COMPARISON BETWEEN INTRAVENOUS PATIENT CONTROLLED ANALGESIA AND PATIENT CONTROLLED EPIDURAL ANALGESIA IN CIRRHOTIC PATIENTS AFTER HEPATIC RESECTION

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Abstract

Background: Postoperative pain is one of the most important problems that confront surgical patients. The aim of this work is to compare pain control using intravenous patient controlled analgesia (PCA) and patient controlled epidural analgesia (PCEA) in cirrhotic patients undergoing elective hepatic resection.

Methods: Thirty four adult patients ASAI and II scheduled for liver resection were randomly allocated into two groups-Group (P) with I.V (PCA) with fentanyl and Group (E) (PCEA) via epidural catheter using Bubivacaine 0.125% plus 2 microgram per ml fentanyl. Coagulation changes were followed and pain score was compared in both groups.

Results: 34 child A cirrhotic patients, undergoing liver resection were studied. The demographic data were comparable in both groups. There was a significant decrease in pain score in both groups during the follow up period when compared to their initial score. When comparing average pain score between both groups, the PCEA group had significantly lower values. The changes in prothrombin time (PT), INR, and hemoglobin (Hb), were significant all over the follow up period compared to their corresponding base line values. 2 cases needed FFP to normalize the INR for epidural removal. There was no significant difference regarding postoperative nausea and vomiting (PONV) in both groups, no clinical manifestation suggesting epidural hematoma, and no cases were recorded to have respiratory depression. There were no significant differences in patient satisfaction and ICU stay.

Conclusion: The two modalities of pain control seems to be nearly equivalent, but considering the risk of epidural catheter insertion and removal in cirrhotic patients who are further exposed to hepatectomy with subsequent additional coagulopathy, it may be wise to consider IVPCA technique as a policy for pain management in cirrhotic patient undergoing hepatectomy.

Keywords*: Post-operative pain, liver resection, Patient controlled intravenus analgesia, Patient controlled epidural analgesia.*

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Introduction

Postoperative pain is one of the most important complications that confront surgical patients. The aim of postoperative pain treatment is to provide subjective comfort in addition to inhibiting trauma-induced nocioceptive impulses in order to blunt autonomic and somatic reflex responses to pain and subsequently to enhance restoration of function by allowing the patient to breathe, cough and move more easily[1-3]. Liver resection is used with increasing frequency for treating primary neoplasms of the liver, which are frequently related to liver cirrhosis. It has been assumed that sufficient pain relief will improve the surgical outcome with reduced morbidity, need for hospitalization and convalescence[1,4]. Postoperative analgesia in cirrhotic patients remains a challenge, mainly because of the narrow dose range between the analgesic and side effects of drugs used,[1] in addition to alteration of the endogenous opioid system which have been reported in patients with liver disease[2,5]. Epidural analgesia is one of the best methods for the provision of postoperative pain relief in patients recovering from major upper abdominal operations. Being an invasive technique, epidural analgesia carries an inherent risk of several complications. Also the remaining liver's capacity to produce clotting factors is decreased for several days following resection which makes the epidural analgesia of concern[3,6]. Among the most commonly used pain-relieving techniques is patient-controlled intravenous analgesia (PCA) with opioids which may be an attractive alternative in this category of patients in whom epidural may carry possible risks. This study aims to compare epidural versus intravenous patient controlled analgesia in cirrhotic patients undergoing hepatic reactions.

Methods

This study was approved by of the local ethical committee and a written informed consent was obtained from each patient. Thirty-four patients ASA I and II, Child A cirrhotic patients, who were undergoing major liver resection, were classified into two groups:

Group (P) received intravenous patient controlled analgesia (PCA) with fentanyl while Group (E) received patient-controlled epidural analgesia (PCEA) with Bubivacaine 0.125% plus 2 microgram per ml fentanyl. All surgeries were performed under standardized general anesthesia.

Patients included in the study are of 25 years or older, not on anticoagulant therapy and undergoing major hepatic resection surgery for tumor removal. Exclusion criteria included failure of the surgery to proceed as planned, development of post operative complications limiting assessment, objection to an epidural catheter or inability to use PCA pump, postoperative need for mechanical ventilation, patients having contraindication to regional technique as infection and anatomical spinal abnormality and preexisting severe pulmonary or psychiatric diseases. In group (E) epidural catheters were placed at (T11-l2) interspaces while the patient is awake before anesthesia, in sitting position using loss of resistance to air technique and a median approach using an 18G touhy needle and a 20G epidural catheter after negative suction of blood and cerebrospinal fluid. A test dose of lidocaine 2% (total test dose of 3ml) was injected. All PCEA pumps were programmed for a basal infusion rate of 6 ml/hr and a patient-activated bolus of 3ml every 15 minutes. All PCEA were initiated within first 2 hours after induction at a basal rate only.

Patients in group (P) with IVPCA were well educated about the pump with detailed description of the plan of pain management. An I.V line was inserted and fentanyl 15 µg bolus was injected with 10 min lock out interval, 90 µg/hr maximum and no back ground infusion.

General anesthesia was induced on for all patients with fentanyl (1-2 µg/kg), propofol (1-2 ml/kg), and rocronium (0.6 ml/kg) and after intubation anesthesia was maintained with isoflurane in a 50% oxygen-air. IV muscle relaxant was administered as appropriate.

Intra operative monitoring included ECG, pulse oximetry, capnography, fraction of inspired O_2, body temperature, urine output, central venous pressure (C.V.P), and blood pressure. Tidal volume and ventillatory rate were adjusted to maintain end tidal CO2 between 35-40 mmHg. Intra operative hypothermia was prevented by forced air surface warming (Model 750-Bair Hugger Temperature Management Unit, Arizant Healthcare Inc, USA).

At the end of surgery, all patients were awakened and extubated in the operating room and transferred to the surgical intensive care unit. Data collected included age, sex, surgery performed, length of surgery, intra- operative blood products requirements, hospital and I.C.U. length of stay and day of epidural catheter removal. Epidural catheters were removed when platelet count was more than 80 x 10^9 and INR <1.4. All patients were contionously observed for clinical signs of spinal cord compression. Blood tests, including complete blood count, prothrombin time (PT), activated partial thromboplastin time, were determined preoperatively, immediately on admission to the recovery room and the third postoperative day (POD).

Base line heart rate and non-invassive blood pressure were continuously monitored.

Post operative pain was assessed by a10cm visual analogue scale (VAS) (0 to 10) 0 no pain, and 10 worst pain at rest and during movements (inspiration and cough). Side effects such as nausea, vomiting and were also noted.

The primary out-come was to compare both techniques regarding pain control. Secondary outcomes included evaluation of complications such as sedation, nausea, vomiting, urinary retention, post operative pulmonary complications, epidural neurological complications, return of bowel function and the length of intensive care and hospital stay.

Statistical procedure

Data was statistically analyzed using SPSS (statistical package for social science) program version 13 for windows and Epi info program version for all the analysis a p value <0.05 was considered statistically significant:

- Data are shown as mean, range or value and 95% confidence interval (95% CI) and frequency and percent.

- Fischer exact test for 2 × 2 tables when expected cell count of more than 25% of cases was less than 5 and p-value <0.05 was considered significant.

- Student t-test was done for normally distributed quantitative variables to measure mean and standard deviation and p-value <0.05 was considered significant.

- Mann-Whitney test was done for quantitative variables which are not normally distributed and p-value <0.05 was considered significant.

- Paired t test was done to detect mean and standard deviation of normally distributed pre and post values of the same variable of the same group of patients and p-value <0.05 was considered significant.

- Wilcoxon test was done to detect mean and standard deviation of not normally distributed pre and post values of the same variable of the same group of patients and p-value <0.05 was considered significant.

- Repeated measures ANOVA test was performed to differentiate changes in different follow up results of normally distributed studied variables and p-value <0.05 was considered significant.

- Friedman test was performed to differentiate changes in different follow up results of different studied variables and p-value <0.05 was considered significant.

All data are tested with kolmogorov-Smirnov Z test and most of them were found normally distributed and so presented with mean ± SD; and using parametric testes on doing association or correlation.

17 patients in arm 1 with intravenous PCA and 17 patients in arm 2 with PCEA were recruited based on the following assumptions: with the power of 80 %, $\alpha = 0.05$ and the ratio of cases to controls = 1:1. The required sample size was determined using PS (power and sample size calculation) software.

Results

Patients' characteristics and operative data are shown in Table 1. The mean arterial blood pressure and heart rat tended to be better controlled in IVPCA group however the comparison was statistically insignificant (P value >0.05) when comparing both groups. PCEA and IV PCA were found to be similar and effective in pain control at rest during the first three days postoperatively, Mean intensity of pain on a numerical analogue scale (0-10) at rest on day 1 was 5/10, day 2 was 3/10, and day 3 was 2/10, but on cough both groups suffered out breaks of pain on

Table 1
Patient characteristics (mean +/- SD)

	IVPCA (n = 17)	PCEA (n = 17)
Age (years)	50.1 +/- 9.7	50.8 +/- 11.5
Sex (M/F)	10/7	15/2
Weight (Kg)	81.7 +/- 15.7	78.8 +/- 14.8
Type of operation (n / %)		
Right hepatectomy (focal lesion)	6/35.3	10/58.8
Right hepatectomy + left radiofrequency (focal lesion)	3/17.6	0/0
Left hepatectomy (focal lesion)	6/35.3	4/23.5
Right hepatectomy (Cyst)	2/11.8	1/5.9
Left hepatectomy (hydatid)	0/0	1/5.9
Right hepatectomy (Haemangioma)	0/0	1/5.9

Data are presented as Mean +/- SD, Student t-test was used comparing age, weight, Intensive care unit; ICU stay between groups; p >0.05 considered not significant.

first day that needed intravenous meperidine. On day 2 and 3; patients of PCEA group suffered less pain during cough (Table 2). Postoperative sedation score showed significant difference between both groups during the first day followed by a significant mean

Table 2
Post-operative pain score on cough Mean +/- SD

Time	IVPCA (n = 17)	PCEA (n = 17)
2hrs POD1	3.18 0.81	3.82 (1.13)
8hrs POD1	6.35 (0.78)	6.59 (0.79)
12hrs POD1	6.76 (0.66)	7.00 (0.71)
24hrs POD1	6.61 (0.69)	6.29 (0.68)
POD2	6.59 (0.94)	5.65 (1.22)*
POD3	6.00 +/- 1.12	4.47 +/- 1.26**

Data are presented as Mean +/- SD, student t-test was used for postoperative pain score, *P <0.05 is considered significant and **P <0.01 is considered highly significant, POD; postoperative day.

Table 3
Sedation score of both groups on POD1

Studied variables	Groups	Mean +/ - SD
Sedation score	IVPCA	3.6 (0.51)
	PCEA	2.94 (1.14)*

Data are presented as Mean (SD), Mann Whitney test was used comparing sedation score, POD1; postoperative day 1,* P <0.05 was considered significant.

decrease in score by 2nd and 3rd days post operatively in the IVPCA group (Table 3). Four out of 17 cases in the epidural group complained of bilateral lower limb numbness during the first postoperative day in the PCEA group, due to the established epidural block, but only one patient developed moderate motor block and in this sole case the epidural infusion was stopped with close follow up of the motor status. Regarding the coagulation changes, there was significant increase in INR and prothrombin time, with peak changes at the 3rd POD with no significant changes in platelets count when compared to corresponding base line values in both groups. The mean time for the epidural catheter stay was 5.88 ± 1.27 days before removal; two cases demanded the infusion of fresh frozen plasma units before removal in order to achieve acceptable level of the prolonged prothrombin time and elevated INR. Patients in the PCEA group were less sedated and had fewer incidences of side effects as nausea/vomiting.

Table 4
Drug consumption differences all over the follow up period in intravenous fentanyl patient controlled analgesia group (IVPCA)

Studied variable	D1	D2	D3
Fentanyl (µg)	1255.6 (287.2)	1318.3 (413.3)*	1163.1 (398.5)**
Bolus number	121.3 (26.4)	136.3 (31.7)*	112.6 (23.2)*
Demand number	83.7 (19.1)	85.2 (28.1)	77.9 (25.9)

Paired t-test was used in fentanyl, bolus and demand to study differences, * indicates statistically significant difference (P <0.05) and ** indicates highly significant difference (P <0.01).

Table 5
Drug consumption differences all over the follow up period in patient controlled epidural analgesia (PCEA)

Studied variable	D1	D2	D3
Marcaine (ml)	352.6 (101.5)	411.6 (183.7)**	362.4 (92.1)
Fentanyl (µg)	575.5 (133.1)	628.6 (119.2)**	577.4 (172.8)
Bolus	107.6 (21.2)	99.5 (21.9)	87.4 (27.7)**
Demand #	60.9 (17.8)	55.5 (24.3)	52.7 (18.6)

Data are presented as Mean (SD), repeated measures ANOVA test was used for Marcaine, Fentanyl and Bolus, P <0.01 was considered highly significant. # Wilcoxon test was used for Demand. Paired t-test was used in Bubivacaine, fentanyl and bolus to study differences with day 1, P <0.05 was considered significant.

Table 6
Satisfaction score analysis differences between patients of both groups

Satisfaction score	IVPCA	PCEA
excellent	2 (11.7)	4 (23.5)
good	7 (41.2)	8 (47.1)
fair	8 (47.1)	5 (29.4)
poor	0 (0.0)	0 (0.0)

Data are presented as number (%), Chi square test; X^2 was used, P-value >0.05 was considered not significant.

There was an increase in the amount of fentanyl used by patients in the IVPCA group by the second day post operatively followed by a decrease in the third day, matching with the PCA boluses and demands trends. The demand (number of button pushes by the patient) increase in the second day post operatively followed by a decrease in the third day, as shown in Table 4. Table 5 data presented the amount of Bubivacaine and fentanyl used by the patients in the PCEA group throughout the follow up period. No significant difference as regard the satisfaction assessment of both groups was reported (Table 6).

Discussion

The main finding of our study was that both PCEA and IV PCA can provide complete control of pain at rest; however, upon movement and coughing PCEA was superior to IV PCEA. Finally, both techniques were equivalent as to patients' satisfactions.

In this study, the pain control was effective and similar during the first postoperative day between PCEA and IV PCA groups, but during movement and on cough both were not efficient enough to control the pain, which mandates use extra analgesic supplementation in both techniques. Both groups required the use of analgesia by the second day more than the first day that may be due to the decline of the residual anesthetic effect and/or the increased frequency of movement and physiotherapy during the second day. By the third day the need for analgesia decreased in both groups and this could be attributed to the normal sequel of the decrease in the stress response.

The PCEA group showed a gradual decrease in VAS score on movement during the follow up period on the 2nd and 3rd post operative days, with less bolus and less demands, but still intravenous opioids were needed to cover for the pain outbreaks for several patients.

No sole technique was able to provide a full pain relief. A multimodal approach in the form of intravenous pethedine and paracetamol was implemented to control pain in 6 out of 17 cases in PCEA group and in 8 out of 17 cases in IVPCA group. The need for supplementary intravenous opioid with PCEA is supported by Revie EJ et al[7] who found that 20% of patients undergoing open liver resection with epidural analgesia for postoperative pain requested additional intravenous opioids for pain control.

The use of continuous background infusion in the PCEA group in this study to reduce the pain on day 2 and 3 was reported also by Komatsu et al and Vercauteree et al who found that the use of a background infusion of a mixture of bupivacaine and fentanyl reduced the incidence of postoperative pain significantly in particular the pain associated with cough and movement after upper abdominal surgery[8].The option of using a back ground infusion of fentanyl in the IVPCA group was omitted for fear of

side effects in particular respiratory depression in this group of cirrhotic patients undergoing liver surgery and expecting a possible temporary postoperative liver dysfunction as reported previously[10].

Previous studies reported effective pain control when a multimodal approach for post-operative pain control was adopted[11,12].

Katz et al[13] added intrathecal morphine and fentanyl with bupivicaine for post-operative pain control and achieved better results with reduction in IV morphine consumption postoperatively. But, as reported by several previous studies, pain management of post liver resection is sometimes difficult to control and out breaks of pain can be reported in particular with early ambulation and physiotherapy which will need additional IV opioids, but the rate of consumption is significantly reduced if a planned multimodal analgesic technique is adopted[14]. The relatively less pain score in PCEA group compared with IVPCA group may also be due to the combined use of local anesthetic with opioid. Brodner et al[15] reported that the production of the proinflammatory cytokines IL-1ß and IL-6 was more increased in the intravenous PCA group compared with the PCEA group, especially at 24 hours after surgery. This may be attributed to the local anesthetics effect which can reduce the postoperative inflammatory response in two ways: first blocking neural transmission at the site of tissue injury and thus may attenuate the neurogenic inflammation, second, having systemic anti-inflammatory properties of their own. This has been proved through reducing the postoperative inflammatory index in patients with continuous epidural analgesia, consisting of local anesthetics and opiates[16].

The use of an epidural catheter in patients undergoing resection remains controversial because of the postoperative changes in the coagulation profiles of these patients suffering from hepatic cirrhosis which are further aggravated by the effect of liver resection.

The prolongation of the prothrombin time and increase in INR were reported in this study, INR increased gradually till the third day and began to normalize by the fifth or the sixth day, which delayed the epidural removal till the 5th and even the 7th day postoperatively in some cases. Two cases needed fresh frozen plasma to help reduce INR to an acceptable level allowing epidural catheter removal. None of the cases developed any clinical manifestation suspecting epidural hematoma or showed signs of neurological deficits.

These results were similar and in agreement with the study by Schumann et al[17] which also showed a transient postoperative coagulopathy after liver resection among their healthy liver patients.

Matot I et al[18] also showed the same findings with a conclusion that the extent of liver resection may affect the magnitude and duration of postoperative coagulation disturbances and, therefore, they concluded that the proper timing of epidural catheter removal need also to be revised with the coagulation laboratory results day by day before removal.

Tran SB et al[19] also documented that in healthy livers subjected to minor liver resection the PT returns to a normal value in one to two days, while in major resection it might need up to 5 days to normalize. All the previous factors may account for a delay of removal of the epidural catheter until day 7 and for the need for fresh frozen plasma transfusion in some cases as reported by the current study and the study of Tran SB.

Most of cases in this study started oral sips of water and juice by the 1st day post operatively. The incidence of nausea and vomiting in this study was (3/17) in the IVPCA group and (1/17) in the PCEA group, few cases needed medical intervention for symptomatic relief, this may be attributed to the choice of using fentanyl in both groups which is known to have a lower incidence of post operative nausea and vomiting than morphine. This was in agreement with Koo PJ, et al[20] and Rob et al[21]. Studies which found that IV PCA fentanyl have a significant lower rate of common opioid side effects (nausea/vomiting) when compared to other methods of analgesia.

In contrast, Bozkurt P et al[22] has reported a higher incidence of nausea and vomiting in children after epidural opioids of approximately 30%, and 87% with IV PCA.. This higher incidence may be due to the different patient populations. This age category variation in incidence was supported by Leman et al[23] who reported that children have an average vomiting incidence more than 40% almost twice as frequent as the rate in adults and the incidence tapers by reaching puberty.

Epidural analgesia with local anesthetics offers potential means to attenuate several mechanisms of postoperative ileus. Sympathetic block from epidural local anesthetics may help attenuate postoperative reflex inhibition of GI motility. Suppression of the surgical stress response and systemic absorption of epidural local anesthetics may reduce the inflammatory response and attenuate the postoperative ileus. Both postoperative pain and use of systemic opioids increase the risk of ileus. In Consistent with these mechanisms, experimental data indicates that epidural analgesia with local anesthetics shortens time of intestinal paralysis, increases the strength of colonic contractions, and does not impair anastomotic healing or increase risk of anastmotic leakage[24,25].

The level of the epidural catheter was intended to be thoracic to keep its tip in the target dermatome for perfect pain control especially with using fentanyl, sparing of lumbosacral segments to minimize urinary retention and limit motor effects as reported by Basse et al[26].

In this study, urinary retention as an expected complication could not be assessed due to the presence of a urinary catheter.

In agreement with Veering BT et al study[27], patients in the epidural group showed better control of systolic blood pressure and heart rate than in the IVPCA group, which may be due to a better pain control.

Respiratory depression in patients undergoing major upper abdominal surgery is of great concern due to impaired of diaphragmatic, intercostal, and abdominal muscle functions and in case of inadequate analgesia the tidal volume will be also further reduced, hence an adequate pain control is of a major priority. In this study we did not record any manifestations of respiratory depression as assessed by continuous monitoring of respiratory rate, oxygen saturation, and degree of consciousness in both groups and no naloxone was required.

In the study by Wu CL[28] epidural modality conferred superior analgesia compared with that from systemic opioids including IVPCA, which may improve voluntary respiratory function. Segmental block from thoracic epidural anesthesia may result in increased tidal volume and vital capacity related in part to improved pain control and also to interruption of the reflex inhibition of phrenic nerve activity, thus improving diaphragmatic activity. However, effects from the typical dilute solutions of local anesthetics and opioids used for thoracic epidural analgesia (TEA) are unclear. It has also been demonstrated that TEA with bupivacaine 0.25% does not impair ventilatory mechanics, respiratory muscle strength, or airway flow even in patients with severe chronic obstructive pulmonary disease[29].

Various degrees of sedation in the post-operative period in cirrhotic patients have to be expected due to use of opioids. Our patients were closely monitored with sedation score. There was a significant degree of sedation all over the study period in both groups with highest score during the 1st day which could be attributed to the residual effect of the general anaesthetic agents and intra operative opioids used, the following declining in scores was associated with a decrease in severity of pain during the following postoperative days and subsequent decrease in drug consumption. Trends of sedation were higher in IVPCA group as expected with the use of IV opioids, with no recorded deep sedation as indicated by absence of any manifestation of respiratory depression. Butkovic, et al[30] found that the type of analgesia either IVPCA or PCEA has no effect on the Ramsay sedation score, implying that both analgesic regimes produced the same level of sedation, however, a meta-analysis of several different studies found less respiratory depression with administration of continuous epidural opioids compared with parentral opioids[31].

In order to encourage early mobilization and achieve patient satisfaction and pain relief, a local anesthetic concentration of 0.125% was used in PCEA group to reduce possible motor weakness, however 4 out of 17 cases complained of bilateral lower limb numbness on the first postoperative day. Only one patient developed moderate motor block and the epidural infusion was stopped with close follow up of the motor status. Christopher[32] reported better pain relief at the expense of higher incidence of motor block with the use of continuous epidural analgesia compared with PCEA. John et al[33] correlated the density and duration of block with the concentration of the local anesthetic as both the 0.125% and 0.25%

groups had significantly denser maximum motor blockade than the 0.0625% group, indicating a degree of dose-dependent response. In this study the effect of various concentrations of bupivacaine was not evaluated, as the study was restricted to one protocol; however pain control and degree of motor and sensory block were acceptable.

In a study by Pitimana et al[34], the satisfaction analysis indicated excellent score in 11%patients of IVPCA and 23% of PCEA group undergoing total knee replacement, this difference may be because of the ability of epidural analgesia to promote patient well being in the form of better pain control particularly on movement, faster recovery of bowel function and earlier patient mobility, but this did not alter the ICU stay when compared to the PCA group[35].

In another study by Butkovic et al[30] IVPCA with fentanyl was as effective as epidural block with bupivacaine and fentanyl in controlling the postoperative pain of children after thoracoscopic surgery for pectus excavatum repair.

One study found no significant differences in patients' satisfaction after living donor liver resection in those receiving either IVPCA opioids or PCEA, also the authors warned from the post operative coagulopathy that may affect the removal of the catheter[36].

In our study, there was no evident clinical significance between the two techniques regarding the efficacy in pain control during rest, but not on movement. There were no differences as well in the severity of any complications including sedation, respiratory and GIT side effects apart from sedation during the first day post operatively. In view of the choice of a safer method to control pain in cirrhotic patients it may be wise to recommend IVPCA in order to avoid the remote incidence of epidural hematoma which may be more prevalent with post liver resection associated coagulopathy particularly when it is not possible to assess the neurological condition of the patients during the long hours of the surgery until recovery.

One of the limitations of the current study is the inability to alter the settings of the PCA pumps for both groups during the course of the study period and the inability to modulate the Bupivacaine concentration. Also, the use of background infusion in cirrhotic patients and their safety need to be studied in further planed research work. Conclusion: IVPCA with fentanyl was used with no reported side effects in Child A cirrhotic patients. Also, PCEA was delivered safely with no clinical evidence of epidural hematoma, but in view of the associated coagulation changes in conventional tests, it seems wiser to recommend the IVPCA opioids for cirrhotic patients. A multimodal approach is recommended as no sole technique was enough to control out breaks of pain for such a surgical procedure. Each patient should be informed and consented before surgery about pros and cons of the two techniques and risks weighed against benefits.

References

1. Crews JC: Multimodal pain management strategies for office-based and ambulatory procedures. *JAMA*; 2002, 288:629-632.
2. Tanaka S, Norio Noguchi F, Ochiai T, et al: Outcomes and recurrence of initially resectable hepatocellular carcinoma. Meeting Milan Criteria: Rationale for Partial Hepatectomy as First Strategy. *Journal of the American College of Surgeons;* January 2009, vol. 204, 1-6.
3. Schecter WP, Bongard FS, Gainor BJ, Weltz DL, Horn JK: Pain control in outpatient surgery. *JAM CollSurg*; 2002, 195:95-104.
4. Cross, SA: Mayo Clin Pathophysiology of Pain. This article on pain mechanisms is still by far the best summary we have. *Anesth Analg*; 2003, 96:548-54.
5. Maddali MM, Mathew J, Fahr J, et al: A prospective study of postoperative nausea and vomiting in a tertiary care hospital in Oman. *Middle East J Anaesthesiol*; 2003, 17:131-41.
6. Breen TW, et al: Epidural anesthesia for labor in anambulatory patient. *Anesth Analg;* 1993, 77:919-24.
7. Revie EJ, Massie LJ, Mcnally SJ, et al: effectiveness of analgesia after liver resection. *Reg Anaesth Pain Med*; 2010, 35:51-60.
8. Komatsu H, Matsumoto S, Mistuhata H, et al: Comparison of patient controlled epidural analgesiawith and without Background Infusion After gasterectomy. *Br J, Anaesth*; 2001, 87:907-10.
9. Vercautereen MI, Coppejans HC, Broecke PW, et al: Epidural sufentanil for postoperative patient-controlled analgesia (PCA) with or without background infusion: a double-blind comparison. *Anesth Analg*; 1995, 80:76-80.
10. Flisberg P, Rudin A, Linner R, Lundberg CJF: Pain relief and safety after major surgery.A prospective study of epidural and intravenous analgesia in 2696 patients. *Acta Anaesthesiol Scand*; 2003, 47:457-65.
11. Ozalp G, Guner F, Kuru N, et al: Postoperative patient-controlled epidural analgesia with opioid-bupivacaine mixtures. *Can J Anaesth*; 2010, 45:938-942.
12. Ming H, Chen K, Kwang M, et al: The Addition of Morphine Prolongs Fentanyl-Bupivacaine Spinal Analgesia for the Relief of Labor Pain. Departments of Anesthesiology and Gynecology and Obstetrics, National Taiwan University Hospital, Taiwan. *Anesth Analg*; 2001, 92:665-8.
13. Katz J, Cohen L, Schmid R, Chan VW, Wowk A: Postoperative Morphine Use and Hyperalgesia Are Reduced by Preoperative but Not Intraoperative Epidural Analgesia: Implications for Preemptive Analgesia and the Prevention of Central Sensitization. *Anesthesiology*; June 2003, 98:1449-1460.
14. Bajwa SJ, Bajwa SK, Kaur J, et al: Admixture of clonidine and fentanyl to ropivacaine in epidural anesthesia for lower abdominal surgery, Department of Anaesthesiology and Intensive Care, Gian Sagar Medical College and Hospital, India. *Anesth Essays Res*; 2010, 4:9-14.
15. Brodner G, Van Aken H, Hertle L, et al: Multimodal perioperative management-combining thoracic epidural analgesia, forced mobilization, and oral nutrition-reduces hormonal and metabolic stress and improves convalescence after major urologic surgery. *Anesth Analg*; 2001, 92:1594-60.
16. Page GG, Blakely WP, Ben-Eliyahu S: Evidence that postoperative pain is a mediator of the tumor-promoting effects of surgery in rats. *Pain*; 2001, 90:191-9.
17. Schumann R, Zabala L, Angelis M, et al: Altered hematologic profiles following donor right hepatectomy and implications for postoperative analgesic management. *Liver Transpl*; 2004, 10:363-87.
18. Matot I, Scheinin O, Eid A, Jurim O: Epidural anesthesia and analgesia in liver resection. *Anesth Analg*; 2002, 95:1179-81.
19. Tran SB, Wellmyer E, Gadassaly SR, Steadman RH: Postoperative coagulation status following liver donor-living transplantation. *Anaesthesiology*; 2001, 95:A186.
20. Koo PJ: Postoperative pain management with a patient-controlled transdermal delivery system for fentanyl. *Am J. Health Syst Pharm*; 2005, 62:1171-1176.
21. Rob W, Hutchison D, Chon E, et al: Comparison of a Fentanyl, Morphine, and Hydromorphone Patient-Controlled Intravenous Delivery for Acute Postoperative Analgesia. *Br J Anaesth*; 2006, 41:659-663.
22. Bozkurt P: The analgesic efficacy and neuroendocrine response inpaediatric patients treated with two analgesic techniques: using morphine-epidural and patient-controlled analgesia. *Paediatric Anaesthesia*; 2002, 12:248-54.
23. Lerman J: Surgical and patient factors involved in postoperative nausea and vomiting. *Br J Anaesth*; 1992, 69:S24-32.
24. Groeben H, Schafer B, Pavlakovic G, et al: Lung function under high thoracic segmental epidural anesthesia with ropivacaine or bupivacaine in patients with severe obstructive pulmonary disease undergoing breast surgery. *Anesthesiology*; 2002, 96:536-41.
25. Fotiadis RJ, Badvie S, Weston MD, Allen-Mersh TG: Epidural analgesia in gastrointestinal surgery. *Br J Surg*; 2004, 91:828-41.
26. Bassel, Linda M, Werner, Mads M, Kehlet: Is Urinary Drainage Necessary During Continuous Epidural Analgesia After Colonic Resection? *Regional Anesthesia & Pain Medicine*; 2000, 25-5:498-501.
27. Veering BT, Cousins MJ: Cardiovascular and pulmonary effects of epidural anaesthesia. *Anaesth Intens Care*; 2000, 28:620-35.
28. Wu CL, Cohen SR, Richman JM, et al: Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. *Anesthesiology*; 2005, 103:1079-88.
29. Eva M, Gruber, Edda M, Tschernko, Meinhard Kritzinger, Elena Deviatko, Wilfried Wisser, David Zurakowski, Wolfram Haider: The Effects of Thoracic Epidural Analgesia with Bupivacaine on Ventilatory Mechanics in Patients with Severe Chronic Obstructive Pulmonary Disease. *Anesth Analg*; 2001, 92:1015-9.
30. Butkovic1 D, Kralik1s, Matolic1 M: Postoperative analgesia with intravenous fentanyl PCA versus epidural block after thoracoscopic pectusexcavatum repair in children. *Journal of Anaesthesia*; 2007, 98 (5):677-81.
31. Carvalho B, Wang P, Cohen SE: A survey of labor patient controlled epidural anesthesia practice in California hospitals. *Int J Obstet Anesth*; 2006, 15:217-22.
32. Christopher L, Cohen M: Efficacy of Postoperative Patient-controlled and Continuous Infusion Epidural Analgesia versus Intravenous Patient-controlled Analgesia with Opioids: A Meta-analysis. *Anesthesiology*; November 2005, 103:1079-1088.
33. John A, Murdoch C, Ursula K, et al: The Efficacy and Safety of Three Concentrations of Levobupivacaine Administered as a Continuous Epidural Infusion in Patients Undergoing Orthopedic Surgery. *Anesth Analg*; 2002, 94:438-444.

34. Pitimana-Aree S, Visalyaputra S, Komoltri C, et al: An economic evaluation of bupivacaine plus fentanyl versus ropivacine alone for patient-controlled epidural analgesia after total knee replacement procedure: A double blinded randomized syudy. *Regional anesthesia and pain management;* 2005, 30:44-451.
35. Orhan-Sungur M, Kranke P, Sessler D, Apfel C: Does supplemental oxygen reduce postoperative nausea and vomiting? A meta-analysis of randomized controlled trials. *Anesth Analg*; 2008, 106:1733-8.
36. Jean-Denis R, Luc Massicotte A: Comparison of Intrathecal Morphine/Fentanyl and Patient-Controlled Analgesia with Patient-Controlled Analgesia Alone for Analgesia After Liver Resection. *Anes Analg*; 2006, 103:990-994.