

A Comparative Study of Intravenous Paracetamol and Tramadol for Post Operative Pain Management in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Accurate management of pain is one of the most important challenges of health care providers and one of the most important concerns of the patients in postoperative period. 160 patient undergoing elective laparoscopic cholecystectomy were divided into 2 groups (60 female in each group and 15 male for each). The first group received Tramadol 1.5 mg per kg intravenously at recovery and then every 8 hours for post operative analgesia. The second group received Paracetamol 5mg per kg intravenously then the same dose every 8 hours. In this study we found that there is no significant differences in behavioral pain score ($p>0.05$) between groups treated with Paracetamol and those treated with Tramadol at recovery period, first hour observation and 8 hour observation. while there was significant decrease in behavioral pain score observation ($p<0.05$) at the hour 24 of patients treated with Tramadol and there were significant decrease in behavioral pain score ($p<0.05$) between male treated with Tramadol and those treated with Paracetamol at recovery period, first hour, 8 hour observation and 24 hours. As conclusion Intravenous Paracetamol appeared as effective as Tramadol in the management of mild to moderate pain in female patients undergoing laparoscopic cholecystectomy in doses used in our study. While Tramadol seems to be more effective than Paracetamol in male groups.

الخلاصة

المعالجة الصحيحة للألم هي واحدة من أهم التحديات التي تواجه من تخصصوا في الرعاية الصحية وواحد من أهم المهوم التي تواجه المريض بعد إجراء العملية الجراحية. في هذه الدراسة ١٦٠ مريض يخضعون لعملية رفع المرارة الناظورية قسموا إلى مجموعتين بواقع ٦٠ امراه لكل مجموعته و ١٥ رجل لكل مجموعته. المجموعة الأولى حققت ١,٥ ملغ لكل كيلو غرام من دواء Tramadol وريديا والمجموعة الثانية حققت ب ٥ ملغ لكل كيلو غرام من دواء Paracetamol وريديا في فترة الاستفاقة وبعد كل ٨ ساعات. توصلت الدراسة للنتائج التالية انه ليس هناك أي فرق معنوي في مقياس معدل الألم السلوكي بين المجموعتين التي عولجت بال Tramadol وريديا ومجموعة ال Paracetamol وريديا ($p>0.05$) في فترة الاستفاقة وساعة المراقبة الأولى والثامنة. بينما كان هناك فرقا معنويا واضحا في مقياس معدل الألم السلوكي بين المجموعتين التي عولجت بال Tramadol وريديا ومجموعة ال Paracetamol وريديا ($p<0.05$) بالنسبة للإثبات في الساعة ٢٤ و بين ذكور المجموعتين في جميع ساعات المراقبة. نستنتج من ذلك ان دواء Paracetamol وريديا هو يكافئ دواء Tramadol وريديا في معالجة الم ما بعد الجراحة الناظورية بالنسبة للإثبات بينما بالنسبة للذكور دواء Tramadol وريديا يبدو أكثر كفاءته في معالجة الم ما بعد الجراحة الناظورية.

Introduction

Accurate management of pain is one of the most important challenges of health care providers. One of the most important concerns of the patients in postoperative period is postoperative

pain. Effective relief of postoperative pain is one of the primary targets as postoperative pain also affects the clinical outcomes of the surgeons.[1,2].

Uncontrollable acute pain may result in prolonged hospital stay and unplanned hospital admissions and

increased hospitalizations besides psychological and physiologic effects[3]. The accurate assessment of pain is challenging because pain perception is subjectively reported and may be influenced by the patient's attitude about health, disease, and personal expectations. These differences may be more than just idiosyncratic, for example, men and women not only experience pain differently, they may respond to analgesics differently. Central sensitization and hyperexcitability developed after surgical incision results in amplification of postoperative pain. Some short-term reduction in postoperative pain and acceleration of recovery and long-term reduction in chronic pain development benefits can be obtained in recovery period by preventing central sensitization through analgesic treatment[4,5].

Pathophysiology of postoperative pain is multifactorial, and predominantly of inflammatory nature from skin incision and tissue damage. Inflammatory cytokines, interleukins and prostaglandins produced from the arachidonic acid pathway induce a neuro-inflammatory soup, which sensitizes peripheral A δ and C fibres. Ischaemia from retraction of tissue, as well as disrupted blood supplies, contributes to pain significantly, characterized by low tissue pH and high lactate levels at the site of incision[6,7]. Opioids are widely used to relieve postoperative pain due to their efficacy and effectiveness[8] However, the authors are concerned about their adverse effects such as nausea, vomiting, and respiratory depression. Nonsteroidal anti-inflammatory drugs(NSAIDs) have been widely applied for postoperative pain management after laparoscopic surgery [9]. Several trials showed that NSAIDs, either selective or non-

selective, were not superior to placebo on shoulder pain control although they could reduce surgical pain or rescue narcotics requirement[10].

Tramadol

Is a synthetic analogue of codeine. Its analgesic effect is moderate. It is the only drug acts upon two different mechanisms. One of its metabolites has a poor affinity to μ -opioid receptor without affecting delta and kappa receptors. The second mechanism is reuptake inhibition of neurotransmitters norepinephrin and serotonin. Tramadol causes less side effects like respiratory depression and sedation encountered with other opioids in postoperative pain treatment [11-13].

Paracetamol

(N-Acetyl-4-aminophenol) also known as "APAP" or "paracetamol" is one of the most widely used medicines. It is a weak COX-1 and COX-2 inhibitor in peripheral tissues and possesses no significant anti-inflammatory effects. Recent evidence suggests that acetaminophen may inhibit a third enzyme, COX-3, in the central nervous system. COX-3 appears to be a splice variant product of the COX-1 gene[13]. The drug is useful in mild to moderate pain such as headache, myalgia, postpartum pain. In Arici S., *et al.* study, it was demonstrated that administration of 1 g Paracetamol intravenously before hysterectomy resulted in better postoperative pain control and lead to decreased use of morphine. [14]

In therapeutic doses, a mild increase in hepatic enzymes may occasionally occur in the absence of jaundice; this is reversible when the drug is withdrawn. With larger doses, dizziness, excitement, and disorientation are seen[15]. This study aim to compare the analgesic efficiency of Paracetamol and Tramadol in relieving post operative pain of patients undergoing

laparoscopic cholecystectomies by using behavioral pain score.

Patients and Methods

In order to standardize the surgical procedure, we chose laparoscopic cholecystectomy since it is a commonly performed procedure universally. 160 patient undergoing elective laparoscopic cholecystectomy in Al-Hyaat Private Hospital were divided into 2 groups (60 female in each group and 15 male for each). The first group received Tramadol 1.5 mg per kg intravenously at recovery and then every 8 hours for post operative analgesia .The second group received Paracetamol 5mg per kg intravenously then the same dose every 8 hours. Anesthesia was standardized for both groups, anesthesia induced by Thiopenton sodium 5mg per kg with Ketamin 0.5 mg per kg for intra operative analgesia, Atracurium was the only muscle relaxant used and anesthesia maintained using Halothane in concentration of 1-1.5 percent .Muscle relaxation was reversed using

Neostigmin with Atropine. Analgesia for post operative pain given toward the end of surgery. Patient monitored in the recovery room for variable time until adequate recovery achieved. Patients considered well recovered when he achieve Aldret score of 10 at this time the first assessment of pain is done , another assessment done after 1 hour then after 8 hours then after 24 hours. There are a lot of methods used for pain assessment; all carries disadvantages; however we chose behavioral pain assessment scale since it is more objective and depend on strict clinical parameters which make assessment more reliable and subjected to less personal variation .If patient suffers sever pain at the first and second assessment another modality of analgesia is used and case with drown. Observers were blinded for the type of analgesia given . All data was analyzed by using SPSS version 17, using independent single t-test, Mann-Whitney U test, Fisher-exact test accordingly. P-value less than 0.05was considered significant.

Table 1 Aldert scoring system for post anesthesia recovery[16].

Discharge Criteria	score
Consciousness	
Fully awake	2
Arousable	1
Not responding	0
O₂saturation	
Able to maintain o ₂ saturation>92% room air	2
Needs O ₂ saturation>90% room air	1
O ₂ saturation<90%with O ₂ supplementation	0
Circulation	
BP 20 mm Hg preop	2
BP 20–50 mm Hg preop	1
BP 50 mm Hg preop	0
Activity	
Able to move 4 extremities	2
Able to move 2 extremities	1
Able to move 0 extremities	0
Respiration	
Able to take deep breath and cough	2
Dyspnea	1
Apnea	0

Table 2 Behavioral pain assessment scale For patients unable to provide a self-report of pain: scored 0–10 clinical [17]

Face	0 Face muscles Relaxed	1 Facial muscle tension, frown, grimace	2 Frequent to constant frown, clenched jaw
Restlessness	0 Quiet, relaxed appearance, normal movement	1 Occasional restless movement, shifting position	2 Frequent restless movement may include extremities or head
Muscle tone	0 Normal muscle	1 Increased tone, Tone flexion of fingers and toe	2 Rigid tone
Vocalisation	0 No abnormal Sounds	1 Occasional moans, cries, whimpers and grunt	2 Frequent or continuous moans, cries, whimpers or grunts
Consol ability	0 Content, relaxed	1 Reassured by touch, distractible	2 Difficult to comfort by touch or talk

1-3 = mild pain 4-6= moderate pain 7-10 = sever pain

Results

In this study we found that there is no significant differences in behavioral pain score (p>0.05) between patients treated with Paracetamol and those treated with Tramadol at recovery

period , first hour observation and 8 hour observation,(table 3). while there was significant decrease in behavioral pain score observation (p<0.05) at the hour 24 of patients treated with Tramadol,(table 3).

Table 3 comparison of behavioral pain score(BPS) mean value of paracetamol and tramadol groups.

Post operative time interval (hours)	Paracetamol group BPS by mean No.75	Tramadol group BPS by mean No.75	P value
Recovery	2.013	1.49	0.129
1 st hour	1.786	1.44	0.097
8 th hour	1.626	1.28	0.064
24 th hour	1.733	0.6	0.00*

* p<0.05

In this study we found that there is no significant differences in behavioral pain score (p>0.05) between female treated with Paracetamol and those treated with Tramadol at recovery period , first hour observation and 8

hour observation,(table 4). while there was significant decrease in behavioral pain score observation (p<0.05) at the hour 24 of female patients treated with Tramadol,(table 4).

Table 4 comparison of behavioral pain score(BPS) mean value of paracetamol and tramadol female groups.

Post operative time interval (hours)	Paracetamol group(female) BPS by mean No.60	Tramadol group(female) BPS by mean No.60	P value
On recovery	1.766	1.6	0.804
1 st hour	1.53	1.51	0.970
8 th hour	1.43	1.43	0.827
24 th hour	1.65	0.65	0.00*

* p<0.05

Also this study found that there were significant decrease in behavioral pain score (p<0.05) between male treated with Tramadol and those treated with

Paracetamol at recovery period , first hour observation, 8 hour observation and 24 hours. (table5).

Table 5 comparison of behavioral pain score(BPS) mean value of paracetamol and tramadol male groups

Post operative time interval (hours)	Paracetamol group(male) BPS by mean No.15	Tramadol group(male) BPS by mean No.15	P value
On recovery	3	1.066	0.006*
1 st hour	2.8	1.133	0.00*
8 th hour	2.4	0.8	0.001*
24 th hour	2.26	0.4	0.00*

* p<0.05

Discussion

Pain is the most frequent complaint leading to delayed discharge after laparoscopic cholecystectomy[18].

This study revealed no significant difference in behavioral pain score (p>0.05) between patients treated with Paracetamol and those treated with Tramadol at recovery period, first hour observation and 8 hour observation, (table 3,4), and when patients divided according to sex female show the same results , this finding may be due to the

number of female enrolled in this study. These results meet with Akarsu S, et al. [19] and Craig M, et al. [20] who state that Paracetamol intravenous 1 g has analgesic activity in moderate-severe post-operative pain similar those have shown ketorolac 30 mg, diclofenac 75 mg, morphine 10 mg. This result support our result even though lower doses of paracetamol was used in current study. But not with Guner et al. [22] study that compared Paracetamol and Tramadol, they

reported Paracetamol and Tramadol reduce opioid requirements after major abdominal surgeries, but alone could not provide adequate analgesia, therefore in major surgeries a multimodal approach have to be needed. This could be explained by the differences of operative method from this study.

On the other hand this study found that there is significant decrease in behavioral pain score ($p < 0.05$) in Tramadol treated patients and female patients at 24th hour observation than Paracetamol treated patients and this result is with and agree Aghamir and coworkers [21] compared IV Paracetamol with IV Tramadol and demonstrated that Paracetamol is an effective and safe analgesic for acute postoperative pain management but it was insufficient in the control of pain compared to tramadol . Aubrun F,et al. [23] who state that women experienced more severe postoperative pain and required a greater dose (+11%) of morphine than men in the immediate postoperative period. Also ,this results comes with McNicol ED, et al. [24] who said that ;A single dose of either propacetamol or i.v. paracetamol provides around 4 h of effective analgesia for about 37% of patients with acute postoperative pain. This finding not agree with Mehran Kouchek et al. [25] who found any statistically significant difference between the IV Paracetamol and IV Fentanyl groups in pain scores at 24 or 48hour. Previous studies addressing influence of gender on pain perception and the requirements of analgesics for pain relief to similar degree of analgesia have reported conflicting results. This could be due to heterogeneity in studies with respect to type and doses of analgesic drugs, type of surgery, different methods of pain relief, end point of treatment, duration, and ethnicity.

This study shows that there is significant decrease in behavioral pain score ($p < 0.05$) between male treated with Tramadol and those treated with Paracetamol at recovery period , first hour observation ,8th hour observation and 24th hours. (table 5), and this comes with Chia ,et al [26] investigated the influence of patient characteristics on postoperative pain at rest and pain on movement in a large sample of Chinese patients. Male sex was associated with increased postoperative pain and morphine requirements.

Limitations of our study such as small sample size, lack of placebo arm were reasons we could not draw further conclusions. However this small study indicates similar pain management properties of IV Paracetamol and IV Tramadol in mild to moderate pain.

Conclusion

Intravenous Paracetamol appeared as effective as Tramadol in the management of mild to moderate pain in female patients undergoing laparoscopic cholecystectomy in doses used in our study till 24 hour . While Tramadol seems to be more effective than Paracetamol in the management of mild to moderate pain in male patients undergoing laparoscopic cholecystectomy in doses used in our study

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