Original Article

Effect of small dose intermittent IV pethidine in combination with diclofenac for post operative pain relief

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Abstract:

Background: Post operative pain is an acute type of pain. There is convincing evidence that unrelieved post operative pain may result in harmful physiological and psychological effects with significant morbidity and even mortality. Complete and effective pain management is an essential for the patient who recovers from surgery. For this reason we used easy available drugs opioid, NSAID and its combination for better post operative analgesia with the aim of avoiding expensive patient controlled analgesia technique, infusion or intramuscular painful roout of administration.

Methods: 120 patients ASA grade-I and II were selected for post operative pain releive in upper and lower abdominal surgery. All patients divided into three groups and each group are equal in number and same type of surgery. Among the three groups, two groups received small intermittent intravenous pethidine and diclofenac pre and post operatively and other groups received intra muscular pethidine with diclofenac pre and post operatively (controlled group). All vital parameter and pain score both VAS and VRS were recorded in perioperative period up to 24 hours postoperatively.

Result: Good level of anaesthesia was achieved in all groups (VAS>30mm) of upper and lower abdominal surgery except early post operative period. In early post operative period significant difference of VAS in group II and III (P<.01) was found with group I. But after half an hour and one hour significant difference of VAS in group II and III (P<0.02, P<0.001) was found with group I. Over all excellent analgesia was possible in group II VAS, VRS always more than 30mm and all vital sign were stable.

Conclusion: Small intravenous intermittent dose of pethidine in combination with diclofenac sodium effectively controlled post-operative pain.

Key Word: Post operative analgesia, small intra venous dose of pethidine, diclofenac.

(Journal of BSA, 2009; 22(2): 40-47)

Introduction:

Pain is one of the most common fears for patients coming into hospital for surgery. Unfortunately the patients worries about and the fears of pain are how on the priority list of the medical staff[1]. One of the reasons frequently mentioned for inadequate post operative pain relieve in the literature is the nurse and doctor fear to administer opioid analgesics because of their side effects[1]. Prevention of post operative complication[2], evidence of shortness hospital stay, increased patients satisfaction with effective relief of post operative type of acute pain[3].

Pain management is not too easy because the variable response to pain. The response to pain can be highly variable between individual as well as in the same individual in different times[4]. It is likely that all form of acute type of post operative pain is poorly managed. A wide range of pharmacological and psychological treatment for post operative pain

is now available inadequate or improper application of knowledge and therapies currently available is certainly one of the most important factor indequate relief of pain[5,6].

The post operative pain relief immediately after major surgery can not be achieved with opioids alone in all patients without respiratory depression or other significant side effects[7]. So it is not always applicable or without side effect and require skill manpower. Now a days another combined analgesic method, opioid with NSAIDs is used to manage postoperative pain[9] with the aim of reduction of opioid doses.[8]

Combined analgesic techniques are also popular for postoperative pain management in this country without definitive effective method of drugs administration. In our setup intramuscular opioids and NSAIDs are popular in combined analgesic techniques. Intramuscular injection is painful and absorption is unreliable, as a result analgesic effect is unpredictable. For this reason we may use easy available drugs and formulation for better post operative analgesia to avoid expensive PCA, infusion or intramuscular route of administration.

In our setting among the NSAIDs diclofenac sodium is commonly used, easily available and very cheap and equianlgesic with ketoprofen, ketorolac and piroxicam[9,10]. Among the opioids pethidine is one which is supplied to the Government hospital though not easily procurable from the open market. So, in this combined study diclofenac sodium and pethidine are included.

This investigation was conducted for better control of postoperative pain and in addition it was done with the intention of reducing the incidence of side effects and to search for better method of pethidine administration while improving the quality of pain relief.

Methods and materials:

A double blind, randomized controlled study of 120 cases of different surgical plans carried out in IPGMR (BSMMU). Sixty adult patients age ranging from 20-50 years, undergoing upper abdominal surgery like open cholecystectomy by subcostal incision and sixty adult of same age range under going lower abdominal surgery like abdominal hysterectomy of not more than 90 minutes duration under general anaesthesia were enrolled in the study. All the patients were in ASA group I & II and weighing between 50 to 70kg. Patients were included in the study after obtaining informed consent. Each surgical plan patients were placed in three different groups. Any patient with known history of sensivity of NSAID, peptic ulcer, bronchial asthma, hepatic or renal disease, any bleeding history or anti coagulant therapy were excluded from study.

Group-I (Control group) This group of patients received diclofenac sodium as rectal suppository 1 mg/kg body weight (bw) half an hour before commencing surgery in the ward / anaesthetic preparation room and 50mg 8 hourly in postoperative period. Time maintained from first dose administered by a nurse who was not aware of the study. This group of patients also received intramaucular pethidine 1.5mg/kg in post-operative period upto 24-hours, when VAS is more than 30mm, not repeated with 2 hours.

Group-II This group of patients received diclofenac sodium as rectal suppository 1mg/kgbw half an hour before commencing surgery in the ward / anaesthetic preparation room and 50mg 8 hourly in post-operative period. Time maintained from first dose administered by a nurse who was not aware of the study. This group also received 1st dose pethidine 0.5mg/kg bw intravenously in postoperative period when VAS more than 30mm. Then 10mg Pethidine was given hourly by intravenously up to 24 hours when VAS is more than 30mm, not repeated within 10 minute.

Group-III: this group of patients received rectal suppository of diclofenac sodium 1mg/kgbw at the end of surgery and 50mg 8 hourly in post-operative period. Time maintained with first dose administered by a nurse who was not aware of the study. This group also received 1st dose pethidine 0.5mg/kg intravenously in post-operative period when VAS more than 30mm. Then 10mg pethidine was given hourly intravenously up to 24 hours when VAS is more than 30mm but not repeated within 10 minute.

Pre operatively all patients were examined properly and record sheet was filled for each patient. 100mm (10 cm) visual analogue scale slide roller and verbal rating rating score were used to assess the level of postoperative pain. The VAS was explained to the patient that one extreme of the scale indicate no pain and other end worst pain possible. The verbal rating score also explained to the patient (No pain,

mild pain, moderate pain and severe pain). All patients were premedicated with midazolam 7.5mg and Ranitidine 150mg orally at night before operation.

In all general anaesthesia was started with pre oxygenation induced with thiopental sodium 5mg/kg and suxamethonium (1.5 mg/kg) body weight and fentanyl 1 µg/kgbw was injected to facilitate intubation. Anaesthesia was maintain with nitrous oxide and oxygen (60:40) and halothane (0.50%). atracurium 0.5mg/kgbw was given as a bolus dose and repeated dose of 0.2mg/kg bw given when necessary to continue relaxation. Fentanyl (0.25µg/kg bw) was given at 30 minute interval for maintaining analgesia and amount of fentanyl given during surgery was recorded. Pulse, Systolic blood pressure, diastolic blood pressure, arterial oxygen saturation and $ETCO_2$ were recorded in the pre, per and postoperative period. Patient was recovered from anaesthesia to maintain by standard procedure. Pain was assessed by VAS and VRS on arrival, 30 minutes, 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 18 hours and 24 hours after arrival in the post-operative ward. Sedation score were recorded with pain assessment in same interval. (awake and alert 1, awake and drowsy 2, asleep and ready arousal 3 and asleep[4]) and also recorded any side effect.

For use of intravenous preparation of pethidine, one ampoule (100mg) pethidine dissolved in 18 ml distilled water in 20ml syringe. So 1ml solution contains 5mg pethidine. Time of first pethidine requirement and total amount of pethedine and diclofenac sodium were recorded postoperatively. Data were analyzed by student's "t", ANOVA test, X^2-test and SPSS version 12 for window were used for comparative analysis. A P value of <0.05 was considered as significant.

Observation and Result:

Observations were made on haemodynamic parameter, analgesic requirement and level of analgesia in perioperative period. Pain (VRS/VAS), level of sedation, haemodynamic parameter, side effects were recorded 24 hours of post operative periods. Demographic data and different parameter were described as mean with standard error in table and graph.

Demographic characteristics in all groups in respect to age, weight, gender and educational status were similar (Table - I). Pre-operative and peroperative parameter like pulse rate, respiratory rate, SBP, DBP, SPO_2 EtCO2 and resting VAS, VRS between the groups were not statistically significant (Table – II & III). There was no significant difference of amount of fentanyl used in intra operative period and duration of surgery (Table-IV) and recovery score.

Pain score (VAS and VRS) at each time of measurement after surgery were mostly in acceptable limit but early post operative period (0 - 1 hours) were significantly different in group-I and group II with group III at arrival ($p < .05$) and at 30 minute and one hour. After two hours VAS and VRS gradually reduced and achieved acceptable level but score was significantly higher in group I and III ($p<0.05 – 0.01$).

Table-I

Demographic data of different study group

	Upper abdominal Surgery			Lower abdominal Surgery		
	Group I (N=20) Mean±SE	Group-2 (N=20) Mean±SE	Group 3 (N=20) Mean ±SE	Group I (N=20) Mean+SE	Group-2 (N=20) Mean+SE	Group 3 (N=20) Mean ±SE
Age (yr)	39. 6± 1.39	39.2±1.99	38.7±1.8	40.30 ± 2.38	42.05±1.46	41.30±1.22
Sex	F 16M4	F 15M5	F 16M4	F 17 M3	F 16M4	F 16M4
Wt (kg)	58.15±0.86	58.00±0.96	59.60±0.8	58.25±0.80	58.50±0.81	59.0±0.75
Edu	UNG 12 G 8	UNG 10 G 10	UNG 11 G 09	UNG 13 G 7	UNG 11 G 9	UNG 12 G 8

Data was analyzed by ANOVA test, Values regarded significant, there in different study group $p<0.05$. no significant difference between the groups, F = Female, M = Male, UNG = Undergraduate, G= Graduate

Table-II

Preoperative parameter of the patients

	Upper abdominal Surgery			Lower abdominal Surgery		
	Group I (N=20) Mean±SE	Group-2 (N=20) Mean±SE	Group 3 (N=20) Mean ±SE	Group I (N=20) Mean+SE	Group-2 (N=20) Mean+SE	Group 3 (N=20) Mean ±SE
ASA	ASA 1 17 ASA 2 03	ASA 1 16 ASA 2 04	ASA 1 16 ASA 2 04	ASA 1 14 ASA 2 6	ASA 1 15 ASA 2 05	ASA 1 14 ASA 2 6
Pulse	79.10±3.37	81.7±1.46	81.15±2.22	82.40±1.29	83.65±1.24	83.40±1.67
Resp	16.50±0.41	16.85±0.37	16.55±0.32	16.70±0.35	17.05±0.35	16.75±0.33
SBP	128.25±2.09	127.25±2.26	125.75±2.18	128.75±2.23	128.50±2.35	126.50±2.26
DBP	79.7±1.05	78.70±1.68	77.95±1.29	79.70±1.10	79.20±1.60	78.05±1.44
Hb	12.75±0.24	12.75±0.26	12.82±0.24	12.87±0.23	12.72±0.24	12.77±0.23
VAS	35.25±2.25	36.45±2.15	33.80±2.20	37.75±2.35	38.23±2.85	36.23±2.75

Data was analyzed by ANOVA test Values regarded as significant value $p<0.05$.

Table: III

Intra operative parameter of different study groups

	Upper abdominal Surgery			Lower abdominal Surgery		
	Group I (N=20) Mean±SE	Group-2 (N=20) Mean±SE	Group 3 (N=20) Mean ±SE	Group I (N=20) Mean+SE	Group-2 (N=20) Mean+SE	Group 3 (N=20) Mean ±SE
Pulse	93.90±1.54	94.30±1.70	93.30±1.85	94.90±1.49	93.65±1.67	92.85±1.56
SBP	129.0±2.26	128.75±1.70	126.0±1.97	127.65±2.23	126.75±1.93	123.05±1.59
DBP	81.5±1.09	81.75±1.01	79.25±1.37	82.45±1.04	82.30±1.14	80.85±1.25
SpO2	98.25±0.16	98.40±0.16	98.45±0.15	98.55±0.15	98.75±0.14	98.60±0.19
ET CO2	40.05±0.23	40.05±0.16	39.95±0.16	38.85±0.34	39.35±0.13	39.45±0.30

No significant different between the three groups

Table-IV

Intra operative amount of fentanyl used and duration of surgery.

	Upper abdominal Surgery			Lower abdominal Surgery		
	Group I (N=20) Mean±SE	Group-2 (N=20) Mean±SE	Group 3 (N=20) Mean ±SE	Group I (N=20) Mean+SE	Group-2 (N=20) Mean+SE	Group 3 (N=20) Mean ±SE
Amount of Fentanyl used (mg)	119.75±3.77	118.50±2.99	119.50±2.98	120.0±3.20	122.0±3.27	120.75±3.16
Duration of surgery (min)	72.5±2.25	73.5±1.70	73.75±1.88	71.75±1.96	75.0±1.76	74.75±1.86

No significant difference between the three groups

Table-V

Post operative VAS of different study groups

	Upper abdominal Surgery			Lower abdominal Surgery		
	Group I (N=20) Mean±SE	Group-2 (N=20) Mean±SE	Group 3 (N=20) Mean ±SE	Group I (N=20) Mean+SE	Group-2 (N=20) Mean+SE	Group 3 (N=20) Mean ±SE
At arrival	34.50±2.88†	36.25±3.07‡	46.0±2.62	34.75±2.95†	33.50±3.14‡	43.45±2.78
30 minute	51.75±3.46	25.0±2.87***‡	35.25±2.00‡‡	45.25±3.56	24.0±2.85 ***‡	33.0±2.52‡‡
One hour	37.0±2.92	28.0±3.59*	28.0±4.38†	32.50±3.23	22.0±3.16*	24.50±3.84†
two hour	26.50±3.42*	17.0±3.06	19.0±2.87†	22.0±3.37	17.0±3.06*	18.75±3.03
Four hour	20.50±3.58	15.25±3.15*	19.50±3.10	20.50±3.58	12.75±3.19*	17.0±2.88
Eight hour	30.50±4.25	20.50±3.93*‡	26.50±3.64	28.50±3.92	18.0±3.44*	19.0±0.62†
Twelve hour	24.50±3.93	17.50±3.54*‡	20.0±3.69†	22.0±0.69	15.00±2.20*	17.50±3.23†
Eighteen hour	21.0±4.03	15.50±3.51**	18.50±3.58	19.50±3.93	11.0±2.89*‡	17.00±3.70
Twenty four hour	19.0±4.03	15.50±3.51*‡	19.0±4.28	16.50±3.99	12.50±2.89*‡	16.0±3.93

Between the Groups
‡/†/*/• P <.05 **p< .01
* group! vs. group2
†p group! vs. group3
‡p group2 vs. group3

Between the Surgical plan
UAS vs. LAS
• Gr. 1vs Gr. I
• Gr. 2 vs. Gr. 2
• Gr. 3 vs. Gr. 3

Table VI

Time of 1st pethidine requirement and total amount of pethidine requirement in different group study.

	Upper abdominal Surgery			Lower abdominal Surgery		
	Group I (N=20) Mean±SE	Group-2 (N=20) Mean±SE	Group 3 (N=20) Mean ±SE	Group I (N=20) Mean+SE	Group-2 (N=20) Mean+SE	Group 3 (N=20) Mean ±SE
Time (min)	29.75±2.54	28.25±2.74	29.60±2.50	30.85±2.63	27.25±2.90	31.25±2.26
Amount (mg)	186.50±6.66	112.75±1.24**‡	122.45±0.96	171.65±4.39	109.45±1.50**‡	120.0±1.50

Between the Groups
‡/†/*/• P <.05 **p< .01
* group! vs. group2
†p group! vs. group3
‡p group2 vs. group3

Between the Surgical plan
UAS vs. LAS
• Gr. 1vs Gr. I
• Gr. 2 vs. Gr. 2
• Gr. 3 vs. Gr. 3

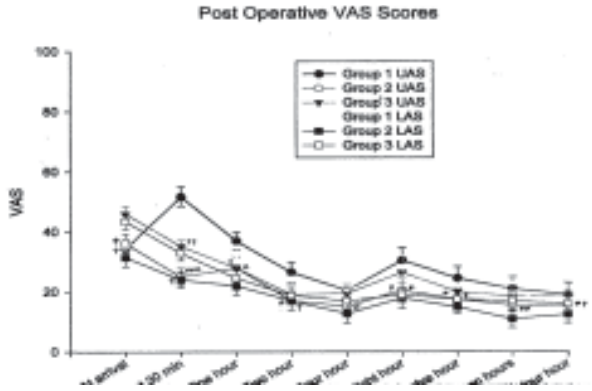

Fig.-1: *Line diagram showing the Post Operative VAS Score in different time.*

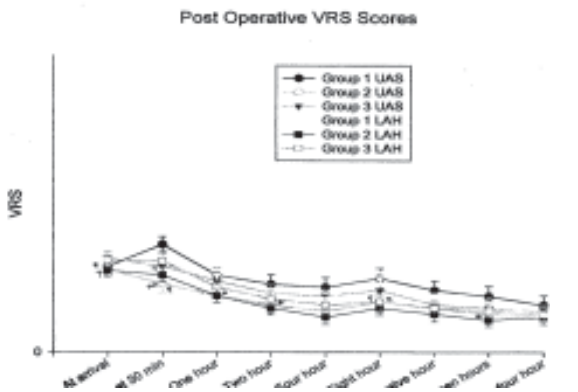

Fig.-2. *Line diagram showing the Post Operative VRS scores in different time.*

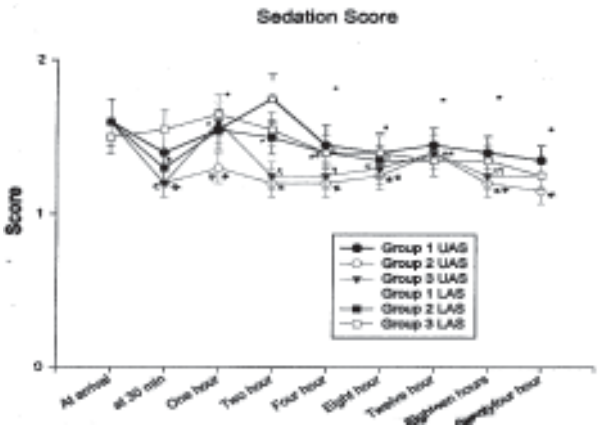

Fig.-3. *Line diagram showing the Post Operative sedation Scores in different time.*

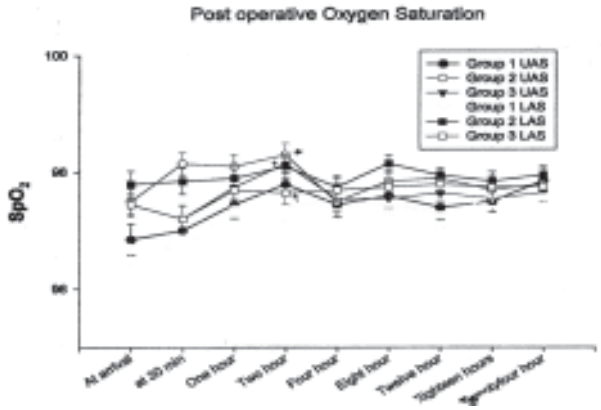

Fig.-4. *Line diagram showing the Post Operative Oxygen Saturation in different time.*

Discussion:

In this study it was found that good level of post operative analgesia (VAS within 30mm) was achieved within one in all groups having both upper and lower abdominal surgery.But excellent quality of analgesia was achieved in group II within half an hour (VAS 25 ±2.87) and continued to maintain with significant lower VAS score than other two groups. Although VAS score appeared to be higher at arrival in the post operative ward in group III but analgesia was achieved within half an hour. The similar analgesic effect was also obtained using other combination such as morphine with indomethacine, morphine with ketoralac and fentanyl with diclofenac etc. however, in those combined studies, routes of drugs administration were different most of such studies opioids were administered by PCA and NSAIDs by intra-muscularly or intra-venously or a suppository forms [7,11,12] .Results of present study was showing better analgesic effect than combination of diclofenac and pethidine or morphine and ketorolac when used by demand basis intramuscularly[14,15,16]. Lancker P et al [17] in 1996 showed that post operative pain score had decreased during the first 2 hour and had reached a lower level by 4 hours with their combined analgesic study with PCA opioid administration. But they used alfentanil as an opioid and piroxicam as an NSAIDs and administrated post operatively. The different NSAIDs and different opioids and different modes of administration used for the comparison and the different setting in which the analgesia was tested makes direct comparison difficult.[18]

Small intermittent dose of intravenous pethidine groups showed effective and safe analgesia in this study which was compared with intravenous PCA based combined analgesic studies using morphine, fentanyl, indomethacine and diclofenac.[7,11,17] Early analgesia (within 30 min) was achieved in this study with small does of intravenous pethidine which was compared with PCA based single opioid therapy[19,20,21,22] . PCA therapy is considered to be a safe but high doses of opioid was required. For this high doses or instrumental error, there was a serious adverse outcome exists[23,24,25]. Life threatening respiratory events associated with the use of PCA have reported [24,26,27,28]. These events were almost always associated with human error, usually related to pump programming major factor limiting the use of PCA other than side effects was patient factors and cost effectiveness [20.22,29,30]. There was different survey of post operative analgesic service with PCA. Semple P, Jackson IJB[31] did survey in 1991 of post-operative analgesia practice in anaesthetic departments in England and wales, PCA was considered by 58% of respondents to be the ideal method of analgesia where there was no limitation in staffing or equipment. However only 18% rated it as the safest technique on normally staffed wards. In contrast 63% of the departments felt on demand I/M analgesia was the safest form of analgesia. PCA technique are offered to fewer than 30% of patients either in North America or in Europe[32]. Present combined technique with small intermittent intravenous dose of pethidine provides excellent level of post-operative analgesia without respiratory depression or severe hypoxeamia. So this pain relief technique was safe and cost effective

compared to PCA based combined analgesia. PCA therapy provides improved analgesia compared with 'as needed intramuscular' opioid administration in patients undergoing a variety of surgical procedures [19,33,34,35]. Present study showed that small intermittent intravenous dose of pethidine provides improved and better analgesia compared with intramuscular pethidine administration (controlled group) in-patient undergoing upper and lower abdominal surgery. Mean VAS of intramuscular pethidine group varied from 19.0±4.03 to 51.75±3.46 (SE) (UAS) and 16.50±3.99 to 45.25±3.56 (SE) (LAS). mean value of intravenous pethidine group varied from 15.25±3.15 to 36.25±3.07 (SE) (UAS) and 11.0±2.89 to 33.52±3.14 (SE) (LAS).

Good analgesia was achieved after one hour in intramuscular pethidine based combined group in this study (VAS 26.50±3.42 & 22.0±3.37 at 2 hour) Iqbal KM et al 1986 [16] demonstrated that analgesia started after one hour and good analgesia was achieved after three hour of postoperative period by using combined intramuscular pethidine and declofenac study (VAS 20.5±1.9 SD). Onset of action and level of analgesia of these study was differed from my study because they used both drugs intramuscularly and post operatively.

In finding of the present study in combined analgesic method showed that the marked reduction of the pethidine dose specially in small intermittent intravenous group can maintain good postoperative analgesia with maintaining good post-operative sedation and respiratory pattern.

Incidence of nausea and vomiting in all groups was similar and it was varied from 40% to 50% and 35% to 45% respectively but frequency of vomiting was more in intrramuscular pethidine group. This finding was due to every patient gets metronidazol post-operatively. Anti-emetic requirement was more in-group I. This finding similar or less than the other same study.

Conclusion:

The combination of pre and post operative application of rectal suppository of diclofenac sodium and post-operative small intravenous intermittent dose of pethidine is an efficient method of treating post-operative pain. It is also effective and better alternative method of intramuscular or PCA based pethidine administration.

References:

1. Mamie C, Kloptenstein CE et al. Comparison of three standard analgesic regimens on postoperative pain and satisfaction. Br. J. Anaesthesia 1996; 70; 130.
2. Atkinson RS, Rushman GB, Davies NJH. Acute pain. Lee's Synopsis of Anaesthesia. 11th edn. Butterworth – Heinemann 1993; 750.
3. Yeager MP, Glass DD et al. Epidural anaesthesia and analgesia in high risk surgical patients. Anaesthesiology 1987; 66: 729-736.
4. Morgan G E, Mikhail MS. pain Management. Clinical Anaesthesiology 2nd ed. Stamford, Appleton and Lange, 1996; 274 - 316.
5. Bonica JJ. Pain research and therapy: past and current status and future needs. In: Ng LKY, Bonica JJ eds. Pain, discomfort and humanitarian care. Amsterdam: Elsevier / North Holland 1980: 1-46.
6. Bonica JJ, Loeser JD. History of Pain conceptes and Therapies. In: Loeser J D eds. Bonica's Management of pain 3rd ed. Lippincott William and Wilkins; 2001; 3-16.
7. Laitinen JL, Nuutinen L. Intravenous diclofenac coupled with PCA fentanyl for pain relief after total hip replacement. Anaesthesiology 1992; 76: 194-198.
8. Acute pain management operative or medical procedures and trauma: Clinical practice guidelines AHCPR pub No. Agency for health Care policy and Research, Public – health Service, US Department of health and Human Services, Rockville, MD. 1992;92;32
9. Rorarius MGF, Suominen P et al. Diclofenac and ketoprofen for pain treatment after elective cesarean section. Br. J. Anaesthesia. 1993; 70: 293 – 297.
10. O'Hanlon J, Miligan K et al. A comparison f the effect of intramuscular diclofenac, ketorolac or piroxicam on postoperative pain following arthroscopy. Br. J. Anaesth. 1996; 70: 132.
11. Sims C, Johnson CM et al. Rectal indomethacin for analgesia after Appendicectomy in Children. Anaesthesia Intensive Care 1994; 22: 272-275.
12. Murphy DF, Medley C. preoperative indomethacin for pain relief after thoracotomy. Comparison with postoperative indomethacin. Br. J. Aanaesthesia 1993; 70: 298-300.

13. Van P, Lancker J et al. Systemic piroxicum as an adjunct to patient controlled analgesia with altentanil for postoperative pain relief. Anaesthesia 1996; 51: 658-662.

14. Cataldo PA, Senagore AJ, Kilbride MJ. Ketorolac and patient controlled analgesia in the treatment of post-operative pain. Surg Gyenocol Obstet 1993; 176: 435-438.

15. Kenny GN McArdle CS, Aitken HH. Parenteral Ketorolac: opiate sparing effect and lack of cardiorespiratory depression in the perioperative patient. Pharmacotherapy 1990; 10: 127 – 131.

16. Iqbal KM, Gour KB et al. Assessment of post operative analgesia: A comparative study of Pethidine and Diclofenac sodium. Journal of Bangladesh College of Physicians and Surgeons. 1986; 4 (1): 1 – 7.

17. Lancker PV et al. Systemic piroxicam as an adjunct to patient controlled analgesia with alfentanil for postoperative pain relief. Anaesthesia 1996; 51: 658 – 662.

18. Turner GA, Anson N, Williamson R. Comparison of intramascular Ketorolac with Indomethacin suppositories in the treatment of pain after oral surgery. Anaesth Intens Care 1996; 24: 665 – 668.

19. Bolish SJ, Collins CL et al. Efficacy of patients controlled versus conventional analgesia for post-operative pain. Clin. Pharm. 1985; 4: 48 – 52.

20. Ferrante FM, Orav EJ et al. A statistical model for pain in patient controlled analgesia and conventional intramuscular opioid regimens. Anasth Analg 1988; 67: 457 – 461.

21. White PF. patient controlled analgesia: a new approach to the management of post operative pain. Semin Anaesth 1985; I.V: 255 – 266.

22. Jamison R, Taft K et al. Psychological and pharmacologic predictors of satisfaction with intravenous patient controlled analgesia. Anaesth Analg 1988; 67: 121-125.

23. Kreitzer JM, Kirschenbaum LP Eisenkraft JB. Safety of PCA devices. Anaesthesiology 1989, 70: 881.

24. Thomas DW, Owen H. patient-controlled analgesia: the need for caution. A case report and review of adverse incidents. Anaesthesia 1988; 43: 770 – 772.

25. White PF, parker RK. Is the risk of using a "basal" infusion with patient controlled analgesia therapy justified (letter). Anaesthesiology 1992; 76:489.

26. Ngan Kee, Warwick D et al. Respiratory depression associated with patient controlled analgesia. Canadian Journal of Anaesthesia 1995; 42 (10): 953.

27. Etches RC. Respiratory depression associated with patient-controlled analgesia: a review of eight cases. CJA 1994; 41(2): 125-132.

28. White PF. Mishaps with patient-controlled analgesia. Anaesthesiology 1987; 66: 81-83.

29. Thomas T, Robinson C et al. Prediction and assessment of the severity of postoperative pain and of satisfaction with management. pain 1998; 75: 177-185.

30. Magnani B, Johnson LR, Ferrante M. Modifiers of patient-controlled analgesia efficacy II. Chronic pain. Pain 1989; 39:23-29.

31. Semple P, Jackson IJB. Postoperative pain control. A survey of current practice. Anaesthesia 1991; 46: 1074-1076.

32. Rawal N eds. Regional opioids in anaesthesiology and pain management. Boston: Little, Brown and Company, 1986; 1-15.

33. Eisenach JC, Grice SC, Dewan DM. Patient controlled analgesia following cesarean section: a comparison with epidural and intramuscular narcotics. Anaesthesiology 1988; 64: 444-448.

34. McIntosh D, Rayburn W. Patient-controlled analgesia in obstetrics andgynecology. Obstet Gynaecol 1991; 78: 1129-1135.

35. Webb, Sterigios D, Rodgers B. Patient-controlled analgesia as postoperative pain treatment for children. J Pediatr nurs 1898; 4: 162-171.

36. Doyle E, Byers G, McNicol LR, Morton NS. Prevention of postoperative nausea and vomiting with transdermal hyoscine in children using patient-controlled analgesia. Br. J. Anaesth. 1994; 72: 72-76.