DISCUSSION

Although there is growing concern with pain management all over the world, it is still under treated and a lot of patients continue to suffer during the post-operative period. Inadequately managed pain can lead to adverse physical and psychological patients' outcomes. The inability to escape from pain may create a sense of helplessness and even hopelessness, which may predispose the patient to chronic pain and depression. A great effort, in the field of anesthesia and surgery, was growing to enhance postoperative pain management and reducing pain consequences on patient's health.[98]

The present study was conducted on 30 patients scheduled for elective open cholecystectomy.

The aim of the present work was to compare intravenous PCA using morphine therapy with Continuous bupivacaine/fentanyl thoracic epidural analgesia for pain control after open cholecystectomy under general anesthesia. The demographic data (age, sex, and weight) was matched between the two groups.

Perioperative pain is the major factor influencing the patient's hemodynamic status.[99] Ledowski et al[100] Studied the correlation between pain and hemodynamic parameters including heart rate (HR), mean arterial pressure (MAP) or cardiac autonomic parameter: heart rate variability (HRV) and respiration rate (RR) in addition to catecholamine plasma levels. They used 4 pain categories of numeric rating scale (NRS) scores (no pain, mild, moderate and severe pain), and they reported that plasma levels for norepinephrine and MAP were significantly different in (severe vs. no pain and severe vs. mild pain).

In the present study there was no significant change in the mean heart rate and mean arterial blood pressure intraoperative or postoperative in comparison to the preoperative value in each of the studied groups.

Comparison of vital signs between both groups showed that heart rate and blood pressure were significantly lower in group I (epidural). Epidural anaesthesia acts by pre-ganglionic sympathetic blockade. Once the sympathetic nervous system is blocked, vascular tone is diminished and subsequent arterial vasodilation and venodilation with venous pooling will lead to a decrease in cardiac filling and mean arterial blood pressure. Reflex bradycardia may occur and further reduces cardiac output and thus arterial blood pressure.[101] IV Morphine acts by stimulation of μ- and/or κ-opioid receptors in the brain at cardiovascular centers, resulting in inhibition of sympathetic outflow, or activation of vasovagal reflexes. Opioid-induced histamine release may also play a role.[102]

In agreement with the present study ,Rigg et al[103] conducted a randomized trial on 915 patients undergoing major abdominal surgery who were randomly assigned into two groups, intraoperative epidural anaesthesia and postoperative epidural analgesia for 72 h or general anaesthesia based on a balanced technique with intraoperative and postoperative opioids. They found that epidural block was associated with significantly lower maximum pulse rate and systolic blood pressure.

Kopacz et al[104] conducted a prospective, randomized, double-blinded study of epidural anesthesia using 0.75% levobupivacaine (20 mL, 150 mg) compared with 0.75% racemic bupivacaine in 56 patients undergoing elective lower abdominal surgery. They found that similar decrease in systolic blood pressure, attributable to sympathetic block accompanying the epidural anesthesia had occurred.[104]

In the current study when visual analogue scale in the two studied groups was compared together, significant difference was detected. VAS was significantly lower in EPI group compared to IV PCA group. This result indicates obvious superior effect for epidural analgesia over IV PCA morphine analgesia technique in the doses used in this study. This is supported also by observing significant delay in requiring first dose of postoperative analgesia and significant elevation of patients' satisfaction score with post-operative analgesia in group EPI.

Many studies revealed results that coincide with the results of this study.

Lin M-C et al[105] conducted a retrospective study. A total of 335 patients who underwent colorectal surgery were included. Patients received IVPCA (n = 200) using morphine (1 mg/mL) plus droperidol (2.5−5 mg in 100 mL of morphine solution) without background infusion, EPCA with 0.0625% levobupivacaine/fentanyl (n = 45), or EPCA with 0.1% levobupivacaine/fentanyl (n = 90) found that epidural analgesia with low-concentration levobupivacaine plus fentanyl provided significantly lower postoperative pain scores during activity than those with IVPCA. The daily satisfaction scores revealed that most patients were satisfied with their postoperative pain management. [105]

Teng et al[106] conducted a retrospective study to determine whether epidural fentanyl-bupivacaine patient-controlled analgesia (PCA) was more efficacious and had fewer adverse effects than intravenous morphine PCA. They found that patients who received epidural fentanyl-bupivacaine had greater satisfaction with overall pain relief than those who received intravenous morphine PCA.

Also R.Wheatley et al [107]conducted a review of randomized controlled trials in which dynamic pain relief was the outcome measure. They stated that epidural analgesia with local anesthetic-opioid combinations had been shown to be significantly better than IV PCA morphine in providing dynamic pain relief after major abdominal surgeries. They stated that combining LA with opioid significantly reduced systemic opioid requirements.[107]

Similarly Hensel et al[108] conducted a prospective case controlled study on 60 women with benign uterine diseases undergoing vaginal hysterectomy (VH) or laparoscopically assisted vaginal hysterectomy (LAVH). Patients were divided for analysis into two groups (n=30 each) according to the postoperative analgesic strategy (EDA group versus IV PCA group).

The study showed that one of the advantages of epidural analgesia compared to intravenous patient-controlled analgesia was reduced pain intensity and lower need for analgesics.

Similarly Flisberg et al [109]conducted a retrospective study on 2696 patients undergoing major surgeries receiving either epidural or intravenous analgesia for

postoperative pain relief after major surgery. They found that numeric rating scale scoring was lower in the EPI Group compared to the IV group both at rest and during mobilization.[109]

Also Ferguson et al [110]conducted a randomized controlled clinical trial including women undergoing laparotomy for a gynecologic disorder. Patients were randomized to postoperative IV morphine PCA (control arm) or to postoperative morphine–bupivacaine PCEA. Patients treated with PCEA had significantly less pain at rest on postoperative day one compared to the IV PCA group. They had better postoperative recovery with an associated improved patient satisfaction compared to conventional IV PCA. [110]

Vural et al [111]conducted a randomized control study on sixty patients, ASA I-III, undergoing Total knee arthroplasty (TKA)who were randomized into three groups. First group (group GA) received IV PCA. The second group (group EA) received epidural anesthesia followed by an epidural PCA. The third group received continuous femoral block. The study stated that epidural analgesia provided better pain relief than IVPCA.[111]

Fischer et al [112] included 90 ASA physical status I—III patients, scheduled for unilateral total hip replacement in a prospective, randomized clinical study. The aim of this study was to evaluate pain and recovery after two treatment approaches: General anesthesia followed by PCA-morphine (GA/PCA) and epidural anesthesia followed by epidural analgesia. They found that wound pain at rest was significantly lower in the EDA group compared with the GA/PCA group. They also found less consumption of the rescue analgesia in EDA group. [112]

These results might be explained by different mechanisms of analgesia of epidural and IV morphine. Local analgesic drugs injected into the epidural space cause nerve blocks at three possible sites; the spinal nerves intra-durally (this is probably the essential site of blockade), the spinal cord and the spinal nerves in the paravertebral space.[47] IV morphine acts by activating opioid receptors within the CNS as well as throughout the peripheral tissues. Opioid receptors located on the presynaptic terminals of the nociceptive C-fibers and A delta fibers, when activated by an opioid agonist, will indirectly inhibit voltage-dependent calcium channels, decreasing cAMP levels and blocking the release of pain neurotransmitters such as glutamate, substance P and calcitonin gene-related peptide from the nociceptive fibers, resulting in analgesia. Opioids activate presynaptic receptors on GABA neurons, which inhibit the release of GABA in the ventral tegmental area. The inhibition of GABA allows dopaminergic neurons to fire more vigorously, and the extra dopamine in the nucleus accumbens is intensely pleasurable. [83]

In contrast to the results of the present study Yimyaem et al[113] compared CEA with IV PCA opioid for postoperative pain control following upper abdominal surgery in cholangiocarcinoma (CHCA) patients via prospective and randomized-controlled trial. Thirty patients were randomized allocated to two groups: Postoperative continuous epidural morphine (0.05 mg/ml) with 0.0625% bupivacaine in CEA group or postoperative IV PCA using morphine sulfate (1mg/ml) in PCA group. They found that the pain scores between both groups were not statistically different. This might be due to using different dose and drug combination in the epidural infusion as they used morhine instead of fentanyl, and a lower concentration of bupivacaine (0.0625%) instead of 0.125%.

In the current study, no local anesthetic toxicity or motor block had been developed in the group which received epidural block. This result could probably be due to the use of bupivacaine at a concentration of 0.125%.

There was no respiratory depression or arrhythmias. The noticed disadvantages in the present study were longer time needed before the start of surgery in the epidural group and In the PCA group it required an educated patient to use this technique.

In the current study postoperative nausea and vomiting were significantly reduced in group I in comparison with group II. This observation may prove the benefit of EPI block in reducing postoperative opioid consumption and its adverse effects. The opioid analgesics produce nausea and vomiting by an action on the medullary chemoreceptor trigger zone, and alter vestibular sensitivity. [89]

In agreement with the current result Hensel et al[108] found that epidural analgesia reduced occurrence of PONV compared to intravenous patient-controlled analgesia. [108]

Teng et al[106] also reported that the incidences of nausea and vomiting caused by I.V. morphine were much higher than that of patients receiving epidural fentanyl-bupivacaine.[106]

Similarly Fischer[112] stated that in the EDA group nausea and vomiting were reported less frequently than systemic opioids.

In contrast to the present study Flisberg et al[109] found that PONV occurred similarly in both groups, this might be due to using morphine in the epidural infusion, as all opioids given in equi-analgesic dose may cause nausea and vomiting by triggering the medullary chemo receptor zone.[109]

Also Lin M-C et al[105] found that the difference in the incidence of nausea/vomiting in the epidural and IV analgesia groups were not statistically significant. This might be because they did not use background infusion of morphine in the IV PCA but only bolus doses. [105]

Ferguson et al[110] found that there were no significant difference in the rates of nausea/vomiting in the epidural and I.V. analgesia groups. This was probably because they used morphine 100 mcg/ml with bupivacaine 0.05% in the epidural infusion.[110]

In the present study, postoperative sedation scale was not significantly different between both groups.

In agreement with this study Yimyaem et al[113] found no significant difference in sedation scale between continuous epidural group and morphine IV PCA group.

On the contrary Teng et al[106] reported that the incidence of sedation was higher in patients receiving IV morphine, this probably because they used higher doses for morphine: background infusion (0.5-2 mg/h) with PCA of 0.5- 3 mg while the dose used in the present study was 0.5 mg and 1 mg respectively.

As regards patient satisfaction, there was significant difference in patient satisfaction in favor of the epidural analgesia.

In agreement with our study Ferguson et al[110] found that patients in epidural group were significantly more satisfied with their pain therapy although they used different concentrations and doses.

On the contrary, Lin M-C et al[105] found that the satisfaction scores revealed that all patients were satisfied with their postoperative pain management with both techniques.[105]

SUMMARY

Introduction:

Postoperative pain is still under treated and a lot of patients continue to suffer after surgery. Unrelieved postoperative pain has several negative impacts on patient health as it increases patient's anxiety, heart rate, blood pressure and catecholamine and cortisone release. It also impairs respiratory function, gastrointestinal motility and carbohydrate and protein metabolisms. Furthermore, it may persist after wound healing and transform to chronic pain. A great effort is still needed to enhance postoperative pain management and reduce its consequences on patient's life.

Aim of the work:

- The aim of the present work was to compare intravenous PCA using morphine therapy with continuous bupivacaine-fentanyl epidural analgesia for pain control after open cholecystectomy under general anesthesia as regards: Analgesic efficacy, side effects and patient satisfaction.

Patient and methods:

The research was carried out on thirty adult ASA I, II patients admitted to the Medical Research Institute hospital, University of Alexandria and scheduled for open cholecystectomy under general anesthesia.

Patients were randomly divided according to analgesia technique using closed envelope method into two equal groups each of fifteen patients:

Group I: Continuous epidural analgesia group (using bupivacaine 0.125 % by a rate of 6 ml/h and fentanyl 100 mcg /24h)

Group II: PCA Intravenous morphine group (Morphine conc. 1 mg/ml, Bolus dose: 2 mg, Patient activated dose: 1 mg, Basal infusion: 0.5mg/h, Lockout time: 8 min and 4 hours maximum dose was 20 mg.)

Evaluation of the patients was carried out on the day before surgery and they were informed with the procedure of epidural block and PCA, they were trained to use the visual analogue scale (VAS) [15].

All patients received midazolam 0.02 mg/kg IV 2 minutes before anesthesia.

Thoracic epidural block in group I was conducted preoperatively through the T7-T8 interspace, with patients in the sitting position using paramedian approach. A 6 ml bolus of bupivacaine (0.25%) with 50 µg fentanyl was administered via the epidural catheter ten minutes prior to surgical incision.

General anesthesia was induced in both groups as following:

Induction of anesthesia was carried out with fentanyl 1.5-2 ug/kg IV, propofol 2 mg/kg IV injected slowly and cisatracurium 0.15 mg/kg IV to facilitate direct

laryngoscopy and endotracheal intubation. Tracheal tubes of ID 7.0 or 7.5 mm were used for female and male patients respectively. Ventilation was maintained at tidal volume 7 ml/kg and respiratory rate to adjust $EtCO_2$ at 35 mmHg using the ventilator "Fabius GS Drager". Anesthesia was maintained with 1.2% isoflurane in 100% O_2 and intermittent boluses of cisatracurium (0.03 mg/kg).

Intraoperative analgesia was conducted in both groups using ketorolac 30 mg IV when needed in fractionated doses.

At the end of surgery anesthesia was discontinued, residual neuromuscular block was antagonized by atropine 0.02 mg/kg and neostigmine 0.04 mg/kg , the trachea was extubated and patients were transferred to postoperative anesthesia care unit (PACU) for the next 24 hours.

Postoperative analgesia*:*

At the PACU Tramadol was administered intravenously throughout the first 24 hours as a rescue analgesic to all patients with VAS>3 as bolus of 30 mg, with maximum daily dose 1-1.5 mg/kg.

- Group (I): Continuous infusion of epidural bupivacaine 0.125 % by a rate of 6 ml/h and fentanyl 100 mcg /24h.
- Group (II): PCA using Fres. , Master PCA, Pilote CIS 3, France.

Morphine 1 mg/ml, Bolus dose: 2 mg, Patient activated dose: 1 mg,

Basal infusion: 0.5 mg/h, Lockout time: 8 min and 4 hours maximum dose was 20 mg.

Measurements:

1. Continuous ECG, heart rate, mean arterial blood pressure, oxygen saturation and end tidal CO2 monitoring were carried out. The measures were recorded every 10 minutes in the first 30 minutes intraoperatively then every 15 min. till the end of surgery and in the PACU, then every hour for the first 4 postoperative hours then every 4 hours for the rest of the first 24 postoperative hours.
2. Pain assessment using VAS pain score was assessed after 30 minutes in the recovery room and every hour for the first 4 hours postoperatively then every 4 hours for the rest of the first 24 postoperative hours.
3. The sedation scores: Was recorded at 30 min., and every 4 hours for the first 24 postoperative hours.

Results:

1. Demographic data were matched in both studied groups
2. Intraoperative and postoperative heart rate and mean arterial blood pressure did not show significant changes compared to pre-operative values within each group. When

the two studied groups were compared together there were significant higher readings at all time points in the postoperative period in group II.

3. The VAS when compared between two groups revealed that significant higher readings were found at all time of measurements in group II.
4. Time of requiring postoperative analgesia was longer in group I (epidural).
5. Postoperative nausea and vomiting were significantly less in group I than group II.
6. Patients were more satisfied with pain relief therapy in group I than in group II.

CONCLUSION

1. Better pain relief can be achieved in patients receiving epidural continuous infusion with fentanyl bupivacaine than with IV morphine PCA in the doses used in this study.
2. The incidence of nausea and vomiting were significantly higher with intravenously administered morphine.
3. Significantly higher readings for heart rate and mean arterial blood pressure were detected in the patients who received I.V. morphine PCA with the concentrations used in this study.
4. There was no significant difference in the sedation scores between both groups with the used concentrations.
5. Patients who received continuous epidural analgesia were more satisfied than those received IV morphine PCA with the concentrations used in this study.
6. No serious complications in the form of arrhythmias, hypotension, respiratory depression or local anesthetic toxicity were detected in both groups with the doses used in this study.