ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

Safety and Efficacy of Transdermal Buprenorphine Versus Oral Tramadol for Treatment of Post-Operative Pain Following Lower Limb Surgery

Burulukui Hembram[1], Subir Kumar Brahma[2], Pradip Kumar Mandal[3], Salman Hussen[4]

[1]Associate Professor, Department of Anaesthesiology, Diamond Harbour Govt. Medical College, Diamond Harbour, West Bengal, India
[2]Assistant Professor, Department of Anaesthesiology, Malda Medical College and Hospital, Malda, West Bengal, India
[3]Associate Professor, Department of Anaesthesiology, Malda Medical College and Hospital, Malda, West Bengal, India
[4]Post graduate Trainee, NilratanSircar Medical College, West Bengal, Kolkata, India

Abstract

Background: Patients who have undergone lower limb surgery are vulnerable to adverse consequences from unrelieved or undertreated postoperative pain after surgery. Tramadol has a broad range of therapeutic indications, from acute to chronic pain, and has been used as a first-line treatment in musculoskeletal system disorders, for relief of persistent postoperative pain, as well as various types of chronic pain. Buprenorphine is a synthetic opioid analgesic used in the management of postoperative pain. **Material and Methods:** This is a prospective and single center study conducted at Orthopaedic operation theatre, General surgery operation theatre, post anesthetic unit, post-operative ward of Tertiary care teaching Hospital over a period of 1 year. Total no of patients were 50, they were allocated as follows. Group A-those who received transdermal buprenorphine 10 micro gm/hr (TDB GROUP). Group B-those who received oral tramadol (50 mg) twice daily (OT GROUP). **Results:** In group-OT, the mean duration of surgery (mean±s.d.) of patients was 118.6800 ± 22.9542 min. In group-TDB, the mean duration of surgery (mean±s.d.) of patients was 129.1200 ± 22.7529 min. Distribution of mean duration of surgery vs. group was not statistically significant (p=0.1128). In group-OT, 14(56.0%) patients had ASA I and 11(44.0%) patients had ASA II. In group-TDB, 11(44.0%) patients had ASA I and 6(24.0%) patients had ASA II. Association of ASA vs. group was not statistically significant (p=0.1355). **Conclusion:** It was found that mean VAS at 24 hr, was significantly lower in transdermal buprenorphine compared to oral tramadol. It was found that mean HR at 24 hr in oral tramadol group was significantly higher than transdermal buprenorphine and that mean post op pain was more in oral tramadol group than transdermal buprenorphine group.

Keywords: Transdermal, Buprenorphine, Lower Limb Surgery.

Corresponding Author: Dr.Pradip Kumar Mandal, Associate Professor, Department of Anaesthesiology, Malda Medical College and Hospital, Malda, West Bengal, India.
Email- pradip38443@gmail,com

Introduction

Major lower limb surgery often leads to very severe post-operative pain due to inadequate use of analgesic in post-operative period.[1] Patients who have undergone lower limb surgery are vulnerable to adverse consequences from unrelieved or undertreated postoperative pain after surgery. This is because pain assessment is often fraught with problems arising from

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

difficulties in measuring and reporting pain intensity, and, in older patients, the presence of cognitiveimpairment.[2]

Inadequate postoperative pain management increases the risk of complications from the surgery and reduces the mobility of patients and may even delay the rehabilitation and recovery process due to the pain.[3] Major lower limb surgery is associated with moderate-to-severe pain on the first day after surgery (median score of 7 on the Numeric Rating Scale [NRS], interquartile range: 5–8).[4] With analgesic treatment, pain intensity generally declines from moderate or severe to mild levels over the first 24–48 h after surgery, but a proportion of patients may continue to experience moderate or severe pain beyond this period.[5]

Although considered a weak opioid because of its much lower affinity for the opioid receptor, tramadol may be prescribed for patients with complicated pain etiology owing to its dual mechanism of action: binding to several opioid receptors as well as inhibiting serotonin and norepinephrine reuptake in the central nervous system.[6] Tramadol has a broad range of therapeutic indications, from acute to chronic pain, and has been used as a first-line treatment in musculoskeletal system disorders, for relief of persistent postoperative pain, as well as various types of chronic pain. However, oral formulations of tramadol have a number of systemic side-effects such as headache, sleep disturbance, constipation, vomiting, sweating, nausea, and dizziness and, like other opioids, prolonged use may be associated with dependence and abuse.[7]

Buprenorphine is a synthetic opioid analgesic used in the management of postoperative pain. A review of the buprenorphine transdermal patch found that it was as effective as other opioids such as oral morphine, oxycodone, and fentanyl in relieving pain and that buprenorphine could be used to achieve the same effect at lower dose equivalents.[8] Studies in patients with chronic postoperative pain suggest that CNS sensitization is also reduced or absent with buprenorphine compared with other agents. Buprenorphine can be administered via various routes. A once-weekly patch for transdermal application is available as a dosing regimen that can maintain an analgesic effect equivalent to tramadol. While the buprenorphine transdermal system (BTDS) has been investigated in a number of studies and, in particular, for the management of chronic pain, its efficacy and safety for the relief of persistent postoperative subacute pain have not been extensively studied.[9]

In a proportion of patients, postoperative pain can be serious and may persist for prolonged periods (several weeks up to several months). Achieving adequate postoperative pain control remains an unmet need during the subacute phase, where pain is present for at least 6 weeks but less than 3 months.[10] Research on the use of analgesics for subacute pain is limited, and a literature search revealed no studies comparing transdermal buprenorphine to oral tramadol/acetaminophen for the treatment of subacute postoperative pain.[11]

Aims and Objectives

To compare the potency of the both drugs, reduction of post-operative analgesia by visual analogue scale.

Material and Methods

This is a prospective and single center study conducted at Orthopaedic operation theatre, General surgery operation theatre, post anesthetic unit, post-operative ward of Tertiary care teaching Hospital over a period of 1 year. Total no of patients were 50; they were allocated as follows.

GROUP A-

Those who have received transdermal buprenorphine 10 micro gm/hr (TDB Group)

GROUP B-

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

Those who have received oral tramadol (50 mg) twice daily (OT Group).

Inclusion Criteria
All the ASA 1 & 2 patient of either sex, age between 25-60 years undergoing lower limb surgery under spinal anaesthesia.
Exclusion Criteria
ASA physical status 3 or more. Patients with contraindication of spinal anaesthesia. Hepatic, renal impairment, obese, myasthenia gravis, delirium, dermatitis at patch site.
Parameter to be monitored- NIBP, SPO2, ECG, Respiratory Rate, Pain Score.

Study Technique- For the patients in the TDB group, a buprenorphine patch of 10 microgram/hr was applied to the upper arm (an effective serum conc for TDB group is achieved after 12-24 hrs). The other group of patients will continue to receive 50 mg tramadol tablets preoperatively. All the patients received 0.25mg alprazolam the night before surgery. Spinal anesthesia was administered with 4 ml of hyperbaric bupivacaine 0.5% along with 50 microgram of fentanyl. It was monitored in both groups whether there was any rescue analgesic needed or not. Post-operative pain was assessed by visual analogue scale (0-100), and numeric rating scale (0-10) at the following time period. Preoperatively and 4,12, and 24 hrs and daily for up to 7 days of post operatively. If patients who have pain score 4 and higher rescue analgesic was to be given. Inj. Diclofenac(75mg), inj. pcm (1gm), inj. pethidine (50mg) may be used as a rescue analgesic if required. Side effects such as giddiness, drowsiness, PONV, constipation, resp. distress, and patch site redness was noted.

Statistical Analysis
For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. p-value ≤ 0.05 was considered statistically significant.

Results
In group-OT, the mean age (mean±s.d.) of patients was 38.6000 ± 10.0582 years. In group-TDB, the mean age (mean±s.d.) of patients was 44.1200 ± 11.1517 years. Distribution of mean age vs. group was not statistically significant (p=0.0723).

Table 1: Distribution of mean age (years): group

		Number	Mean	SD	ep-value
Age	Group-OT	25	38.6000	10.0582	0.0723
	Group-TDB	25	44.1200	11.1517	

Table 2: Distribution of mean duration of surgery (min) : group

		Number	Mean	SD	p-value
Duration of surgery	Group-OT	25	118.6800	22.9542	0.1128
	Group-TDB	25	129.1200	22.7529	

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

In group-OT, the mean duration of surgery (mean±s.d.) of patients was 118.6800 ± 22.9542 min. In group-TDB, the mean duration of surgery (mean±s.d.) of patients was 129.1200 ± 22.7529 min. Distribution of mean duration of surgery vs. group was not statistically significant (p=0.1128).

Table 3: Distribution of mean SBP at different time of interval in two groups

		Number	Mean	SD	p-value
SBP0 min	Group-OT	25	129.0400	7.0680	0.7516
	Group-TDB	25	129.6000	5.2361	
SBP 4HRS	Group-OT	25	128.0800	5.5447	0.2393
	Group-TDB	25	129.7200	4.0776	
SBP 12 HRS	Group-OT	25	127.5600	5.0339	0.5336
	Group-TDB	25	128.5600	6.1852	

Distribution of mean SPB at 0 minin two groups was not statistically significant (p=0.7516). Distribution of mean SPB at 4 hrs in two groups was not statistically significant (p=0.2393). Distribution of mean SPB at 12 hrs in two groups was not statistically significant (p=0.5336).

Table 4: Distribution of mean DBP at different time of interval in two groups

		Number	Mean	SD	Minimum	Maximum	Median	p-value
DBP 0 min	Group-OT	25	78.6800	3.8375	70.0000	85.0000	78.0000	0.7548
	Group-TDB	25	79.0800	5.0820	70.0000	88.0000	80.0000	
DBP 4HRS	Group-OT	25	78.8000	3.6056	74.0000	84.0000	78.0000	0.2229
	Group-TDB	25	80.0400	3.4938	72.0000	84.0000	82.0000	
DBP 12 HRS	Group-OT	25	80.0800	3.6733	74.0000	88.0000	80.0000	0.7894
	Group-TDB	25	79.8000	3.6968	72.0000	88.0000	80.0000	

Distribution of mean DBP at 0 min in two groups was not statistically significant (p=0.7548). Distribution of mean DBP at 4 hrs in two groups was not statistically significant (p=0.2229). Distribution of mean DBP at 12 hrs in two groups was not statistically significant (p=0.7894).

Table 5: Distribution of mean SPO2 at different time of interval in two groups

		Number	Mean	SD	Minimum	Maximum	Median	p-value
SPO2 0 min	Group-OT	25	98.0400	1.2069	96.0000	100.0000	98.0000	0.9103
	Group-TDB	25	98.0800	1.2884	96.0000	100.0000	98.0000	
SPO2 4HRS	Group-OT	25	98.0000	1.0801	96.0000	100.0000	98.0000	0.9007

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

	Group-TDB	25	97.9600	1.1719	96.0000	100.0000	98.0000	
SPO2 12 HRS	Group-OT	25	97.9600	1.3687	96.0000	100.0000	98.0000	0.4907
	Group-TDB	25	98.2400	1.4799	96.0000	100.0000	98.0000	

Distribution of mean SPO2 at 0 min in two groups was not statistically significant (p=0.9103). Distribution of mean SPO2 at 4 hrs in two groups was not statistically significant (p=0.9007). Distribution of mean SPO2 at 12 hrs in two groups was not statistically significant (p=0.4907). Distribution of mean SPO2 at 24 hrs in two groups was not statistically significant (p=0.5899).

Table 6: Distribution of mean VAS at different time of interval in two groups

		Number	Mean	SD	Minimum	Maximum	Median	p-value
VAS 0 hr	Group-OT	25	89.2000	7.0238	80.0000	100.0000	90.0000	0.6980
	Group-TDB	25	88.4000	7.4610	80.0000	100.0000	90.0000	
VAS 4 hr	Group-OT	25	89.6000	7.3485	80.0000	100.0000	90.0000	0.8507
	Group-TDB	25	89.2000	7.5939	80.0000	100.0000	90.0000	
VAS 12 hr	Group-OT	25	89.2000	7.5939	80.0000	100.0000	90.0000	0.7120
	Group-TDB	25	90.0000	7.6376	80.0000	100.0000	90.0000	
VAS 24 hr	Group-OT	25	76.2000	13.7541	50.0000	90.0000	80.0000	<0.0001
	Group-TDB	25	68.4000	14.9108	50.0000	100.0000	70.0000	

Distribution of mean VAS at 0 hr in two groups was not statistically significant (p=0.6980). Distribution of mean VAS at 4 hr in two groups was not statistically significant (p=0.8507). Distribution of mean VAS at 12 hr in two groups was not statistically significant (p=0.7120). Distribution of mean VAS at 24 hr in two groups was statistically significant (p<0.0001).

Table 7: Association of ASA status: group

ASA status		Group-OT	Group-TDB	Total
I		14	19	33
Row	%	42.4	57.6	100.0
Col %		56.0	76.0	66.0
II		11	6	17
Row	%	64.7	35.3	100.0
Col %		44.0	24.0	34.0
TOTAL		25	25	50
Row	%	50.0	50.0	100.0
Col %		100.0	100.0	100.0

Chi-square value: 2.2282; p-value:0.1355

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

In group-OT, 14(56.0%) patients had ASA I and 11(44.0%) patients had ASA II. In group-TDB, 11(44.0%) patients had ASA I and 6(24.0%) patients had ASA II. Association of ASA vs. group was not statistically significant (p=0.1355).

Table 8: Association of RESCUE Analgesia: group

Rescue Analgesia		Group-OT	Group-TDB	Total
No		19	25	44
Row	%	43.2	56.8	100.0
Col %		76.0	100.0	88.0
Yes		6	0	6
Row	%	100.0	0.0	100.0
Col %		24.0	0.0	12.0
Total		25	25	50
Row	%	50.0	50.0	100.0
Col %		100.0	100.0	100.0

Chi-square value: 6.8182; p-value: 0.0090

In group-OT, 6(24.0%) patients had rescue analgesia. In group-TDB, 25(100.0%) patients had no rescue analgesia. Association of rescue analgesia vs. group was statistically significant (p=0.0090).

Discussion

We found that in group-OT, the mean age (mean±s.d.) of patients was 38.6000 ± 10.0582 years. In group-TDB, the mean age (mean±s.d.) of patients was 44.1200 ± 11.1517 years. Distribution of mean age vs. group was not statistically significant (p=0.0723). Height and weight were not statistically significant. Distribution of mean duration of surgery vs. group was not statistically significant (p=0.1128).

Tang J et al,[12] (2017) found that the pain status, degree of satisfaction, adverse effects, and condition in which the patient received tramadol hydrochloride for uncontrolled pain were recorded on the night before surgery, postoperative day 1, postoperative day 3, and postoperative day 5. The degree of patient satisfaction in Group C was higher than that in Groups A and B, with minimal adverse effects.

We found that in group- TDB, the mean HR at 24 hrs was higher than group-OT. Distribution of mean HR at 24 hrs in two groups was statistically significant (p<0.001).

It was found that Distribution of mean VAS at 24 hr in two groups was statistically significant (p<0.0001). In group- OT, the mean VAS on the 2nd day was higher than group-TDB. Distribution of mean VAS at 2nd day in two groups was statistically significant (p<0.0001).

Desai SN et al,[13] (2017) found that resting pain scores and pain on movement were significantly lower in TDB Group on all 7 days starting from 24 h post-operatively. Rescue analgesic requirement was significantly lower in TDB Group compared to OT Group. All the patients needed rescue analgesic in OT Group whereas 68% of the patients needed the same in TDB Group. Incidence of vomiting was less and satisfaction scores were much higher in TDB Group as compared to OT Group (79% vs. 66%, P< 0.001). Transdermal buprenorphine can be safely used for post-operative analgesia and is more efficacious in reducing post-operative pain after 24 hours, with fewer side effects when compared to oral tramadol.

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

Niyogi S et al,[14] (2017) found that time to first post-operative rescue analgesic (tramadol) requirement was much delayed in TDB Group than TDP Group (708.0 ± 6.98 min vs 54 ± 0.68 min, P< 0.001) and the total tramadol requirement was higher in TDB Group (490.60 ± 63.09 average vs162.93 ± 63.91 mg, P< 0.001). Intra-and post-operative haemodynamic status was also stable in TDB Group without any adverse event. A TDB patch (10 μg/hour) applied 24 hours before surgery can be used as a postoperative analgesic for lumbar fixation surgery without any drug-related adverse effect.

Kim HJ et al,[15] (2017) found that the VAS score (primary outcome) for postoperative back pain at 7 days after surgery in the Buprenorphine group was not inferior compared to the Tramadol group. The overall changes in VAS scores for postoperative pain during follow-up assessments over a 2-week period did not differ between both groups. However, the VAS scores for postoperative pain significantly improved with time after surgery in both groups. The patterns of changes in the VAS scores for postoperative pain during the follow-up period were not significantly different between the both groups. The efficacy of buprenorphine TDS was not inferior to that of oral tramadol medication for alleviating postoperative pain in the subacute period from 72 h after surgery, following PCA administration. In addition, adverse events were similar between both groups.

Liaqat N et al,[16] (2018) found that age and gender distribution in both the groups were comparable. Pain score noted in both Groups was equal in both groups at 0- hours. however at 1-hour, 2-hour and 4-hour, pain score was slightly more in Group-B. But at 8-hours mean pain score was markedly raised in Group-B as compared to Group-T (3.32 ± 1.42 vs 2.45 ± 1.35). Only complication noted in patients was vomiting which was higher in Group T. Locally infiltrated Tramadol is a better choice than bupivacaine as a local anestheticfor pain management in children after inguinal herniotomy.

It was found that in group-OT, 6(24.0%) patients had rescue analgesia. In group-TDB, 25(100.0%) patients had no rescue analgesia. Association of rescue analgesia vs. group was statistically significant (p=0.0090).

Choudhury K et al,[17] (2018) found that commonest primary cancers were breast in females and head and neck in male individuals in both arms. Initial VAS scores of arm A and arm B were 81.25 and 82.26 respectively. By 1st week, 11 arm A patients were relieved from pain. Another 17 patients of arm A became pain free by 2nd week, total dose of 40 μg/h. Only 4 patients needed 60 μg/h for pain relief. In arm B, 2 patients were relieved by 1 week with total 30mg/day morphine, 11 patients were relieved with 60 mg/day by 2nd week and 12 patients with 90 mg/day. 6 patients were relieved with 120 mg/day dose at the end of 4th week. Nausea and constipation were statistically higher in Arm B compared to that of Arm-A. TD Buprenorphine had similar efficacy with oral morphine, with better toxicity profile and better compliance.

Kadapamannil D et al,[18] (2018) found that all patients received general anesthesia following standardized protocol. Postoperative pain was assessed using numerical rating scale (NRS). The Mann–Whitney U test and independent t-test were used for statistical analysis. NRS was significantly high in group A for up to 30 h postoperatively as compared to group B. From 36 to 48 h, it was comparable. The need for rescue analgesia was significantly high in group A as compared to group B. Significant numbers of patients in group B experienced nausea and vomiting (53.33% vs. 26.67%) and sedation (20% vs. 13.33%) in the preoperative period. Transdermal buprenorphine patch applied 72 h preoperatively provided better analgesia than the one applied 48 h before surgery.

Conclusion

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

It was found that mean VAS at 24 hr, 2nd day and 5th day was significantly lower in transdermal buprenorphine compared to oral tramadol. We found that rescue analgesia was given in oral tramadol but it was not required in transdermal buprenorphine and this association was statistically significant. It was found that mean HR at 24 hr in oral tramadol group was significantly higher than transdermal buprenorphine and that mean post op pain was more in oral tramadol group than transdermal buprenorphine group.

References

1. F. Auburn and F. Marmion, "The elderly patient and postoperative pain treatment," Best Practice and Research: Clinical Anaesthesiology, vol. 21, no. 1, pp. 109–127, 2007.
2. D. E. Eissa, "Analgesic efficacy of intrathecal diamorphine for postoperative pain relief after major lumbar spine surgery," Ain Shams Journal of Anesthesiology, vol. 4, p. 3, 2011.
3. H. J. Gerbershagen, S. Aduckathil, A. J. M. van Wijck, L. M. Peelen, C. J. Kalkman, and W. Meissner, "Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures.," Anesthesiology, vol. 118, no. 4, pp. 934–944, 2013.
4. D. K. Kim, S. H. Yoon, J. Y. Kim, C. H. Oh, J. K. Jung, and J. Kim, "Comparison of the effects of sufentanil and fentanyl intravenous patient controlled analgesia after lumbar fusion," Journal of Korean Neurosurgical Society, vol. 60, no. 1, pp. 54–59, 2017.
5. S. H. Lee, K. H. Kim, S.-M. Cheong, S. Kim, M. Kooh, and D. K. Chin, "A comparison of the effect of epidural patient-controlled analgesia with intravenous patient-controlled analgesia on pain control after posterior lumbar instrumented fusion," Journal of Korean Neurosurgical Society, vol. 50, no. 3, pp. 205–208, 2011. ·
6. M. Sommer, J. M. de Rijke, M. van Kleef et al., "The prevalence of postoperative pain in a sample of 1490 surgical inpatients," European Journal of Anaesthesiology, vol. 25, no. 4, pp. 267–274, 2008.
7. X. Capdevila, P. Biboulet, and Y. Barthelet, "Postoperative analgesia. specificities in the elderly,AnnalesFrancaisesd'Anesthesie et de Réanimation, vol. 17, no. 6, pp. 642–648, 1998.
8. K. T. Hegmann, M. S. Weiss, K. Bowden et al., "ACOEM practice guidelines: Opioids for treatment of acute, subacute, chronic, and postoperative pain," Journal of Occupational and Environmental Medicine, vol. 56, no. 12, pp. e143–e159, 2014.
9. P. Lavand Homme, "The progression from acute to chronic pain," Current Opinion in Anaesthesiology, vol. 24, no. 5, pp. 545–550, 2011. View at Publisher · View at Google Scholar · View at Scopus
10. W. Meissner, F. Coluzzi, D. Fletcher et al., "Improving the management of post-operative acute pain: priorities for change," Current Medical Research and Opinion, vol. 31, no. 11, pp. 2131–2143, 2015.
11. R. B. Raffa, E. Friderichs, W. Reimann, R. P. Shank, E. E. Codd, and J. L. Vaught, "Opioid and nonopioid components independently contribute to the mechanism of action of tramadol, an 'atypical' opioid analgesic," The Journal of Pharmacology and Experimental Therapeutics, vol. 260, no. 1, pp. 275–285, 1992.
12. Tang J, Fan J, Yao Y, Cai W, Yin G, Zhou W. Application of a buprenorphine transdermal patch for the perioperative analgesia in patients who underwent simple lumbar discectomy. Medicine. 2017 May;96(20).
13. Desai SN, Badiger SV, Tokur SB, Naik PA. Safety and efficacy of transdermal buprenorphine versus oral tramadol for the treatment of post-operative pain following surgery for fracture neck of femur: A prospective, randomised clinical study. Indian journal of anaesthesia. 2017 Mar;61(3):225.

ISSN: 0975-3583,0976-2833 VOL13,ISSUE02,2022

14. Niyogi S, Bhunia P, Nayak J, Santra S, Acharjee A, Chakraborty I. Efficacy of transdermal buprenorphine patch on post-operative pain relief after elective spinal instrumentation surgery. Indian journal of anaesthesia. 2017 Nov;61(11):923.
15. Kim HJ, Ahn HS, Nam Y, Chang BS, Lee CK, Yeom JS. Comparative study of the efficacy of transdermal buprenorphine patches and prolonged-release tramadol tablets for postoperative pain control after spinal fusion surgery: a prospective, randomized controlled non-inferiority trial. European Spine Journal. 2017 Nov 1;26(11):2961-8.
16. Liaqat N. Comparison of Local Infiltration of Bupivacaine and Tramadol in post-operative pain management in children after inguinal herniotomy. Iranian Journal of Pediatric Surgery. 2018 Dec 4;4(2):54-60.
17. Choudhury K, Dasgupta P, Paul N, Choudhury KB, Roy B, Maity S. A comparative study of transdermal buprenorphine and oral morphine in the treatment of chronic pain of malignant origin. Indian journal of palliative care. 2018 Oct;24(4):500.
18. Kadapamannil D, Rajan S, Tosh P, Kumar L. Comparison of efficacy and safety of transdermal buprenorphine patch applied 48 versus 72 hours preoperatively in providing adequate postoperative analgesia following major abdominal surgeries. Indian Journal of Pain. 2018 Jan 1;32(1):46.