
4. Brisk response to glabellar taps
5. Sluggish response to glabellar taps
6. No response to glabellar taps

Throughout the study, patients were observed for any adverse effects like Nausea, Vomiting, dizziness, sedation.

Statistical Analysis: The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2019) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA).

Quantitative variables were described as means and standard deviations or median and interquartile range based on their distribution. Qualitative variables were presented as count and percentages. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

Table 1: Demographic Data

	Group B	Group T	Student t test	P value	inference
Age	36.32±16.80	28.16±8.19	2.1830	0.0340	NS
Sex(M/F) *	(11/14)	(12/13)	-	-	-
ASA Grade (1/2/3) *	(0/10/15)	(0/9/16)	-	-	-

Table 1 shows demographic data of two groups. The groups were comparable with respect to age, Sex and ASA grading. Mean age in group B years and group T years is comparable and statistically not significant. (P value >0.05)

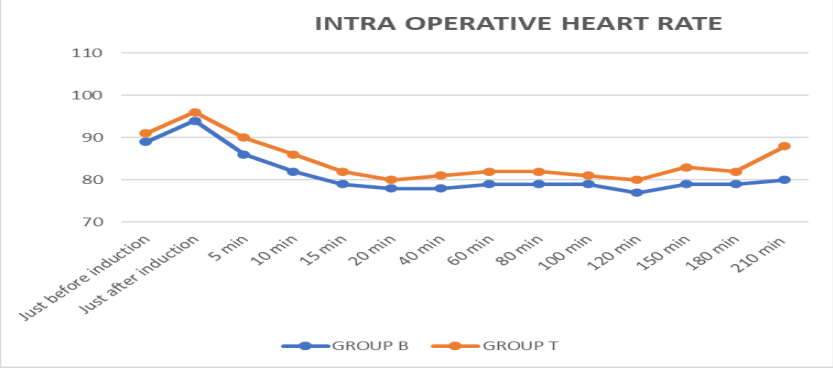

Figure 1: Intra Operative Heart Rate

The heart rate was reduced in both groups, but it was reduced statistically significant from 5 min in group B (86.56±3.76) than in group T (90.4±5.7) (p value 0.0074).

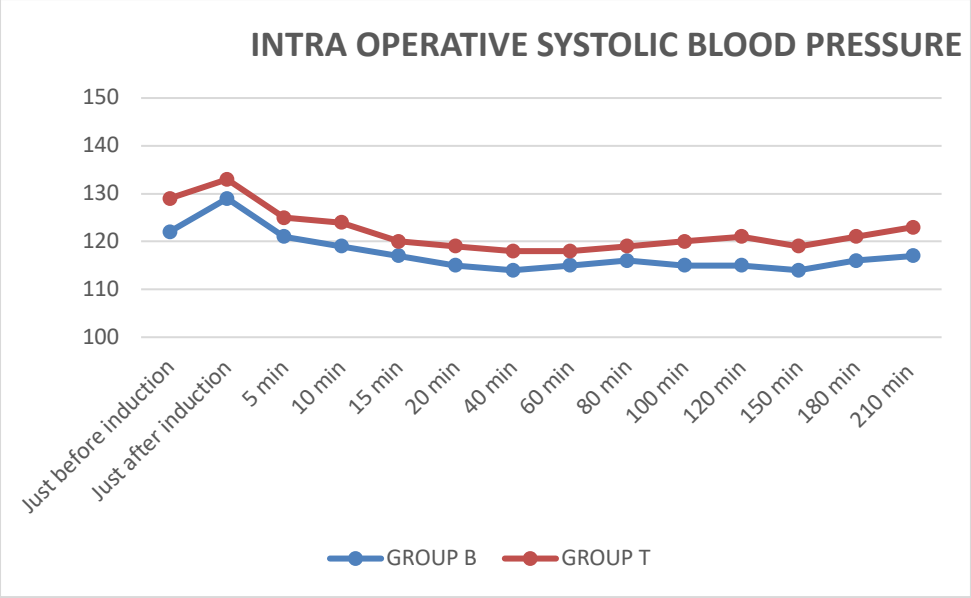

Figure 2: Intraoperative Systolic Blood Pressure

The systolic blood pressure was reduced in both groups, but it was reduced statistically significant just after induction in group B (129.04±7.05) than in group T (133.28±5.79) (p value 0.0244**).**

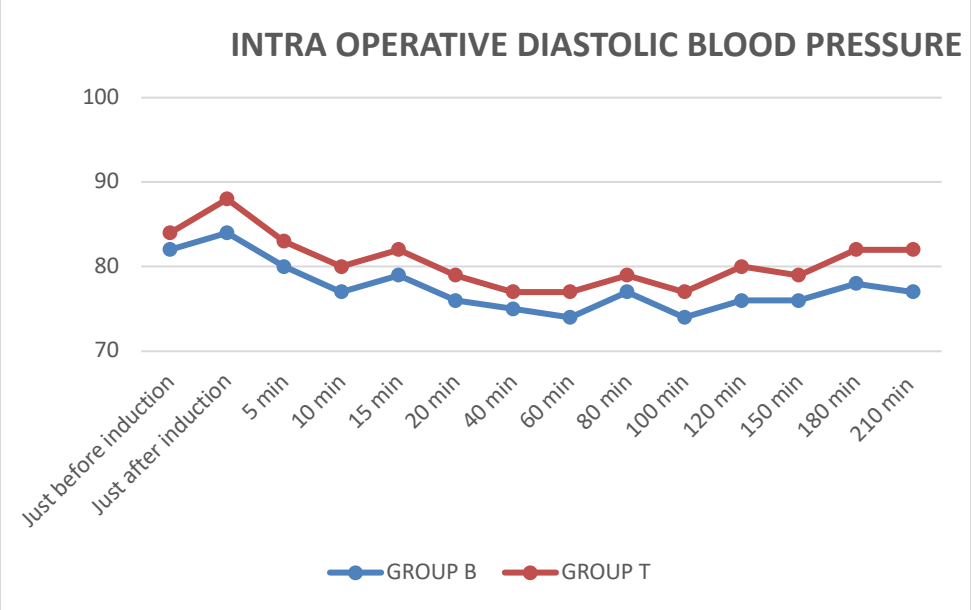

Figure 3: Intraoperative Diastolic Blood Pressure

The diastolic blood pressure was reduced in both group, but it was reduced statistically significant just after induction in group B(84.80±3.95) than in group T(88.24±7.46) (p value 0.0244).

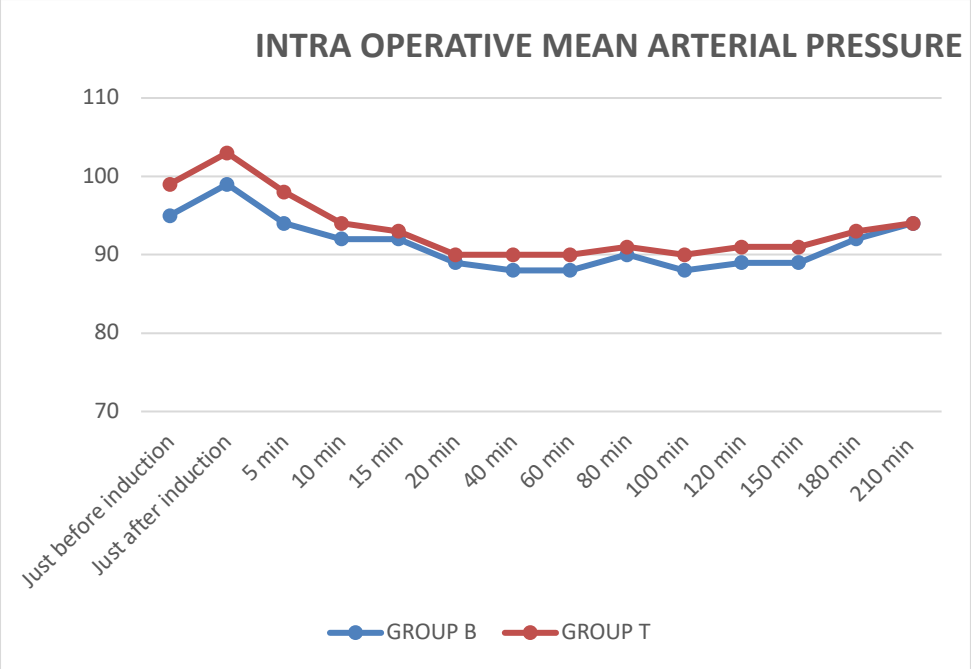

Figure 4: Intraoperative Mean Blood Pressure

The mean blood pressure was reduced statistically significant just after induction in group B (99.92±4.40) than in group T (103.6±6.33). (P value- 0.0210) till 10 minutes. After that the mean blood pressure was statistically not significant in both groups.

Table 2: Duration Of Surgery

	Group B	Group T	Student t test	P value	inference
Duration of surgery	147.2±33.72	154.8±40.93	0.7166	0.4771	NS

Mean duration of surgery in group B (147.2±33.72) minutes and group T (154.8±40.93) minutes and it is not statistically significant. (>0.05)

Table 3: Ramsay Sedation Score

	Group B	Group T	Student T Test	P value	Inference
Time	Mean ±SD	Mean ±SD			
0 min	1.66 ± 0.2	1.96±0.2	1.5137	0.1367	Ns
2 hr	2±0	2±0	-	-	-
4 hr	2±0	2±0	-	-	-
6 hr	2±0	2±0	-	-	-
8 hr	2±0	2±0	-	-	-

We compared sedation score with the help of "RAMSAY SEDATION SCORE" in both groups postoperatively at 0 min, 2hr, 4hr, 6hr and 8hr. And there was no significant difference in Ramsay Sedation Score in both groups.

Table 4: VAS Score

Variable	Group B	Group T	Student T Test	P value	Inference
Time	Mean ±SD	Mean ±SD			
0 min	0.8±0.4	1.2±0.5	3.1235	0.0030	S
2 hr	1.44 ± 0.76	2.2 ± 0.72	3.6298	0.0007	HS
4 hr	2.44 ± 0.91	3.44 ± 0.58	4.6334	0.0001	HS
6 hr	3.33 ± 0.73	4 ± 0	1.2709	0.2177	NS
8 hr	4 ± 0	-	-	-	-

Vas score are comparatively less in group B at 0 min, 2 , 4 and 6 hour compared to group T which was statistically significant. (P value 0.0030, 0.0007, 0.0001 at 0 min, 2 hr and 4 hr respectively)

Table 5: Total Duration of Analgesia

Variable	Group B	Group T	Student T Test	P value	Inference
	Mean ±SD	Mean ±SD			
Time	390±56.12	294 ± 22.9	7.9187	0.0001	Hs

Table 5 shows mean duration of analgesia. Mean duration of analgesia in group B is 390±56.12 minutes and in group T is 294±22.91 minutes and are statistically significant in group B than group T (0.0001).

Table 6: Total Tramadol Consumption (mg/kg) in 24 hour postoperatively

	Group B	Group T	Student T Test	P Value	Significance
Total Tramadol Consumption (mg/kg)	1.75 ±0.44	2.20±0.34	4.0463	0.0002	S

Total Post-operative Mean consumption of Tramadol in 24 hours in Group B was 1.75mg/kg and in Group T was 2.20mg/kg and it is statistically significant (p-<0.0001).

In group B , 2 out of 25 patients developed nausea postoperatively whereas in group T, 1 out of 25 developed nausea, which is not statistically significant. In group B, 1 out of 25 patients developed sedation postoperatively whereas in group T, no cases of sedation found, which is not statistically significant. There was no incidence of postoperative complication like bradycardia, hypotension and respiratory depression.

Discussion

Adequate pain control is a key element in successful recovery after head and neck surgery. Inadequate postoperative pain management has been correlated with poor functional recovery. Furthermore, continuous unrelieved postoperative can resulting in postsurgical wound infection and poor wound healing. Inadequate pain control can also reduce patient mobility. Effective postoperative pain control can shorten hospital stay, improve short- term postoperative outcome, and decrease morbidity. Poorly managed acute postoperative pain is often associated with chronic pain. Buprenorphine has been used in various doses to supplement anesthesia. Sublingual buprenorphine offers an effective alternative to parenteral route especially in the management of postoperative pain, but only limited studies are available with it as a premedicant. [9,10]

The primary objective was to find out the efficacy of analgesia in term of intraoperative hemodynamics. The secondary objectives were VAS Score in postoperative period, duration of analgesia, defined as the period from the administration of the drug as premedication to the requirement of first rescue analgesia in postoperative period (VAS >4), total requirement of rescue analgesia, and the side effects of the drug such as sedation, nausea and vomiting.

In our study, both Group B (36.32±16.80) & Group T (28.16±8.19) were demographically comparable and there was no statistically significant different between the two groups. (P value>0.05) The heart rate was reduced in both group but it was reduced statically significant from 5 minutes in group B (86.56±3.76) than in group T (90.4±5.74) (p value 0.0074). At 5 minutes and 10 minutes, the heart rate was reduced statistically very significantly. At 10 min in group B (82.48±3.47) than group T (86.56±5.52) (P value 0.0030). SCOTT, et al [11] in their study observed that Buprenorphine injection was followed by a slight decrease in mean heart rate, which was greatest at 25 min and still present when observations ceased 30 minutes after injection. The greatest changes in individual patients were isolated values of + 9 and -8 beats/minute after morphine and + 10 and - 10 beats/minute after buprenorphine.

The systolic blood pressure was statistically significantly decreased, just after induction in group B (129.04±7.05) than group T (133.28±5.79). (P value 0.0244). The systolic blood pressure was reduced statistically significant in group B than group T. Martinez, et al [12] observed that During isoflurane anesthesia, buprenorphine administration caused significant (P < or = 0.05) reductions in diastolic arterial pressure, mean arterial pressure, systolic arterial pressure, cardiac index, and heart rate.

The diastolic blood pressure was statistically significantly decreased, just after induction, in group B (84.80±3.95) than group T (88.24±7.46) (P ≤0.0471). The diastolic blood pressure was significantly reduced in group B. SCOTT, et al [11] in their study observed that Arterial pressure decreased slightly in both buprenorphine and morphine groups. Diastolic arterial pressure decreased more after buprenorphine. As we have compared sublingual buprenorphine and injection tramadol, we observed more decreased in diastolic blood pressure in buprenorphine group.

The mean blood pressure was statistically significant just after induction, in group B (99.92±4.40) than group T (103.6±6.33) (P value0.0210). The mean blood pressure was significant till 10 min after that the mean blood pressure was statistically not significant in both groups. Martinez, et al [12] observed that During

isoflurane anesthesia, buprenorphine administration caused significant (P < or = 0.05) reductions in diastolic arterial pressure, mean arterial pressure, systolic arterial pressure, cardiac index, and heart rate. Duration of surgery in group B was (147.2±33.72) minutes while in group T was (154.8±40.93) minutes which was comparable in both group and no statistically significant difference was observed in both groups.

Ramsay sedation score (RSS) in group B and group T in postoperative period. We compared sedation level with the help of "Ramsay Sedation score" in both the groups postoperatively at 0 min. 2 hr, 4 hr, 6 hr and 8 hr. Sedation score immediately after extubation in Group B was (1.66±0.2) and in Group D was (1.96±0.2), which was statistically not significant. Both the drugs have minimal sedative properties, as we have used sublingual buprenorphine, sedation and respiratory depression was not statistically significant. In our study we did not find any significant difference in sedation score of both the groups.

VAS SCORE in post-operative period at 0 min, 2 hr, 4 hr was significantly less in group B than in group T (P value 0.0030, 0.0007, 0.0001) which was statistically significant. Vaidiyanathan, et al [13] have measured the intensity of postoperative pain by VAS score at 2nd, 4th, 6th, 12th, 18th, and 24th h after surgery. VAS score was significantly less in buprenorphine group compared to the morphine group. Akhavan Akbari, et al [14], concluded that the average pain score in the Buprenorphine group was significantly lower than the Morphine group in 8 ($p=0.025$), 16 ($p<0.044$) and 24 ($p<0.003$) hours after surgery. All of above studies shows that buprenorphine used as premedicant and as analgesic agent causes statistically significant lower VAS SCORE in comparison to other study groups. We also found that buprenorphine has less VAS SCORE than tramadol.

In our study, in group B total duration of analgesia was 390±56.12 minutes and group T was 294±22.91 minutes. This study showed that mean duration of total analgesia was significant higher in group B than group T (0.0001). Kiabi FH et al**8** concluded that there was a significant difference in pain score in buprenorphine group at 1, 6 ,12 and compared with placebo ($p<0.0005$). In the control group, the use of analgesic was more than the buprenorphine group.

Total Tramadol consumption in 24 hours postoperatively. Mean Tramadol consumption in Group B is 1.75mg/kg and in Group T is 2.20mg/kg which is statistically significant. Since the Tramadol consumption is less in Group B, and it is associated with fewer side effects and superior analgesic effect compared to Group T. Vaidyanathan et al [13] time of first rescue analgesic requirement was significantly longer in Buprenorphine group and post-operative Diclofenac requirement were significantly less in buprenorphine group compared to Morphine group.

In group B, 2 out of 25 patients developed nausea postoperatively whereas 1 patient developed nausea in group T, which is not statistically significant. Opioids are highly prone for complications like nausea and vomiting. Head and neck surgeries are also prone for PONV. So, considering these we have used Palonosetron as anti-emetic. In our study, 2 patients in buprenorphine group have complaint of nausea, in 1 patient we gave Inj dexamethasone 8mg and in another patient we gave Inj metoclopramide 10mg IV slowly.

Buprenorphine is a synthetic opiate analgesic with mixed agonist-antagonist properties. It has been shown to be effective by the sublingual route in postoperative pain, and the suitability of the drug for this route is suggested by its high lipophilicity, high first pass effect, long duration of action and low addiction potential. So, Sublingual buprenorphine can be better choice to give good analgesia with intra operative hemodynamic stability without complications and side effects for head and neck surgery.

Conclusion

Sublingual buprenorphine 2 mg can be used as premedicant and analgesic for postoperative pain in head and neck surgery similar to that of injection tramadol 1.5mg/kg. Sublingual buprenorphine improves quality and duration of postoperative analgesia compare to injection tramadol. Buprenorphine is a partial agonist at μ-opiate receptor, and an antagonist at the ƙ-receptor. The unique pharmacology of buprenorphine at the μ-opiate receptor (results in buprenorphine having a good safety profile, and flexibility in dose scheduling. Buprenorphine is a potent analgesic drug with a high affinity for opiate receptor. The slow dissociation of the drug receptor complex results in prolonged duration of action. Sublingual buprenorphine can be used as a safe and effective premedicant in head and neck surgery with good analgesia and perioperative hemodynamic stability and less requirement of postoperative analgesia.

References

1. F.M. Perkins, H. Kehlet (Chronic pain as an outcome of surgery. A review of predictive factors Anesthesiology. 2000;93: 1123-1133
2. S.A. Schug, G.M. Palmer, D.A. Scott, et al. Acute pain management: scientific evidence (4th ed.), Australian and New Zealand College of Anaesthetists and Faculty of Pain Management, Melbourne. 2015.

3. Carr DB, Goudas LC. Acute pain. Lancet 1999; 353:2051–8.
4. Breivik H. Postoperative pain management: why is it difficult to show that it improves outcome? Eur J Anaesthesiol. 1998; 15:748–51.
5. Practice guidelines for acute pain management in the perioperative setting: a report by the American Society of Anesthesiologists Task Force on Pain Management, Acute Pain Section. Anesthesiology. 1995; 82:1071–81.
6. Twersky R, Fishman D, Homel P. What happens after discharge? Return hospital visits after ambulatory surgery. Anesth Analg. 1997; 84:319–24.
7. Hale M, Garofoli M, Raffa RB. Benefit-Risk Analysis of Buprenorphine for Pain Management. J Pain Res. 2021; 14:1359-1369. Published 2021 May 24.
8. Kiabi FH, Emadi SA, Shafizad M, Jelodar AG, Deylami H. The effect of preoperative sublingual buprenorphine on postoperative pain after lumbar discectomy: A randomized controlled trial. Ann Med Surg (Lond). 2021 May 1; 65:102347.
9. Norozi V, Ghazi A, Amani F, Bakhshpoori P. Effectiveness of Sublingual Buprenorphine and Fentanyl Pump in Controlling Pain After Open Cholecystectomy. Anesthesia Pain Med. 2021 Aug 8; 11(3):e113909.
10. Ghazi, A., Far, K., Asl, M. E., & Vakili, A. (2018). Comparison of the Effect of Sublingual Buprenorphine and Intravenous Fentanyl on Pain Control after Cesarean Surgery.
11. Scott, David Ht, G. Richard Arthur, and D. Bruce Scott. "Haemodynamic changes following buprenorphine and morphine." Anaesthesia.1980;35(10): 957-961.
12. Martinez, E. A., Hartsfield, S. M., Melendez, L. D., Matthews, N. S., & Slater, M. R. Cardiovascular effects of buprenorphine in anesthetized dogs. American journal of veterinary research, 1997;58(11): 1280-1284.
13. Vaidiyanathan, Bhavani, Sangeeta Dhanger, and I. Joseph Raajesh. "Sublingual buprenorphine versus intravenous morphine as a premedicant and postoperative analgesic in laparoscopic appendectomy under general anesthesia—A randomized control trial." Indian Journal of Pain. 2018;32(2): 102.
14. Akhavan Akbari, G., Ghazi, A., Mohammadian Erdi, A., & Mirza Rahimy, T. Comparison of Efficacy of Intravenous Morphine and Sublingual Buprenorphine for Analgesia after Lower Limb (below the Knee) Orthopedic Surgery. 2018.