Research Article

Intra-peritoneal Xylocaine Spraying for Postoperative Pain Control in Laparoscopic Cholecystectomy: A prospective study at Al-Yarmouk Teaching Hospital

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Abstract

Background: The concept of minimal access surgery was introduced to achieve several objectives; among which was to minimize post-operative pain by bringing access trauma to the lowest possible level without compromising the clarity of the operative field. **Objectives:** To study the effect of using local intraperitoneal application of xylocaine, in 2 different concentrations applied directly as near as possible to the intra-abdominal operative field in laparoscopic cholecystectomy, on post-operative pain control. **Patients and methods:** 110 patients with symptomatic gall stone disease were treated with laparoscopic cholecystectomy. These were divided into 3 groups, the first group, of 40 patients, was operated upon using the classical steps of that surgery and the final step was always to wash the field with normal saline followed by sucking extra fluid before terminating the surgery. In the second group (36 patients) a step was added; and that is the application of local Xylocaine (3 ml of 2% solution-without adrenaline- diluted with 7 ml of normal saline to a total of 10 ml- i.e. 0.6% solution) sprayed as near as possible to gall bladder bed (after excising the gall bladder) and kept in. In the third group (34 patients), 5 ml of the 2% Xylocaine were diluted up to 10 ml (ending with a 1% solution) sprayed in the same way. These 3 groups were followed post-operatively regarding the level of pain and magnitude of post-operative pain control and the amount of post-operative analgesia needed for each of them. **Results:** The first group of patients who did not receive intraperitoneal xylocaine, expressed higher levels of post-operative pain, and needed higher (or more frequent) doses of post-operative analgesia, than the 2nd and the 3rd groups who did receive intra-peritoneal xylocaine sprays. This was expressed as better post-operative pain control in these patients. There was no significant difference in pain control between the 2nd and the 3rd group patients. Using this simple technique will add no more than a minute or two to the time of the operation at its end. Pain control will be significantly aided if subcutaneous Xylocaine was also used in addition at the port site wounds. **Conclusions:** Using local intraperitoneal xylocaine sprayed at the gall bladder bed in laparoscopic cholecystectomy (as the end step after excising the gall bladder) gives a better post-operative pain control and decreases the need for higher or more frequent doses of post-operative analgesia.

Key words: Postoperative pain, laparoscopic cholecystectomy (LC), xylocaine, intraperitoneal spray, Wong-Baker pain scale

INTRODUCTION

Pain has been defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage".[1] This definition also recognizes that group of patients who experiences chronic pain for which no physical cause can be established and where psychological factors are operating. The main categories of such pain are:

1. Nociceptive pain: is produced by stimulation of normal nerves by thermal, chemical or physical injury and is further subdivided into somatic (transmitted by peripheral nerves), e.g. postoperative wound pain and

joint inflammation pain, or visceral (transmitted by splanchnic nerves), e.g. biliary colic.

2. Neuropathic pain: is the result of diseased or damaged components of the nervous system with pain arising in the absence of any peripheral stimulation.

3. Pain due to psychological factors: this type is an important component in chronic pain.[2]

Post-operative pain control was always one of the corner-stones in the management of surgical patients. The goal of proper management of postoperative pain is to eliminate pain and discomfort with the possible minimal side effects.[3] Poor pain control in the postoperative period will definitely lead to increased postoperative morbidities and poor quality of life. Furthermore, an emerging clinical literature suggests that acute pain may rapidly evolve into chronic pain if poorly treated.[4] The concept of minimal access surgery was introduced to achieve several objectives; among which was to minimize post-operative pain by bringing access trauma to the lowest possible level, by minimizing the size of the laparotomy wounds (which are now referred to as laparoscopic port-site wounds, which are mostly 5-10mm in size), without compromising the clarity of the operative field.[5] And since post-operative pain is the sum of both pain caused by the access wound plus that caused by the internal trauma inflicted by the main surgical act, so the aim of post-operative analgesia is to combat these 2 components of pain.

The mainstay of postoperative pain control is to use opioid analgesia (although non-opioid analgesics are often used also, mainly NSAIDs which act by inhibiting the enzyme cyclooxygenase (COX) thereby blocking the production of prostaglandins resulting in an anti-inflammatory response. Injectable acetaminophen is also used for the same purpose.[6,7]

In addition to opioids, epidural analgesia, via a catheter inserted into the epidural space in the thoracic or lumbar regions with continuous infusion of local anesthetic agent results in better postoperative analgesia.[8]

Local anesthetic drugs (e.g. Lidocaine), may be used to provide anesthesia on their own by local infiltration, by the use of regional anesthetic techniques or by providing neuraxial blockade (intrathecal or epidural anesthesia), or as an adjunct to general anesthesia by providing pain relief extending to the post-operative period. Surgical site local xylocaine infiltration was an added factor serving to minimize post-operative pain control.[9] Lidocaine, to act as local anesthetic, it modifies dorsal horn neurons, has anti-inflammatory effect as it inhibit migration and activation of leukocytes. In addition, it positively assists the return of gastrointestinal motility, thought to be due early mobilization.[10]

Among the goals achieved by using minimal access surgery was to decrease access trauma pain by minimizing the size of the laparotomy wounds (which are now referred to as laparoscopic port-site wounds, which are mostly 5-10mm in size).[4] This has decreased post-operative pain significantly. Still on asking our patients post-operatively about pain they always refer to deep local right hypochondrial pain at the site of the surgical procedure denoting that part of the post-operative pain yielded at the local site of the true surgical work.

Local intraperitoneal infiltration of local anesthetics is an uncommonly used technique, but as the peritoneal membrane is an excellent absorptive membrane, it is logical that using these agents in contact with this membrane would allow rapid local absorption at the site where they were applied, furthermore any raw area created by dissection, as with what happens after cholecystectomy, makes exposed nerves in contact with the action of these drugs. This is the idea that inspired us to use local intraperitoneal Xylocaine spraying at the end of laparoscopic cholecystectomy as a mean of pain control for the immediate post-operative period. Before starting such maneuver, the issue was discussed with many of my colleagues (especially surgeons, anesthetists and physicians) regarding complications. Such anticipated complications can be local, such as infection or bleeding from the gall bladder bed on spraying fluid on it (washing established clots) or systemic, due to over-dosage as a result of rapid absorption, leading to toxic blood levels. Single application of a topical Xylocaine preparation does not lead to systemic side effects, toxicity may result from:

1. Excessive high plasma concentration.

2. Accidental intravascular injection or too rapid injection.

The systemic toxicity mainly involves the CNS and the CVS. CNS complications may include lightheadedness followed by drowsiness, numbness of the tongue and perioral region, restlessness, paranesthesia, blurred vision, headache, tinnitus nausea and vomiting and may even cause muscle twitching, tremors and even convulsions. CVS effects include myocardial depression, hypotension due to peripheral vasodilatation, arrhythmias and even standstill.[11]

The sensible upper dose limits for the lignocaine (xylocaine®) is 3mg/ kg. For lignocaine with adrenaline (1:200 000), it is 7mg/ kg). Lignocaine 1% is effective for most sensory blocks. Thus around 50 ml of lignocaine 1% (10mg/ ml) with adrenaline can be

infiltrated into the tissues of a 70kg patient. Bupivacaine 2mg/ kg, (30 ml of 0.5% bupivacaine is more cardiotoxic than lignocaine but has a longer lasting effect) 2. In our study 2% Xylocaine® was used, the maximum allowed dose is 10ml (i.e. 200mg) for a 70kg patient, so the decision was to use half of this dose as a maximum single dose for intraperitoneal spraying. Table 1 demonstrate some of those drugs criteria.

Table1: The most common local anesthetic drugs in use

Name	Dose limit	Conc.	Comments
Lignocaine	3 mg kg^{-1} (7 mg kg^{-1} with adrenaline)	1%, 2%	early onset, short acting, good for sensory blocks
Bupivacaine	2 mg kg^{-1}	0.25%, 0.5%	longer lasting, more cardiotoxic, must never be injected into a vein
Ropivacaine	225 mg	0.2%, 1%	less cardiotoxic, greater sensory than motor block
Prilocaine	400 mg	1%	methemoglobin toxicity
Levobupivacaine	150 mg	0.25%, 0.5%, 0.75%	an isomer of bupivacaine, less cardiotoxic

Local anesthetics are used in different techniques; such as topical anesthesia, local infiltration, regional blockade anesthesia including spinal and epidural anesthesia, and the intravenous regional anesthesia (Bier's block), where a tourniquet is applied for at least 20 min. and an intravenous anesthetic is given to block a whole upper limb.

The use of intraperitoneal local anesthetic was the idea behind this paper. We thought that dissection of the gall bladder from its bed and the injury inflicted to the liver capsule locally with the injury of the visceral peritoneum during dissection at Callot's triangle are contributory factors to the postoperative pain. The entry wound also passes through sensitive skin, fascia, muscles and definitely through the parietal peritoneum which is densely innervated by somatic spinal nerve sensitive to pain and these will add to the magnitude of post-operative pain. We thought that direct application of lignocaine intra-peritoneally to these areas just by spraying a diluted solution will have some post-operative analgesic effect. These patients were followed regarding their post-operative level of pain and the amount of analgesia needed and the results were tabulated and compared to another group of patients who were spared this technique.

PATIENTS AND METHODS

During a period of 30 months (from July 2013 up to January 2016, one hundred and ten (110) patients were admitted to the surgical dept. at Al-Yarmouk teaching hospital. All had symptomatic gall stone disease (usually in the form of chronic calculous cholecystitis or history of acute cholecystitis), for which laparoscopic cholecystectomy was done. They were 91 females and 19 males. Exclusion criteria followed in this study was to exclude any patient older than 60 years of age, any patient with uncontrolled hypertension (& those on blockers), and any patient with history of drug allergy (especially to Lidocaine itself), any patient with disturbed liver functions, and those with cardiac ischemia or dysrhythmia proved by ECG. Ethical issues were considered, as thorough explanation and a written informed consent was prepared and presented to the patients to be signed by them or their families.

Table 2: Sex incidence

Sex	Number	Percentage
Males	19	17.27%
Females	91	82.73%
Total	110	100%

These patients were divided randomly into 3 groups, the first one, of 40 patients (34 females and 6 males) had the classical laparoscopic cholecystectomy, the end step of which was to do lavage with normal saline before terminating the surgery and closing the port site wounds. In the second group (including 36 patients; 28 females and 8 males), and after performing the last step mentioned above, and after returning the patient into the supine position from "head up, right up position", we pushed local intraperitoneal Xylocaine; 3 ml of 2% solution diluted with 7ml of normal saline (a total of 10ml), sprayed to the area of dissection, i.e. beneath the liver at or near the gall bladder bed. A syringe of 10ml was used connected to the gas-valve-connector of the 5mm port inserted in the Rt. hypochondrial area, after directing its tip to that area, followed by injecting 10ml of air using empty syringe, to ensure that none of the solution was left within the tubing of that port kept in by the positive intra peritoneal pressure. Following that the pneumoperitoneum was emptied through the sub-umbilical port, and the port site wounds closed. If the patient needed a drain for any reason (since we don't put a drain for every patient), the drain was kept clamped near its exit from the skin, till the patient is out in the

ward where that clamp was released to ensure enough time for the anesthetic to go into action. In the third group (34 patients; 29 females and 5 males), the same was done except for the dose of Xylocaine. Here 5 ml of 2% solution was used and diluted by adding another 5 ml of normal saline to make a total of 10 ml of diluted Xylocaine solution. The age of these patients varied from 18 to 56 years and the mean age was 37.5 years.

All these 3 groups of patients were followed regarding the level of post-operative pain and the amount and frequency of injectable analgesics (opiates or otherwise) used to combat that pain. These incidences were recorded, tabulated and compared. One of the methods used to assess post-operative pain, was to ask the patient to describe it whether it is mild, moderate or severe. Where mild pain was explained to the patient as being the one which, according to his opinion, is not interfering with usual daily activities, while moderate pain to be the one interfering with those activities but not to the degree keeping him or her in bed, while severe pain was the one keeping them bed ridden. On the other hand, the visual pain scale was used and shown to the patient to score their pain and both results were compared. These estimations were repeated 3 times in the day of surgery; (immediately after surgery when the patient was fully awake, during the evening round and late at night). It was also repeated 3 times in the 1st post-operative day depending on how quick the patient was discharged home. According to those estimations the patient was offered an analgesic drug. The drugs used were all parenteral and include: Tramadol 100mg ampoules, Diclofenac 75mg ampoules and pethidine 100mg ampoules. The amount, different combinations and frequency of these drugs given to the patient depend on how severe his or her pain was. These doses given to the patients were also recorded, tabulated and compared.

Figure 1: Wong-Baker pain scale

RESULTS

On asking the 1st group of patients (the one spared the intraperitoneal Xylocaine®) about their pain, 32 of them insist on their pain being sever during the day of surgery. In that day 29 of them had received 2 interrupted doses of Tramadol 100mg each given i.m. and in 24 of them two shots of Diclofenac 75mg i.m. were also given. In 3 out of these 32 patients the pain was so severe that a shot of pethidine of 100mg was given replacing the first dose of Tramadol, but they received their night dose of Tramadol plus an ampoule of Diclofenac 75mg (Pethidine was not readily available). 6 patients of the 1st group described their pain as moderate, and they received 2 shots of Tramadol 100mg i.m. for it, while only 2 described their pain as being mild and they received a single shot of Tramadol 100mg i.m. immediately post-operatively and Diclofenac 75mg i.m. at night. The 2nd group of patients who received intraperitoneal xylocaine involved 36 patients. 10 of them described their pain as being severe, and those received 2 shots of Tramadol 100mg i.m. plus 2 doses of Diclofenac 75mg i.m. in 8 of them (in 2 divided doses immediately postoperatively when the patient is fully awake and at night). Pethidine was not used in these 10 patients. 14 patients of the 2nd group described their pain as being moderate, and they received 2 doses of Tramadol 100mg i.m. 12 patients of the 2nd group described their pain as being mild. 8 of them received a single dose of Diclofenac immediately post-operatively and a single dose of Tramadol at night. And the last 4 received only 2 doses of Diclofenac 75mg i.m. In the 3rd group (those who received 5ml of Xylocaine® diluted into 10ml with normal saline), 7 patients described their pain as severe pain and they all receive 2 doses of Tramadol 100mg i.m. plus 2 doses of Diclofenac 75mg i.m. 13 patients described their pain as being moderate, so they were giver 2 interrupted i.m. shots of Tramadol 100mg only. The remaining patients of this group (14 patients) described their pain as mild. 5 were offered 2 interrupted shots of i.m. Diclofenac only, while 9 of them needed a single dose of Diclofenac immediately postoperatively and a single dose of Tramadol at bed time. Pethidine was not needed.

Comparing the 3 groups regarding pain severity and the need for different types of analgesics, using Data

Regression through ANOVA test (Microsoft Excel-2007), we found a significant difference in the number of patients with severe pain (P value of 0.0188) and also regarding the number of Tramadol 100mg ampoules needed for group 2 patients when compared with group 1 (P value of 0.0327), while there was no such difference when compared with group 3 (P value of 0.1422 & 0.0637 successively). Postoperatively, our patients were routinely monitored regarding their vital signs, any unusual sense of dizziness, nausea, vomiting (although these are expected postoperatively), palpitation, chest pain or dyspnea.

Most of our patients were discharged home in their 1st post-operative day (at noon time), and only 10 out of the 110 patients were discharged beyond their 1st postoperative day (mostly in the 2nd), and only two patients (ladies) were kept for more than 2 post-operative days, and the reason was postoperative complications (temporary bilious fluid leak) rather than pain. During this additional day (or 2) rarely we resort to more parenteral analgesics and oral drugs were used (except for those who developed the leak; as they were kept nil by mouth).

Postoperatively 8 of the patients of the 1st group developed palpitation (pulse rate < 100 bpm). On ECG, no ischemic changes were detected and no significant dysrhythmias were reported other than sinus tachycardia (most likely secondary to pain). No bradycardia, left sided chest pain, or dyspnea were reported in this group.

Table 3: Pain level (& postoperative analgesia given/ 1st 24h) in group 1

Level of pain	Number	Percentage	Comments
Mild	2	5%	Single dose Diclofenac, single dose Tramadol
Moderate	6	15%	2 shots of Tramadol
Severe	32	80%	2 shots of Tramadol in 29 (plus 2 shots of Diclofenac in 25) And a shot of Pethidine in 3
Total	40	100%	D: 55, T: 75, P: 3

Table 4: Pain level (& postoperative analgesia given/ 1st 24h) in group 2

Level of pain	Number	Percentage	Comments
Mild	12	33.33%	(8) Single dose of Diclofenac & single dose of Tramadol (4) 2 doses of Diclofenac
Moderate	14	38.89%	2 doses of Tramadol
Severe	10	27.78%	2 doses of Tramadol Plus 2 doses of Diclofenac in 8 of them
Total	36	100%	D: 32, T: 56, P: 0

Table 5: Pain level (& postoperative analgesia given/ 1st 24h) in group 3

Level of pain	Number	Percentage	Comments
Mild	14	41.18%	(9) Single dose of Diclofenac & single dose of Tramadol (5) 2 doses of Diclofenac
Moderate	13	38.24%	2 doses of Tramadol
Severe	7	20.59%	2 doses of Tramadol Plus 2 doses of Diclofenac in 8 of them
Total	34	100%	D: 33, T: 49, P: 0

Table 6: Comparing pain level and no. of Tramadol ampoule in the 3 groups

Group	No of patients	Severe pain	P-value	Tramadol	P-value
G1	40	32	(0.05)	78	(0.05)
G2	36	10	0.0188	56	0.0327
G3	34	7	0.1422	49	0.0637

In the 2nd group; tachycardia was reported in the immediate post-operative 6 hours, in 7 patients, and ECGs did not prove any significant dysrhythmias or ischemic changes. 3 cases had pulse rate below 70 (64, 68, 68) but none had pulse rate below 60 bpm. None of the patients of this group had left sided chest pain or significant shortness of breath. In the 3rd group 12 patients had these attacks of palpitation and again no ischemic changes were found on ECG and no added treatment was given. 6 patients develop pulse rate below

70 (really 2 of them had pulse rate of 60 bpm). Again, no significant dyspnea or left sided chest pain was reported in this group.

Light-headedness, sever dizziness, convulsive seizures were not reported in all the three groups in the immediate postoperative period and our patients were followed for all the above symptoms for 10 postoperative days (when nearly all of them had their sutures removed). Even sever hypotension below 100/60 was not reported in our patients. No immediate postoperative mortality was recorded up to one month following their surgery.

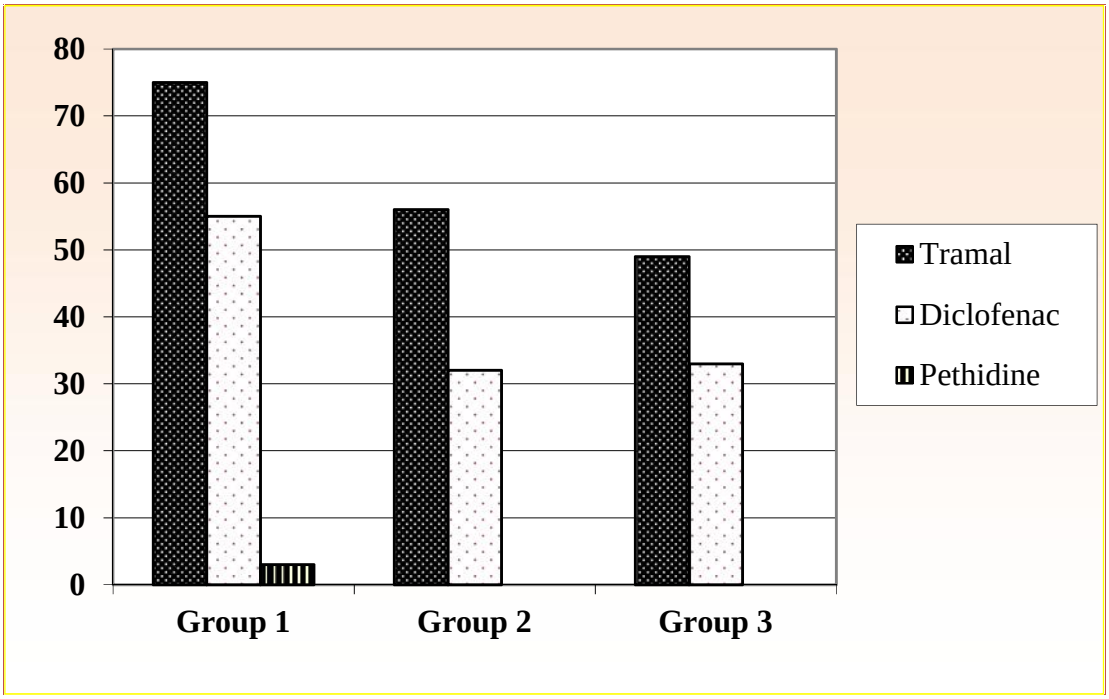

Figure 2: Column chart comparing the 3 groups regarding number of analgesics ampoules needed

Table.8: Postoperative cardiovascular observations

Group	Tachycardia	Pulse rate < 70 bpm	Left sided chest pain	Dyspnea	Tota l
1st	8	0	0	0	8
2nd	7	3	0	0	10
3rd	12	6	0	0	18
Total	27	9	0	0	36

DISCUSSION

Local anesthetic drugs are potent effective drugs known for a long period of time, and their use includes different types of local, regional, spinal…etc. of anesthesia and analgesia. Limitations and difficulties facing us during issuing this study were:

1. To know exactly the effective (and at the same time the safe) dose first.
2. Secondly if we are going to use it intraperitoneally how can we keep it at the site where we think that pain is initiated preventing its dissemination inside the peritoneal cavity where it can be diluted (or absorbed) and thus losing its local effect?
3. Thirdly, since peritoneum is a very wide absorptive surface, there is a chance for the applied dose (if left for enough time), to be absorbed and side effects would be anticipated, and whether the analgesic effect was due to the local action of the drug or its systemic effect after being absorbed.
4. Applying drainage following surgery will rapidly evacuate any amount of fluid installed inside the peritoneal cavity if it is applied at the end of the procedure.
5. And lastly, we don't have facilities to assess the level of the drug in the blood following such application.

So, our plan was to use diluted solution of Xylocaine (within the permitted dose for each patient according to his/her weight) to avoid toxic effects. This diluted solution was applied in laparoscopic cholecystectomy procedures because it is optimal regarding the small incisions used (thus leaking of the drug is nearly impossible), and the site of tissue dissection (and initiation of pain) is limited to small areas. Also, the solution can be installed and kept inside for a fairly logical time. Drains are not always applied in these

procedures (as I don't put a drain in lap. cholecystectomy if it is not complicated by hemorrhage and the gall bladder was kept intact with no bile or pus leaking out of it). Also, the ports used are a very nice tool to install the solution right to the site of visceral peritoneal dissection area i.e. the liver bed of the gall bladder and the hepato-duodenal ligament area.

Intra-peritoneal instillation of local anesthetics is uncommon and few papers discussed this type of usage, its methodology, doses, effectiveness and side effects. And if such papers are found, they are devoid of details. One such study (by El-Sherbiny W. et al) concluded that, intraperitoneal instillation of lidocaine was effective in reducing postoperative pain after minor gynecological laparoscopic procedures.[12]

Another paper from Egypt (by Shahin AY. and Osman AM.) published in 2010 in the Clinical Journal of Pain; compared the effect of 200 mg of intraperitoneal lidocaine with normal saline as control in patients having Caesarean section after closing the parietal peritoneum, and concluded that lidocaine instillation decreased the incidence and scores of post cesarean pain.[13]

Our study concluded that intraperitoneal installation was effective in reducing immediate postoperative pain following LC, while the study conducted by Habibollah Hosseini et al in 2013 showed that intraperitoneal administration of lidocaine 200 mL after elective laparoscopic cholecystectomy has no considerable effect on the abdominal and scapular pain.[14]

A clinical trial published at "ClincalTrials.gov" involved a double-blind study to compare the effect of intravenous and intraperitoneal application of 100 mg of Xylocaine on postoperative pain control following abdominal hysterectomy.[15] These trials concluded that a reduction in postoperative analgesic requirements by 40% during (4-24) hours and the investigators found that LA injected intermittently intra-abdominally resulted in better pain relief compared to intra-abdominal infusions.

Yang SY et al, in 2014 performed randomized, double-blind, placebo-controlled trial evaluated intraperitoneal (IP) lidocaine administration, and concluded that it significantly reduced postoperative pain and opioid consumption in laparoscopic cholecystectomy (LC) patients, compared with control infusions.[16] Although he concluded that IP administration places additional burden on the surgeon, possibly because of the anticipated side effects.

Finally, Kahokehr A, et al, performed Meta analytic study in September 2010, and published in the Journal of hepatobiliary & pancreatic sciences concluded that; there is evidence in favor of intraperitoneal local anesthetic (IPLA) in LC.[17]

Conclusions:

• Local anesthetic agents can be used intra-peritoneally easily and with relative safety to achieve postoperative pain relief, as it was significantly proved by this study to achieve better pain control by themselves and significantly reduced the need for higher and more frequent doses of Injectable post-operative analgesia.

• There is no need for any added devices or tools to achieve the goal of pain control as all what we used was a syringe to achieve intra-peritoneal spraying of Xylocaine (as a diluted solution).

Recommendations:

• Further studies covering higher numbers of patients will confirm (or reject) our results, and until that time we believe that we can recommend using this technique as it is simple, economic and effective.

• Using local anesthetics subcutaneously at port-site incisions as the final step on concluding laparoscopic cholecystectomy, as we thought, will achieve considerable pain control in these patients, putting in mind the maximum dose safe to be given for each patient. And this may need further study to prove this concept.

• We do believe that preparing certain lab tools and investigations to estimate serum levels of those drugs after intra-peritoneal injection will help researchers and give them solid base upon which they can manipulate the dose used in their study and this can be solidified by continuous more invasive monitoring of those patients to assess their side effects (although this is not practical in straight forward surgical procedures as laparoscopic cholecystectomy).

• The use of different modes of applying post-operative analgesics and pain killers other than intravenous or intramuscular routes, like dermal patches, suppositories…etc may significantly add to the armamentarium of post-operative pain relief, especially when there is some difficulty or contraindication to the use of such routes.

REFERENCES

1. http://medical-dictionary.thefreedictionary.com/pain
2. Mehta V, Langford R and Haldar J, Anaesthesia and pain relief. Bailey & Love's Short Practice of Surgery 26th edition. CRC Press, Taylor & Francis Group, 2013; 17: 238-246
3. Sukhminder J S, Managing acute post-operative pain: Advances, challenges and constraints. Indian Journal of Anaesthesia 2017; 61(3): 189–191.
4. Bruce J, Quinlan J. Chronic Post Surgical Pain. Review in Pain. 2011; 5(3): 23–29.
5. Darzi A and Purkayastha S, Principles of laparoscopic and robotic surgery. Bailey & Love's Short Practice of Surgery 26th edition. CRC Press, Taylor & Francis Group, 2013; 7: 93-104
6. Toms L, McQuay H J, Derry S, Moore R A. Single dose paracetamol (acetaminophen) for postoperative pain in adults. Cochrane Database Syst Rev. 2008; (4): CD004602.
7. Maund E, et al. Paracetamol and selective and non-selective NSAID for the reduction in morphine-related side-effects after major surgery: a systemic review. Br J Anaesth. 2011:106(3):292-297.
8. Garimella V, Cellini C. Postoperative Pain Control. Clinics in Colon and Rectal Surgery. 2013; 26(3): 191-196.
9. Christopher D Press, MD; Chief Editor: Erik D Schraga, MD. Infiltrative Administration of Local Anesthetic Agents: Medscape; Drugs & Diseases; updated: 2015. http://emedicine.medscape.com/article/149178-overview
10. Zengin S.U, Saracoglu A, Eti Z, Umuroglu T and Gogus F.G, The effects of preoperative oral Pregabalin and perioperative intravenous Lidocaine infusion on postoperative morphine requirement in patients

undergoing laparotomy. Pain Research and Management 2015; 20(4): 179–182

11. Local Anaesthesia, toxicity and side effects, page 877. BNF 68 September 2014- March 2015. Published jointly by BMJ Group Tavistock Square, London, WC1H 9JP, UK
12. El-Sherbiny W. et al. Effect of intra-abdominal instillation of lidocaine during minor laparoscopic procedures. International Journal of Gynaecology & Obstetrics 2009 Sep; 106(3):213-5.
13. Shahim AY and Osman AM Intraperitoneal Lidocaine Instillation and Postcesarean Pain after Parietal Peritoneal Closure: A Randomized Double Blind Placebo-Controlled Trial. The Clinical Journal of Pain 2010; 26(2):121-7.
14. Habibollah Hosseini et al. Study of the Effect of Intra-abdominal Lidocaine on Postoperative Abdominal and Scapular Pain in Elective Laparoscopic Cholecystectomy Candidates. Journal of Biology and Today's World, Volume 2, 2013, Issue 5, Pages 95-101.
15. Anil Gupta, Örebro University, Sweden. Intravenous or Intra-abdominal Local Anesthetics for Postoperative Pain Management. (PoPuLAR), ClincalTrial.gov; A service of the U.S. National Institutes of Health, ClinicalTrials.gov Identifier: NCT01492179. First received: December 12, 2011. Last updated: May 25, 2014. Last verified: May 2014.
16. Yang SY, Kang H, Choi GJ, Shin HY, Beak CW, Jung YH, Choi YS. Efficacy of intraperitoneal and intravenous lidocaine on pain relief after laparoscopic cholecystectomy. The Journal of international medical research. 2014; 42(2):307-19.
17. Kahokehr A, Sammour T, Soop M, Hill AG. Intraperitoneal use of local anesthetic in laparoscopic cholecystectomy: systematic review and meta-analysis of randomized controlled trials. Journal of hepato-biliary-pancreatic sciences. 2010; 17(5):637-56.