—Regular Articles—

Postoperative Effects of Opioid Analgesics Administered via Continuous Perfusion and Patient Controlled Analgesia after Open Heart Surgery

Deniz Seher OZTEKİN,*[,a] İlhan ÖZTEKİN,[b] Halim İŞSEVER,[c] Onur GÖKSEL,[b] Bayer ÇINAR,[b] and Sevim CANİK[b]

[a]*İstanbul University, Florence Nightingale School of Nursing, Abide-i Hürriyet cad. 34360 Şişli, İstanbul, Turkey,* [b]*Siyami Ersek Thoracic and Cardiovascular Surgery Center, Haydarpaşa, İstanbul, Turkey, and* [c]*İstanbul University, İstanbul Medical Faculty, Department of Public Health, Şehremini, İstanbul, Turkey*

(Received March 10, 2006; Accepted April 13, 2006)

Critical care nurses and physicians are familiar with the principles of patient controlled analgesia and the opioid analgesics' regimens and observations necessary for pain control in the postoperative cardiac surgical patients. The objective of the study was to compare the effects of morphine, fentanyl, meperidine, remifentanil and tramadol which were administered by patient controlled analgesia and continuous intravenous infusion combination on the various parameters. This study was designed as prospective randomised trial. Fifty patients undergone open heart surgery with sternotomy were entered equally into five randomized groups. Visual analog scale was used by researcher nurse to assess the patient' pain status. Respiratory rate, heart rate and blood gases (pO_2, pCO_2, SaO_2), radial arterial blood pressures were measured in the first 24 hrs postoperatively. Bolus requirements were determined by physicians and side effects of the analgesics were documented. Fentanyl group showed statistically higher levels of mean pO_2 ($p=0.002$). Meperidine had the lowest number of bolus doses ($p=0.001$). There were no significant differences between the groups for pain management except higher visual analog scales on tramadol. Headache, stomachache and, palpitations were observed in our patients. Remifentanil, meperidine, fentanyl and morphine showed similar effect with each other for pain relief except tramadol.

Key words——morphine; fentanyl; meperidine; remifentanil; tramadol; opioid

LITERATURE REVIEW

The expected outcome for a postoperative cardiac surgical patient is complete relief of pain such that the patient indicates that he or she is comfortable. Critically ill patient in early postoperative period of open heart surgery is not always able to communicate expressions of pain.

A major challenge to the critical care nurse (CCN) is assessment of the presence and amount of pain as well as the effectiveness of treatment for the pain. Since the subjective expression of pain by the cardiac surgical patient is not always possible, the nurse must anticipate pain, interpret pain signals, and rely on less reliable objective indicators of pain.[1—8)]

Pain relief must be achieved without any adverse and side effects of treatment. It is important for the CCN to establish a regular routine of pain medication administration while the cardiac surgical patient is still in critical care unit (CCU). This will encourage the patient to be aware of his or her nursing care and to be an active participant in activities to help in convalescence. With patient controlled analgesia (PCA), cardiac surgical patients are able to self-administer their analgesic medications. The patient makes a judgement about pain and sedation levels and can choose a balance between them. If patient feel ''in control'' of his/her pain management, anxiety and distress associated with pain can be easily minimized.[1—7)]

Although some researchers have established the effectiveness of PCA,[9)] little researches have been conducted of PCA use in critically ill patient.

Purpose We aimed to investigate and compare the effects of morphine, fentanyl, meperidine, remifentanil and tramadol administered to patients with continuous perfusion and PCA methods for analgesic, hemodynamic, respiratory and side effects to help convalescence in early postoperative period.

Hypothesis

- Remifentanil, meperidine, fentanyl and morphine had maximal pain relief used doses in the study.

Present address: Tütüncü Mehmet Efendi Cad. İffet AP. 40/3 Göztepe 34726 Kadiköy İstanbul Turkey
*e-mail: dnzoztekin@hotmail.com

- Fentanyl effects higher pO_2 levels than other opioid analgesics' effects.

Design This study was designed as prospective randomised trial.

Sample Fifty patients undergoing open heart surgery with standard midline sternotomy were included in our study.

The patients were eligible for inclusion in the study if:

- they were co-operated and agreed about research goals when treatment plan is presented.
- they were ready for extubation procedure.
- their movements and facial expressions, blood pressures, heart and respiratory rates were thought to be the possible causes of pain.
- their visual analog scale (VAS) values were higher than 5 or 6.

Two patients in fentanyl, 3 patients in remifentanil, 1 patient in morphine, 2 patients in meperidine group were excluded from the study. None of the patients were excluded from tramadol group.

The patients were excluded in the study if:

- their extubation time was more over than 8 hrs in early postoperative period,
- their respiratory functions had lower than normal rates,
- they supported by positive inotropic agents such as dopamine, dobutamine, adrenaline, etc...,
- their haemorrhagic drainages were more than 300 cc. during the first hr in of early postoperative period (4 hrs),
- their heart rates were higher than 130 per minute,
- their blood gases (pCO_2 50 mmHg↑, pO_2 80 mmHg↓) were found hypoxemic and SaO_2 values were lower than 90.

METHODS

Patient education on effective postoperative pain relief was carried out in the preoperative period. It took place in the pre-anaesthetic screening clinic. Pamphlets on intravenous PCA were given to reinforce the information provided by the anaesthesiologist and researcher nurse. Researcher nurse in the pre-screening clinic demonstrated the functions of intravenous PCA and explain the concept of PCA. A short videos postoperative analgesia are viewed by patients while they are waiting to be interviewed. In the postoperative period patient education is reinforced by researcher nurse and other members of research team. The patients are counselled on the importance of communicating about inadequate pain relief and the usage of PCAs.

Patients who had extubated in 4—8 hrs postoperatively were selected randomly. Patients were divided equally into five different groups each having a different kind of postoperative analgesia namely; morphine, fentanyl, meperidine, remifentanil and tramadol (10 patients in each group; $n=10$). Patients in five groups were treated with the same institutional narcotic anaesthesia protocol, which included fentanyl (35 μg/kg), propofol (7 mg/kg) and pancuronium (0.1 mg/kg).

In each group, particular analgesic agent was given intravenously in a loading dose followed by a constant maintenance dose. PCA pumps allowed for additional boluses of the drugs as well as keen scrutiny of the perfusion doses and durations. Table 1 depicts loading and maintenance doses of the analgesics used as well as the locking times of the PCA pumps.

At the end of the first 24 hrs in postoperative period, the efficacy of each analgesic treatment (pain status) after coughing determined with VAS (characterized pain status 0—10, 10 being the maximum possible-defined as the worst pain ever experienced) for pain intensity. At the end of the first 24 hrs postoperatively, minute ventilation rate, heart rate (heart beat /minute), arterial blood gases (pO_2, pCO_2, SaO_2), systolic blood pressure (SBP-radial) and side effects of the analgesics were observed by research team and noted by researcher nurse. Additionally, the number of bolus doses of the analgesics at the end of 24 hrs were noted.

McGill Melzack Pain Question Form (MPQF) was used as a data collecting tool for pain assessment in the study.[10] The validity and reliability of this form was tested for using in Turkey.[11]

The validity of factor of the form was analyzed by using the analysis of factor. It was seen that all items were collected on three factors in the rotation of the factor matrix. The accounted reliability of co-efficiency with Cronbach alpha was found as 0.98. The item reliability coefficients are; 0.52—0.72 second part (pain assessment), 0.50—0.70 third part (pain relation with time), 0.50—0.58 fourth part (pain severity) of the form.[11]

Analysis of Data Statistical analysis were done using Kruskall-Wallis test for variables with scores VAS and One-way ANOVA for continuous variables

Table 1. Loaded, Maintenance and Bolus Doses of Analgesics, Locking Times of the PCA Pumps

Demographics / Analgesics	Morphine	Fentanyl	Meperidine	Remifentanil	Tramadol
Sex (M/F)	8/2	6/4	8/2	7/3	7/3
Age	58.8±7.96	55.1±6.98	49±15.18	57.12±11.99	55.33±12.75
Weight	68.6±9.94	72.5±10.98	70.2±0.7	74.25±11.08	70.77±12.60
Bolus number	12.9±5.21	12.9±2.99	2.3±1.84*	10.75±6.23	12.6±4.99
Loaded dose	1 mg	100 mcg	100 mg	80 mcg	50 mg
IV infusion dose (kg/hr)	0.1 mg	0.3 mcg	0.7 mg	0.6 mcg	0.07 mg
Locking time	20′	15′	10′	5′	20′
Bolus dose (kg/hr)	1 mg	25 mcg	10 mg	10 mcg	10 mg
Total dose	24±5.12 mg	922.5±71.15 μg	863.21±24.1 mg	1157.5±178.21 μg	278.8±34.43 mg

* $p=0.001$

Table 2. Effects of the Analgesic Drugs

Analgesics	Morphine	Fentanyl	Meperidine	Remifentanil	Tramadol
Parameters (Mean)	Mean; SD	Mean; SD	Mean; SD	Mean; SD	Mean; SD
SBP	137±12.51	134±6.99	115.2±38.05	125.81±10.25	138.88±13.64
HR	91.9±7.15	90.4±10.47	83.8±7.95	91.56±11.29	95.55±7.17
PCO_2	37.1±2.7	37.2±2.65	37±2.49	35.5±1.41	37.66±2.12
PO_2	131.7±22.62	162.9±26.01**	133.1±25.77	118.31±14.58	128.66±18.66
SaO_2	98	98	97	98	97
Respiratory rate	14.1±1.44	14.4±0.96	14.2±1.31	14±1.71	14.88±1.45

SBP: Systolic Blood Pressure (mmHg), HR: Heart Rate (min), SaO_2: Arterial O_2 Saturation, Respiratory Rate (min) ** $p=0.002$

($p<0.05$).

Ethics Permission to conduct the study was obtained from the local ethical committee of our Hospital. The nature of the study was explained to all unit consultants and members of the multidisciplinary team who have significant input into the critical care unit's pain control protocol. Anonymity of participants was guaranteed and protection of the participants was of paramount importance. Relatives of the patients included in the study were informed by research team and informed consents were taken from patients and their families' members.

FINDINGS

Groups were compared for demographically. Age (mean), body weight (mean), sex were demonstrated no significance (Table 1).

Ninety percent of the patients (n: 45) underwent aortocoronary bypass grafting (CABG) procedures and 10% patients (n: 5) had mitral valve replacement procedures.

Mean levels of minute ventilation rate, heart rate, pCO_2, SaO_2 and systolic blood pressure at the end of the first 24 hrs postoperatively did not show any significant difference among groups. However, we observed tramadol group showed slightly higher heart rates, whereas meperidine group had more acceptable SBP and heart rates (Table 2).

Fentanyl group showed statistically higher levels of mean pO_2 levels at the end of the first 24 hrs postoperatively ($p=0.002$), as shown in Table 2. Tramadol group, however had significantly lower median value of VAS scores ($p=0.001$); this finding was supported in the clinical practice (Fig. 1).

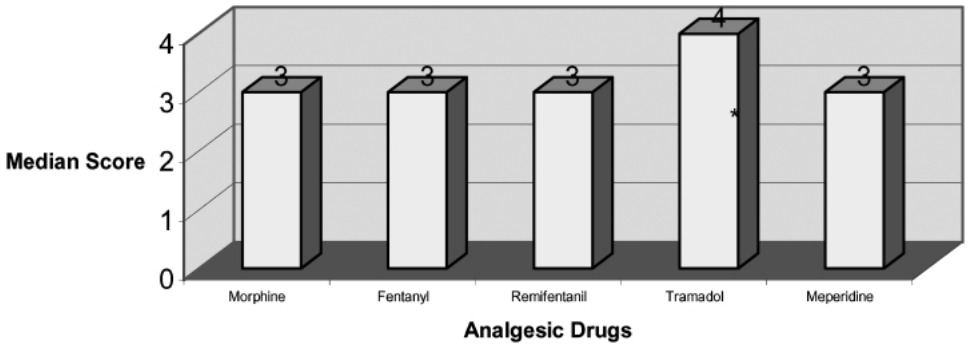

Fig. 1. Comparison of VAS Values for the Five Analgesic Drugs
(*) p: 0.001.

Possible side effects of the analgesics used in the study are observed. Low quantity of the side effects experienced hindered a statistical analysis. In the remifentanil group, 1 patient had headache and 1 patient had stomachache, and palpitations were seen in equal frequencies in fentanyl and tramadol groups. No significant differences were seen among 5 groups in median scores of sedation at the end of the first 24 hrs postoperatively.

Analysis of the PCA doses yielded that meperidine group had the lowest number of additional bolus doses of the particular analgesic (twice in average in 24 hrs), ($p=0.001$) followed by the remifentanil group (Table 1).

DISCUSSION

There are several reports in the medical literature on postoperative pain control using opioid analgesics.[7,9,12,13] However, most of those reports were designed to compare different routes of administration of one or two agents.

It was reported that continuous drug perfusion and PCA is superior to conventional intermittent doses of analgesics,[12] however, other researchers,[13] noted in their report that such a comment still needs further investigations. Some researchers compared epidural route and the above mentioned method and noted that there exists no difference in efficiency, but former route is more advantageous for additional doses and that both methods are superior to intermittent dosing.[14] It was reported that intravenous analgesia with PCA after CABG operations is superior to conventional nurse determined analgesic administration as significantly less postoperative atelectasis with the former method.[9] In previous researches, it had been shown that patients in PCA group after CABG procedures had more rapidly decreasing VAS scores than those in conventional analgesia group.[15] The authors had also advocated that VAS scores were lower in the former group at the time of extubation and on 3rd postoperative day, and thus lower incidences of myocardial ischemia were found.[15]

In the present study, continuous infusion and PCA administration methods were used on patients that have undergone sternotomy in widely accepted dosing regimens. In addition to continuous infusion, approximately 12 times of bolus doses of the analgesics had to be used in all 4 groups except the meperidine group. The fact that infusion doses of the analgesics were adequate. It reflected that their minimal effective concentrations were also adequate. Need for additional bolus doses of the analgesics seemed to be due to cough- or movement-induced pain.

It is understood from the literature that, there is a good relationship especially between pain relief scales,[16] so that, we used pain categories in numerical scores for pain relief and checked these scores by comparison with concurrent VAS measurement.

In spite of the fact that only tramadol group showed to be significantly higher VAS scores, clinically observed lower VAS scores in the other groups can be due to appropriateness of perfusion doses of the analgesics as well as a possible rise in the postoperative levels of endogenous morphine confirming with the studies of researchers.[17,18]

The effects of intravenous tramadol and morphine given with PCA after mammary surgery were compared where they used similar bolus doses and locking times as well as other characteristics such as sedation, nausea and vomiting.[19] In their study, it was reported that both analgesics had similar VAS scores,[19] whereas in the present study, we observed that mor-

phine and the other analgesics showed statistically and clinically lower VAS scores than tramadol did. The findings in a previous research supported our findings.[20] Other researchers reported similar results to our findings in postoperative effects of tramadol, meperidine and nalbuphine on nausea, vomiting and headache;[21] in the present study we observed more cases of nausea and vomiting with tramadol and remifentanil group had one case of headache and one case of abdominal pain, although not statistically shown to be significant. We concluded that two cases of palpitations in tramadol group arose from the agent's monoaminergic effects. Other researchers had also reported a higher incidence of nausea and vomiting with tramadol.[22]

Similar side effects for tramadol and morphine were reported earlier.[23] Tramadol caused a higher incidence of nausea and vomiting, which concurred with our findings except that meperidine group showed a higher tendency for sedation. In the present study, it was observed that side effects such as nausea and vomiting were more often in tramadol group than morphine, fentanyl and meperidine group. We have not seen nausea and vomiting in remifentanil group. These number of side effects might be depended on drug doses used in the present study.

We have seen PO_2 value in fentanyl group was significantly higher than the other groups. This result might be depended on other cardiopulmonary changes in the postoperative period and less pulmonary depression of fentanyl dose.

Reports reminded that comparison of different agents and different routes of administration carry some difficulties.[24] The fact that some of the findings in the present study showed clinical, but no statistical significance can be due to low number of patients involved.

To minimize pain and discomfort after open heart surgery with sternotomy, analgesia combined with PCA and continuous infusion is easy and effective with low minimal effective concentrations. Meperidine showed to be superior for pain relief by less bolus among the drugs. Remifentanil had also shown less superiority than meperidine for pain relief. When regarding IV bolus doses, meperidine is the most effective choice by the dosages used as analgesic and remifentanil is the second choice. Tramadol showed the highest VAS value as far as pain intensity are concerned by doses used in the study. Meperidine and remifentanil caused less side effects and fentanyl showed superiority as far as pO_2 levels are concerned.

It is concluded that, there were no significant differences among the groups for pain management except the highest VAS value on tramadol. The side effects such as nausea, vomiting, headache, stomachache and respiratory depression of the narcotic analgesics were observed in this study. Remifentanil and meperidine in the study had shown less side effects than other three drugs. All these side effects need to be checked frequently and form the basis for the nursing interventions in the postoperative period.

Further studies with higher number of patients are needed to establish statistically more reliable results, especially for side effects.

REFERENCES

1) Chrubasik J., Buzina M., Schulte-Monting J., Atanassoff P., Alon E., *Eur. J. Anaesthesiol.*, **9**, 23–28 (1992).
2) Joshi G. P., White P. F., ''Patient Controlled Analgesia, The Management of Pain,'' eds. by Ashburn M. A., Rice L. J., Churchill Livingston, Philadelphia, 1998, pp. 577–611.
3) Puntillo K. A., Casella V., ''Pain Analgesia and Sedation, AACN Clin Ref Crit Care Nurs,'' 4th ed., eds. by Kinney M. R., Dunbar S. B., Brooks-Brunn J. A., Molter N., Vitello-Cicciv J. M., Mosby, St Louis, 1998, pp. 61–87.
4) Cambitzi J., Harries M., Raders E. V., ''Postoperative Pain Management, Surgical Nursing Advancing Practice,'' eds. by Manley K., Bellman L., Churchill Livingstone, Edinburgh, 2000, pp. 466–506.
5) Barilaro C., Rossi M., Martinelli L., Guarneri S., Cimino A., Schiavello R. L., *Minerva Anestesiol.*, **67**, 171–179 (2001).
6) Krenn H., Oczencki W., Jellinek H., Krumpl-Stroher M., Schweitzer E., Fitzgerald R. D., *Eur. J. Pain*, **5**, 219–226 (2000).
7) Ersek M., Poe C. M., ''Pain, Medical Surgical Nursing,'' 6th ed., Vol. 1, eds. by Lewis S. M., Heitkemper M. M., Dirksen S. R., Mosby, St. Louis, 2004, pp. 131–159.
8) Foubert J., Vaessen G., *Eur. J. Oncol. Nurs.*, **9**, 21–32 (2005).
9) Gust R., Pecher S., Gust A., Hoffman V., Bohrer H., Martin E., *Crit. Care Med.*, **27**,

2218–2223 (1999).
10) Melzack R., Katz J., Te MC Gill., ''Pain Questionnaire: Appraisal and Current Status, Handbook of Pain Assessment,'' The Guilford Press, New York, 1992, pp. 152–168.
11) Kuğuoğlu S. Y., Aslan F. E., Olgun N., ''Adölesan ve erişkinlerin postoperatif ağrı değerlendirilmesinde McGill Melzack Ağrı Soru Formu (MASF)' nun kullanımına yönelik bir çalışma (The Study which is used to the McGill Melzack Pain Questionnaire (MPQF) on the assessment of postoperative pain of adolescents and adults),'' International Participation VI. National Nursing Congress, Ankara, 1998.
12) Parker R. K., Holtmann B., White P. F., *JAMA*, **266**, 1947–1952 (1991).
13) Owen H., Szekely S. M., Plummer J. L., Cushnie J. M., Mather L. E., *Anaesthesia*, **44**, 11–13 (1991).
14) Grant R. P., Dolman J. F., Harper J. A., White S. A., Parsons D. G., Evans K. G., Merrick C. P., *Can. J. Anaesth.*, **39**, 214–219 (1992).
15) Searl N. R., Roy M., Bergeron G., Perrault J., Roof J., Heermans C., Courtemanche M., Demers C., Cartier R., *Can. J. Anaesth.*, **41**, 198–205 (1994).
16) Scott J., Huskisson E. C., *Pain*, **2**, 175–184 (1976).
17) Brix-Christensen V., Tonnesen E., Sanchez R. G., Bilfinger T. V., Stefano G.B., *Int. J. Cardiol.*, **62**, 191–197 (1997).
18) Wilder-Smith C. H., Hill L., Wilkins J., Denny L., *Anesthesiology*, **91**, 639–647 (1999).
19) Silvasti M., Svartling N., Pitkanen M., Rosenberg P. H., *Eur. J. Anaesthesiol.*, **17**, 448–455 (2000).
20) Naguib M., Seraj M., Attia M., Samarkandi A.H., Seet M., Jaroudi R., *Can. J. Anaesth.*, **45**, 1168–1175 (1998).
21) Van der Berg A. A., Halliday E., Lule E.K., Baloch M. S., *Acta Anaesthesiol. Scand.*, **43**, 28–33 (1999).
22) Ng K. F., Tsui S.L., Yang J. L., Ho E. T., *Eur. J. Anaesthesiol.*, **15**, 565–570 (1998).
23) Hopkins D., Shipton E. A., Potgieter D., Van derMerwe C. A., Boon J., De Wet C., Murphy J., *Can. J. Anaesth.*, **45**, 435–442 (1998).
24) White D. C., Pearce D. J., Norman J., *B.M.J.*, **2**, 166 (1979).