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"A COMPARATIVE STUDY OF POST OPERATIVE ANALGESIC EFFECT OF INTRAPERITONEAL INFILTRATION WITH ROPIVACAINE V/S ROPIVACAINE PLUS TRAMADOL IN LAPAROSCOPIC CHOLECYSTECTOMY SURGERIES."

Anesthesiology

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ABSTRACT

AIM: To compare the postoperative analgesic effect of Ropivacaine with Ropivacaine plus Tramadol in patients undergoing laparoscopic surgeries. **METHODS:** Comparative prospective descriptive observational study. Study population Patients undergoing laparoscopic cholecystectomy. Conducted from Department of Anesthesiology in association with Department of Gastrointestinal Surgery at Santokba Durlabhji Memorial Hospital cum Medical Research Institute, Jaipur after taking approval from hospital ethical committee. During January 2018 to August 2019. **RESULTS:** The Current study was observed that at 0-1 hrs. in group A 70% of cases required first dose of rescue analgesia compared to group B 26.67% cases required first dose of rescue analgesia. in Group A ,(P=0.002) Time to requirement of first dose rescue analgesia was prolong in the group B (7.61 hours) compared to group A (5.81 hours), indicating better and longer pain relief in the group B compared to groups A. The Urinary retention was found in 20% cases in group A as compared to 3.33% found in Group B and PONV found only in Group B 10 % ,found not significant(P=0.108). **CONCLUSION:** Combination of Ropivacaine with Tramadol not only reduces the intensity of post-operative pain, but also reduces the total dose of rescue analgesia needed. Post operatively first request of rescue analgesia is also prolong in group with Ropivacaine and Tramadol. So, addition of Tramadol with Ropivacine for intraperitoneal instillation in laparoscopic cholecystectomy is better as compared to single use of Ropivacaine.

KEYWORDS

Laparoscopic Cholecystectomy, Post-Operative Analgesic Effect, Intraperitoneal Infiltration, Ropivacaine

INTRODUCTION

The International Association for the Study of Pain defines pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"[1].

Surgical pain is due to inflammation from tissue trauma (i.e. surgical incision, dissection, burns) or from direct nerve injury (i.e. nerve transaction, stretching, or compression)[2]. The pain after laparoscopic cholecystectomy may be caused due to stretching of the abdominal wall during the pneumoperitoneum and release of inflammatory mediators, local dissection and irritation of the peritoneum produced by blood, bile spillage or CO2 used for pneumoperitoneum[3].

Cholecystectomy is the most common surgery of the biliary tract and the second most common operative procedure[4,5]. Laparoscopic Cholecystectomy (LC) is the treatment of choice in treating gallbladder disease substituting the conventional Open method of Cholecystectomy (OC)[6], unless there is no contraindication found related to laparoscopic procedures. This is because open cholecystectomy surgery are more prone to infection[7]. Although it is the belief of patients that laparoscopy has shown a pain-free era, but the fact remains that the patients complain more of visceral pain after laparoscopic cholecystectomy in contrast to parietal pain experienced in open cholecystectomy surgery[8]. Although Laparoscopic cholecystectomy has improved surgical outcome in terms of reduced pain, morbidity and duration of convalescence compared to open cholecystectomy[9] but it is not a pain-free procedure, as many LC patients refrain from early recovery to normal activity which imperils the feasibility of LC as a low morbidity procedure[10]. The pain following laparoscopic cholecystectomy is variable in intensity and duration and is highly unpredictable. Pain after LC is generally lesser than open cholecystectomy however postoperative shoulder and abdominal pain can cause considerable distress[3]. Patients often suffer from visceral pain during coughing, respiration and mobilization that can increase the hospital stay, which further leads to increase in morbidity and costs[11].

Provision of adequate postoperative pain relief is of utmost important to enhance recovery. There are various modalities available for postoperative pain relief ranging from parenteral analgesia (NSAIDS and opioids), epidural analgesia, peripheral nerve blocks, incisional infiltration or intraperitoneal instillation using local anaesthetics[12, 13]. Multimodal analgesics have been tried to relief pain following laparoscopic cholecystectomy. Over the years intraperitoneal use of local anesthetics during laparoscopy for postoperative pain relief has gained interest.

Intraperitoneal local anesthetic administration[6] and rectus sheath block (RSB)[14,15] have been used as a method for reducing postoperative pain[16]. Intraperitoneal local anesthetic acts on visceral nociceptors of peritoneum, whereas rectus sheath block, with successful blockade of intercostal nerves, provides full thickness anesthesia of anterior abdominal wall[17].

Instillation of intraperitoneal local anaesthetics like lignocaine, bupivacaine, levo-bupivacaine and ropivacaine has been used following laparoscopic surgeries to reduce postoperative pain through randomized trials for many years[8,18-24]. One of the important property of long acting local anesthetics are that, they act by reversible blockade of generation and propagation of action potential in nerves and other excitable tissue, at the level of sodium channels[19,25], thus causing a prolonged sensory or motor blockade which is appropriate for anesthesia in different types of surgeries[25].

Ropivacaine, is a long acting amide group of local anesthetic, structurally related to bupivacaine[25], pure S-enantiomer but unlike bupivacaine, has less lipophillic and cardiotoxicity property. Ropivacaine when given intraperitoneally, initiates its action in 15-20 minutes and reduces postoperative visceral and shoulder pain following laparoscopic cholecystectomy[26].

Although a number of these studies have reported a significant reduction in postoperative pain after the intraperitoneal instillation of local anesthetics, while many have reported no benefit or reduction in analgesic requirement[26]. The effectiveness of local anaesthetic, instilled intraperitoneally either alone or mixed with drugs, has shown in number of studies including surgery like laparoscopic cholecystectomy[27]. Intraperitoneal instillation of local anaesthetic, Ropivacaine at the beginning of laparoscopic cholecystectomy combined with normal saline is an effective method for reducing pain after surgery[28].

Bupivacaine is well established long acting local anesthetics which like all amide group of anesthetics has been associated with cardiotoxicity when used in high concentration or if accidently administered intravascularly[29], compared to Ropivacaine, a newer amide group of local anesthetic, released in 1996, may be preferred due to less risk of cardiovascular toxicity and central nervous system side effects.

Study conducted on the effect of Ropivacaine for combined port site, mesosalpinx infiltration and peritoneal instillation and thus recorded lower pain scores, less use of opioids and lower incidence of post-

operative nausea and vomiting[30].

Tramadol is an atypical opioid analgesic that has been advocated to have local anesthetic action[31] besides its central action on mu opioid receptors along with noradrenergic and serotonergic effects. Study have shown that intraperitoneal administration of bupivacaine (0.125%) with tramadol is an effective and apparently safe method of postoperative pain control following laparoscopic cholecystectomy[32,33].

There have been many studies on intraperitoneal use of Bupivacaine but few on Ropivacaine , so Ropivacaine has been chosen as drug for this study.

METHODS

AIM

1. To compare the postoperative analgesic effect of Ropivacaine with Ropivacaine plus Tramadol in patients undergoing laparoscopic surgeries.

OBJECTIVES

1. Assess the demand of rescue analgesia.
2. Study adverse events due to Ropivacaine Vs Ropivacaine plus Tramadol

STUDY DESIGN: Comparative prospective descriptive observational study.

STUDY POPULATION: Patients undergoing laparoscopic cholecystectomy. Conducted from Department of Anesthesiology in association with Department of Gastrointestinal Surgery at Santokba Durlabhji Memorial Hospital cum Medical Research Institute, Jaipur after taking approval from hospital ethical committee. During January 2018 to August 2019.

INCLUSION CRITERIA

1. Patients in the age group of 18 – 60 years of age,
2. Having ASA (American Society of Anesthesiologists) grade I & II
3. Patients with no contraindication to use of Ropivacaine
4. Patients who give informed written consent to be included in study
5. Patients for elective surgery.

EXCLUSION CRITERIA

1. Age less than 18 years and more than 60 year
2. Having ASA (American Society of Anesthesiologists) grade III
3. Patients with known allergy to the study drugs
4. Patients with anticipated difficult airway
5. Patients with hemodynamic instability
6. Patients presenting with sepsis and contraindication to use of ropivacaine (inadequate amount of cholinesterase enzyme , Mysthenia Gravis , disease of the heart and blood vessels , liver problems , kidney disease with reduction in kidney function , allergies to amide type of anesthetics)

Data Collection Procedures

The Sixty (60) patients posted for elective laparoscopic cholecystectomy surgery under general anesthesia belonging to (ASA) physical status (I or II), aged 18-60 years were selected for the study. All patients underwent a pre- anesthetic assessment a day before surgery. Patients were randomly allocated into two groups, Group A as control group and other experimental group as Group B. After informing the patients about the study and possible side effects of drug administration (like nausea, vomiting, hypotension, bradycardia, sedation, respiratory depression, and urinary retention) informed consent of the patient for participation in the study is taken. On the day of surgery, after checking the patient identity preoperatively, confirming NBM status of patient, checking all the equipments, patient was taken for surgery and was pre-medicated with iv midazolam (0.07 – 0.15 mg/kg) and iv glycopyrrolate 0.2 mg . Induction of anaesthesia was done with propofol (1 – 2.5 mg/kg) intravenous (iv) and fentanyl (2 µg/kg) iv. After 3 min of preoxygenation , tracheal intubation was facilitated with iv succinylcholine (1 - 2 mg/ kg) following ryles tube insertion. Anesthesia was maintained with isoflurane (MAC 1) and 60% oxygen with air. Muscle relaxation was maintained with non-depolarizing muscle relaxant- Atracurium with loading dose of (0.5 mg/kg)iv followed by incremental doses of (0.1mg/kg)iv given every 15-20 minutes. Patients were monitored using MP40 Philips monitor. Intraoperative monitoring include continuous electrocardiogram (ECG), non−invasive blood pressure at 5 min intervals (NIBP), oxygen saturation(SpO_2) and end−tidal carbon dioxide ($ETco_2$) .Patient's lungs was ventilated by intermittent positive pressure ventilation using a circle system to maintain normocapnia. Heart rate (HR) and mean arterial pressure (MAP) was maintained within 20% of the pre−operative value. After making Ports by the surgeon, categorised groups received intraperitoneal infiltration by the surgeon with respective study material, as Group A with 50 ml of 0.25 % of Ropivacaine and Group B with 50 ml of 0.25 % of Ropivacaine with 100 mg Tramadol to the subdiaphragmatic and subhepatic space. All patients received Diclofenac (1.5 mg/kg) iv 40 min before completion of surgery and Ondansetron (0.1 mg/kg) iv 30 min before the completion of surgery . After the completion of surgery, residual neuromuscular block was antagonised with appropriate dose of Neostigmine (0.04-0.08 mg/kg) iv and glycopyrrolate 0.2 mg iv for each 1 mg of neostigmine.. Tracheal extubation was performed on meeting the standard criteria for extubation. The patients were then evaluated postoperatively for postoperative pain at 1, 4, 8, 12, 24 hours. Postoperative rescue analgesia was provided with first Diclofenac (1.5 mg/kg) or Tramadol (1.5 mg/kg) along with Ondansetron (0.1 mg/kg) iv (for nausea caused due to Tramadol administration) if needed. The results then was compiled and analysed statistically. Appropriate treatment was given in case of any side effects.

STATISTICAL ANALYSIS

Statistical analysis was performed with the SPSS, Trial version 23 for Windows statistical software package (SPSS inc., Chicago, il, USA) and Primer for the generation of descriptive and inferential statistics.The Categorical data were presented as numbers (percent) The quantitative data were presented as mean and standard deviation. The difference in proportion was analyzed by using chi square test and the difference in means were analyzed by using student T test. Probability P value <0.05 was considered statistically significant

OBSERVATIONS AND RESULTS

The Observations are presented as Mean ± Standard Deviation or as percentage as is applicable.

Table No. 1: Distribution of the cases according to Age

Age Groups (years)	Group A (N=30)		Group B(N=30)		Total (N=60)	
	No.	%	No.	%	No.	%
20 to30	7	23.33	6	20.00	13	21.67
31 to40	6	20.00	7	23.33	13	21.67
41 to50	9	30.00	5	16.67	14	23.33
51 to 60	8	26.67	12	40.00	20	33.33
Total	30	100.00	30	100.00	60	100.00
Mean ±SD	41.63±12.05		44.83±12.27		43.23±12.16	
Gender	**Group A**		**Group B**		**Total**	
	No.	%	No.	%	No.	%
Female	17	56.67	21	70	38	63.33
Male	13	43.33	9	30	22	36.67
Total	30	100.00	30	100	60	100.00

Table no. 1.shows mean age of patients in both groups. It was observed that there were no significant differences found between study groups according to age, Chi-square = 2.097 with 3 degrees of freedom; P=0.755. According to gender .It was observed that although no significant differences found between the group according to gender , but females were significantly more than male in both study groups, Chi-square = 0.646 with 1 degree of freedom; P = 0.422

Table No: 2. Distribution of the cases according to ASA grade

	Group A		Group B		Total	
ASA GRADE	No.	%	No.	%	No.	%
1	16	53.33	15	50	31	51.67
2	14	46.67	15	50	29	48.33
Total	30	100.00	30	100	60	100.00

Table no. 2 shows distribution of cases according to ASA grading and no significant differences between study groups was observed, Chi-square = 0.000 with 1 degree of freedom; P = 1.000

Table No: 3-Distribution of the cases according to diagnosis

	Group A		Group B		Total	
DIAGNOSIS	No.	%	No.	%	No.	%
Acute cholecystitis	7	23.33	5	16.67	12	20
Cholelithiasis	4	13.33	4	13.33	8	13.33
Resolving biliary pancreatitis	1	3.33	1	3.33	2	3.33
Symptomatic gall stone disease	18	60	20	66.67	38	63.33
Total	30	100	30	100	60	100

Table 3 shows distribution of cases according to diagnosis and observed no significant differences between study groups, however, Symptomatic gall stone disease found to be much higher in both the groups A & B followed by Acute cholecystitis, Chi-square = 0.439 with 3 degrees of freedom;

Table No: 4- Distribution of the cases according to Time to first request of analgesia in postoperative period

	Group A		Group B		Grand Total		P Value
0-1hr	**No**	**%**	**No**	**%**	**No**	**%**	
NO	9	30.00	22	73.33	31	51.67	0.002
YES	21	70.00	8	26.67	29	48.33	
1-4hr							
NO	30	100.00	24	80.00	54	90.00	0.031
YES	0	0.00	6	20.00	6	10.00	
4-8hr							
NO	20	66.67	25	83.33	45	75.00	0.233
YES	10	33.33	5	16.67	15	25.00	
8-12hr							
NO	25	83.33	26	86.67	51	85.00	1.0
YES	5	16.67	4	13.33	9	15.00	
12-24hr							
NO	22	73.33	21	70.00	43	71.67	1.0
YES	8	26.67	9	30.00	17	28.33	

Table 4 shows the distribution of cases according to time to first request of analgesia in post-operative period. It was observed that at 0-1 hr in group A 70% of cases required first dose of rescue analgesia compared to group B 26.67% cases required first dose of rescue analgesia. in Group A ,(P=0.002) Time to requirement of first dose rescue analgesia was prolong in the group B (7.61 hours) compared to group A (5.81 hours), indicating better and longer pain relief in the group B compared to groups A.

Table No: 5-Distribution of the cases according to Adverse Events

	Group A(N=30%)		Group B(N=30)		Total (N=60)		P Value
ADVERSE EVENTS	**No.**	**%**	**No.**	**%**	**No.**	**%**	
NONE	24	80.00	26	86.67	50	83.33	0.72
PONV	0	0.00	3	10.00	3	5.00	0.23
URINARY RETENTION	6	20.00	1	3.33	7	11.67	0.108
Hypotension	0	0	0	0	0	0	NA
Bradycardia	0	0	0	0	0	0	NA
Respiratory Depression	0	0	0	0	0	0	NA
Total	30	100.00	30	100.00	60	100.00	

Table 5 shows the distribution of cases according to adverse events. Although the Urinary retention was found in 20% cases in group A as compared to 3.33% found in Group B and PONV found only in Group B 10 % ,but statistically the difference among groups was not significant(P=0.108)

DISCUSSION

Laparoscopic techniques have gained popularity in the recent years, mainly because of the fact that it involves small incision, short hospital stay and early ambulation. Though it has got various advantages on its own, the peritoneal stretching due to the insufflations of gases results in excessive pain postoperatively. Various modes of providing analgesia were tried. The techniques that can be used for providing pain relief in Laparoscopic surgeries include surgery under subarachanoid block, parenteral opioids and NSAIDs, Instillation of local anesthetics intraperitoneally, etc.

Instillation of local anaesthetic solution intraperitoneally, as a mode of providing postoperative analgesia, has been studied extensively. It has the added advantage of early ambulation, reduced incidence of postoperative nausea vomiting and reduces the use of parenteral opioids and NSAIDs.

The rationale for intraperitoneal administration of drugs for the treatment of the pain that follows laparoscopic surgery is that the small incisions at the abdominal wall cause visceral component of the pain and shoulder pain. With this in mind, many authors have tried to diminish pain via the peritoneal route. Intraperitoneal local anaesthetic is likely to blockade free afferent nerve endings in peritoneum.

This study was done on patients between age group of (18-60 years), with ASA grade I and II, posted for laparoscopic cholecystectomy to compare the postoperative analgesic effect of Ropivacaine and Ropivacaine and Tramadol which were instilled intraperitoneally. Both groups were also compared according to effect on hemodynamic, need for rescue analgesia, drugs used for rescue analgesia, time to first request of rescue analgesia and any adverse events if occurred.

Effect on hemodynamic

Baseline heart rate was77.73 ±9.34 in group A and 75.53 ±10.80 was in group B. The Baseline Systolic blood pressure was 126.47±9.5in group A and 131.7±13.33was in group B , while the Baseline Diastolic blood pressure was 75.83±7.37 in group A and 79.03±8.16 was in group B, overall baseline vital parameters among the groups were comparable

Heart rate (HR)

The heart rate was also monitored postoperatively and was compared among the groups. Though there were changes in the heart rate in both the groups, they were comparable initially. The Baseline heart rate was 77.73 ±9.34 in group A and 75.53 ±10.80 was in group B. The heart rate was decreasing up to 30 min 74.93±6.32 in group A while in group B it was 72.77±8.90 then increasing and were shown to be statistically insignificant between the groups.

Systolic blood pressure (SBP)

The SBP was also monitored postoperatively and was compared among the groups. Though there were changes in the SBP in both the groups, they were comparable initially. The Baseline SBP was 126.47±9.5 in group A and 131.7±13.33 was in group B. The SBP was decreasing upto 20 min 122.9±6.72 in group A while in group B it was 126.03±11.42 then increasing and were shown to be statistically insignificant between the groups.

Diastolic blood pressure (DBP)

The DBP was also monitored postoperatively and was compared among the groups. Though there were changes in the DBP in both the groups, they were comparable initially. The Baseline DBP was 75.83±7.37 in group A and 79.03±8.16 was in group B. The DBP was decreasing upto 20 min 73.9±4.4 in group A while in group B it was 76.67±7.44 than increasing and were shown to be statistically insignificant between the groups.

Mean Arterial Pressure (MAP)

The Mean Arterial Pressure was monitored post operatively in all the groups and was analyzed statistically. The hemodynamic in all the groups was stable and was found to be statistically insignificant among the groups at different follow up periods. The Baseline MAP was 92.67±7.44 in group A and 96.63±9.33 was in group B. The MAP was decreasing upto 20 min was 90.3±4.5 group A while in group B it was 93.3±7.88 then increasing and were shown to be statistically insignificant between the groups. Rapolu S et al.[45] observed that vital parameters like heart rate, blood pressure are important indicators of patients comfort as the values correlated well with high VAS scores.

Visual Analogue Score (VAS score)

In our study VAS score was significantly higher in Group A as compared to Group B with (p-value 0.017S) at (1-4 hrs.). Our results were consistent with results of Kalsotra S et al.[43] who observed that over all VAS score over 24 hrs. also showed statistically significant difference ($p<0.05$) with group RD having least mean VAS compared to other two groups RT and R. similarly Shukla U et al[48] also noted that VAS at different time intervals were statistically significantly lower at all times in Group Bupivacaine + Dexmedetomidine than Group Bupivacaine + Tramadol and Group Bupivacaine. Jamal A et al.[33] ,found reduction in postoperative pain at 4 and 8 h postoperatively when Group BT (bupivacaine and tramadol group) was compared with Group T (tramadol group) or Group B (bupivacaine group) ($P < 0.01$).

Drugs and dose of rescue analgesia needed

Results from study showed that in group A 90% of cases needed rescue analgesia as compared to group B only 60% needed rescue analgesia. Although among the drugs given for rescue analgesia, there were no significant differences found among the groups. However, dose of 75mg diclofenac was far ahead from the others during the study.

Kalsotra S et al.[43] concluded in study that total analgesia consumption of injection Diclofenac in 24 hours postoperatively was least in group

RD followed by RT group and highest requirement was in R group with 81.70 mg, 109.80mg and 140.60mg, respectively.

Time to first request of analgesia in post-operative period

At 0-1 hr, In Group A, Time to first request of analgesia in post-operative period covers 70% cases as compared to Group B only 26.67% cases needed, with significant P value (P=0.002).Thus Time to requirement of first dose rescue analgesia was prolong in the group B (7.61 hours) compared to group A (5.81 hours), indicating better and longer pain relief in the group B. Kalsotra S et al.[43]study also showed that time to first request of analgesia was longest in RT (116.9±23.12 min, range 45-181 min) and Group R (63.7±11.97 min, range 32-130 min). The statistical difference was significant among the study groups (p<0.001). Similar result was shown by Jamal A et al.[33] that time to first dose of rescue analgesic was also significantly prolonged in Group BT compared to Group B or T

Adverse event

Although the Urinary retention was found in 20% cases in group A as compared to 3.33% found in Group B, but statistically it was not significant(P=0.108) and PONV found only in 10% of Group B ,but statistically the difference among groups was not significant (P=0.108).

Kalsotra S et al.[43] observed in the study that shoulder pain, pruritis, nausea and vomiting more in group R, RT compared to RD but hypotension and bradycardia were more in RD group but stastistically not significant. Rapolu S et al.[45] found the incidence of shoulder pain significantly low in group Bupivacaine and Dexmedetomidine compared to group Bupivacaine. Similarly Jamal A et al.[33] observed the incidence of nausea and vomiting was comparable in all the study groups. There was a lower incidence of nausea and vomiting in Group BT compared to other groups, but it was not statistically significant.

CONCLUSION

Intraoperitoneal instillation of local anesthetic is an easy, cheap and non-invasive method that provides good analgesia in the post-operative period after laparoscopic cholecystectomy surgery. The combination of intraperitoneal instillation of Ropivacaine with Tramadol is superior to use of only Ropivacaine for reducing post-operative pain in patients ,who underwent laparoscopic cholecystectomy without any significant increase in adverse events. Combination of Ropivacaine with Tramadol not only reduces the intensity of post-operative pain, but also reduces the total dose of rescue analgesia needed. Post operatively first request of rescue analgesia is also prolong in group with Ropivacaine and Tramadol.

So, addition of Tramadol with Ropivacine for intraperitoneal instillation in laparoscopic cholecystectomy is better as compared to single use of Ropivacaine.

LIMITATIONS

1. Nausea and vomiting or Urinary retension may be due to general anesthesia may be wrongly considered as side effect of drug.
2. As drugs are intra peritoneal instilled just after placing ports by surgeons, so some volume of drugs may get suctioned during surgery, hence might decreasing the volume concentration of drugs from its actual value.

FUTURE IMPLICATIONS

Our study group was small; therefore study on the larger group of patients is required before drawing any further conclusion.

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Conflict of Interest: The authors declare that they need no conflict of interest.

ABBREVIATIONS

ASA Grade : American Society Of Anesthesiologist Grade
LC : Laparoscopic Cholecystectomy
OC : Open cholecystectomy
VAS Score : Visual Analogue Score
NSAIDs : Non Steroidal Anti Inflammatory Drugs
PONV : Post operative nausea and vomiting
NIBP : Non Invasive Blood pressure monitoring
ECG : Electrocardiogram
HR : Heart Rate
SBP : systolic Blood Pressure
DBP : Diastolic Blood Pressure
MAP : Mean Arterial Pressure
sPO2 : Oxygen Saturation
IV : Intravenous
SD : Standard deviation
Mcg : microgram
Mg : milligrams
Kg : kilograms

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