Original Article

Use of Ketorolac As An Adjuvant in Bier's Block

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Abstract

Background: *Bier's block has been most commonly used for hand and wrist surgery of short duration. Though it reduces the potential complication of general anaesthesia, significant post-operative pain is very common just after tourniquet release. Many adjuvants eg. fentanyl, pethidine, morphine, sodi-bi-carb, pancuronium, ketorolac etc. have been used so far with local anaesthetic to produce a dense block and to provide adequate post-operative analgesia. Of them Ketorolac was used very successfully as it has got less potential side-effects. This study was done to see the effect of ketorolac in Bier's block whether and how much it provides post-operative analgesia after tourniquet release.*

Method*: The effectiveness of combination of Lignocaine and Ketorolac as an anaesthetic solution in Bier's block was assessed in terms of reduction of tourniquet pain, quality of anaesthesia, the time of first analgesic demanmd and the amount of total analgesic needed in post-operative 24-hours period. A total of sixty patients of ASA grade-1 and ASA grade-2 undergoing hand and wrist surgery of less than 40 minute duration were enrolled for the study. Patients in control group (Gr-L) were received forty ml of 0.5%Lignocaine and patients in trial group (Gr-LK) were received 39-ml of 0.5% Lignocaine with 1 ml (30 mg) of Ketorolac as an anaesthetic solution. Patient was observed postoperatively for 24 hours.*

Result: *Pain was assessed in terms of VAS , and by measuring Heart rate and Blood pressure to assess sympathetic stimulation due to pain. Tourniquet pain was significantly less in Gr- LK ($p<0.000$). Postoperative analgesia was also significantly prolonged in Gr- LK (76.40 ± 11.78 min) than in Gr- L (27.30 ± 8.18 min). The number of total analgesic demand in postoperative 24 hours period was also significantly reduced in Gr-LK ($p<0.000$)*

Conclusion*: The Lignocaine and Ketorolac mixture in Bier's block produces significant anaesthesia and also provides adequate postoperative analgesia and causes less analgesic demand in postoperative period. These advantages ensure cost-effectiveness, shorter hospital stay and ultimately satisfactory patient outcome.*

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Introduction

Bier's Block, also known as Intra Venous Regional Anaesthesia (IVRA) has been commonly used for surgical procedures of short duration involving the hand and wrist. Although this technique avoids the potential complications of General Anaesthesia, it can result in significant post-operative pain.

The use of Lignocaine for IVRA or Bier's Block has been the mainstay for controlling peri-operative pain, but it provides little or no benefit for post-operative pain. Increased opioid analgesic used, longer hospital stay, poor patient outcome & decreased patient satisfaction are associated with inadequate post-operative pain management.

Ketorlac-a parenterally prepared Non Steroidal Anti Inflammatory Drug (NSAID) can be used to

treat these type of pain. Ketorolac, a peripherally acting analgesic that causes inhibition of Prostaglandin synthesis and thus it decreases the inflammatory response to surgical trauma. It has duration of action of about 6 – 8 hours. So when Ketorolac is used with Lignocaine in Bier's block, it can provide analgesia in the Post-operative period as well as it improves the quality of block.

In several studies various adjuvants were mixed to Local Anaesthetic solution to provide post-operative analgesia. In this context-NSAIDs,,Opioids, Muscle relaxants etc. have been used[7].Clinical use of opioid analgesic is based on the principle of their dose-response relationship.The relation between the dose of NSAID and its analgesic effectiveness is less well established, although a similar concept probably applies. Thus administration of Ketorolac to an isolated extremity would be expected to produce more intense analgesia in that extremity than would occur when the same dose was given systemically.

In present study,combination of Lignocaine0.5% and Ketorolac-30mg has been used and compared the degree of anaesthesia and duration of post-operative analgesia while using Lignocaine alone in other group. During IVRA,the hand and forearm are isolated from the rest of the body. Some leakage of drug into the general circulation can occur when injected distal to tourniquet. However, steps were taken to minimize this.The principle site of anaesthesia was debated[11].Tourniquet ischaemia alone will produce anaesthesia[8],but a considerable slow rate than in combination with local anaesthetic agent. Local anaesthetic agents probably act at two sites,anaesthetizing both large sheathed nerves at the elbow and also affecting small unsheathed nerve peripherally.[12]

The administration of Ketorolac locally decrease the incidence of systemic side-effects while providing the analgesic benefits suggested by Lundel et el[1]. Ruben et el used pethidine in Bier's block. They used 75mg of pethidine,but even this large dose failed to block conduction in median nerve[2]. Also large dose lead to a more frequent incidence of side effects without significant prolongation of post-operative analgesia. With pethidine , there were unexpected adverse clinical effects such as severe skin vasodilatation, associated with severe pruritus[15]. With this large dose post-operative analgesia lasts approximately 5 hours, but Teinbage et el studied that addition of Ketorolac 30mg to local anaesthetic in Bier's block provides effective post-operative analgesia without side effects for 10 hours[3]. In our study also postoperative analgesia lasted for more than 10 hours with Ketorolac.

In another study, Abdulla and Fadhil obtained successful analgesia in 100% of cases with combination of Lignocaine (100mg) + Fentanyl (50mcg) + Pancuronium (0.5mg). Although they obtained better loss of motor power however,no improvement in post-operative analgesia was found[15]. Another study done by Ruben et el in which they used Ketorolac, has been reported to improve regional anaesthesia both in terms of dosage and post-operative analgesia[17].Rivera et el studied that the use of 20mg of Ketorolac in IVRA reduces the total post-operative analgesic demand following non-traumatic hand and wrist surgery[5]. Malik et el studied that adding of Ketorolac 30mg in Bier's block provides effective post-operative analgesia for ambulatory hand surgery[4]. The doses used in this study were equivalent to those administered systemically.The administration of Ketorolac locally could possibly decrease the incidence of side effects while providing analgesic benefits along with systemiceffects[11].

Considering all the above mentioned studies, this study was done to see the effect of Ketorolac 30mg in Bier;s block whether and how much it prolongs the duration of block and whether it reduces the post-operative analgesic demand both in traumatic and non-traumatic hand and wrist surgery.

Aims & objectives of the study

(A) General:
To see the effects of Ketorolac in Bier's block.

(B) Specific:

i) To compare the degree of Analgesia

ii) To compare the duration of Anaesthesia

iii) To asses the need of Post-operation analgesia between the two groups using Lignocaine alone & Lignocaine plus ketorolac in Bier's block.

Materials & Methods

Place & Period of study:

This prospective randomized study was carried out in the Department of Anaesthesiology & ICU, Dhaka Medical college Hospital, Dhaka, during the period of July ' 2010 to January ' 2011.

Population of the study:

Sixty patients, admitted in the Department of Orthopedic Surgery, General Surgery & Neuro-Surgery of Dhaka Medical College Hospital, Dhaka was included in the study.

Inclusion Criteria:

- Patients belonging ASA-I & II
- Age between 20 – 60 yrs
- Weight between 40 – 60 kg
- Patients Scheduled for minor Hand Surgery & short Orthopedic & Neuro-surgical procedure of the fore-arm & Wrist joint less than Forty minutes duration.

Exclusion Criteria:

- Patients refusal
- Patients with known allergy to Local Anaesthetics & ketorolac
- Patients with Hepatic dysfunction.
- Patients with sickle cell disease
- Patients with any known convulsive Disorder
- Deficient peripheral Circulation
- Myasthenia Gravis
- Decompensate Heart Disease
- Obese patients

Study Design:

All the sixty patients undergoing surgery under Bier's block was divided into two groups.

· Group-L (n=30) :(Thirty patients)	Bier's block using Lignocaine alone (L)(lignocaine 0.5% = 39 ml + D/W = 1 ml)Total volume = 40 ml
· Group-LK (n=30) :(Thirty patients)	Bier's block using Lignocaine & ketorolac (LK)(ligocaine 0.5% = 39 ml + Ketorolac -30mg = 1 ml)Total volume = 40 ml

Methods

Each patient was selected according to the inclusion & exclusion criteria of the protocol. Pre-anaesthetic check-up was done for each patient on the day before surgery. Each patient was kept fasting for at least 8 hours pre-operatively. After taking informed consent in the special consent form for the study, each patient was entered into the operation theatre. Two intra-venous canula were inserted on the dorsal metacarpal vein of each hand. All equipments were checked for leaks & malfunction and all resuscitative drugs & equipments including Anaesthesia machine were kept ready. The hand, on which surgery was done, elevated for 5 minutes. Exsanguination was done by means of Esmarch bandage to reduce the venous pressure. An orthopedic tourniquet of the correct size was applied over padding on the upper-arm. The touruiquet was inflated to a pressure of 100 mm of Hg above the patients systolic pressure. Then the proposed drug for each group for Bier's block were injected through the intra venous cannula over 2 – 3 minutes. Full monitoring according to the Data-sheet . The touruiquet was released after 30 minutes.

The patient was sent into Post-operative ward and was observed for 24 hours. The time of need of first analgesic after the Bier's block and the need for total post-operative analgesic drug in 24 hours, were noted in the data-sheet of each group.

Data Processing

All statistical analysis was carried out using SPSS statistical package. All results are expressed as mean ± SD or in frequencies as applicable. The results were compiled and analysed using student's 't' test, chi square and ANOVA as appropriate. Results were considered significant if 'p' < 0.05 (confidence interval; CI - 95%).

Results

Observation of the present study was analyzed in the light of comparison among the subject groups (Gr-L, Gr-LK) each group having n = 30. Results

were expressed as mean ± standard deviation (SD) or in frequencies as applicable. The studied groups became statistically mathched for Age (p<0.628), Sex (p<0.197), Weight (p<0.981)(Table-01,Fig-1), ASA physical status (p<0.796), the duration of surgery (p<0.868), the baseline pulse rate (p<0.131) and the mean arterial pressure (p<0.348) other than the types of surgery (p<0.001).

Table 1 *Demographic data.*

Group/Variblen	Gr-L30	Gr-LK30	P value
Age in years	35.36 ± 11.56	33.93 ± 11.22	**0.628**
Weight in kg	57.90 ± 4.99	57.93 ± 5.71	**0.981**
Duration of surgeryin minutes	49.78 ± 1.20	50.96 ± 1.46	**0.867**

Values are expressed a mean ± SD. Between groups analyses were done by student's 't' – test.
Vales are expressed as significant if p<0.05 (CI-95%).
* = Significant ;
** = Highly significant.

Table 2 *ASA physical status and Sex distribution*

		Gr-Ln (%)	Gr-LKn (%)	Totaln (%)	Chi-square	P value
ASA	I	18 (60%)	17(56.7%	35 (58.31%)	0.067	0.796
	II	12 (40%)	13(43.3%	25 (41.65%)		
Female		14 (46.7%)	17(56.7%	31 (51.46%)	1.667	0.197
Male		16 (53.3%)	13(43.3%	29 (48.14%)		

Between group analysis was done by chi-square test. Values are expressed as frequency: Within parenthesis is percentage over column total. Values are expressed significant if p<0.05 (CI-95%).
* = Significant ;
** = Highly significant.

The ASA physical status of the patients included in present study was ASA class-I and ASA class-II. Out of 60 patients 35 (58.31%) were from ASA class 1 and 25 (41.65%) were from ASA class 2. p< 0.796 (Table-02,Figure-02). The male patients are 29 (48.14%) and the female patients are 31 (51.46%) out of total 60 patients. The p value is <0.197(Table-02,Fig-03).

The nature of surgery was hand 12 (20%), wrist 06 (10%), elbow joint 16(26.6%) and the forearm 26 (43.16%) out of total 60 patients. And the p value is <0.001. Mean duration for surgery for group L was 49.78 ± 1.20 and for group LK was 5.96 ± 1.46; p<0.867(Table-03).

Table-III *Comparison of types of surgery*

Types of surgery	Gr-L n (%)	Gr-LK n (%)	Total n (%)	Chi-square	P value
Hand	16 (53.28%)	10 (33.3%)	26 (43.16%)	15.600	0.001**
Wrist	05 (16.65%)	11 (36.63%)	16 (26.6%)		
Elbow joint	04 (13.32%)	02 (06.66%)	06 (10%)		
Forearm	05 (16.65%)	07 (23.31%)	12 (20%)		

Between group analysis was done by chi-square test. Values are expressed as frequency: Within parenthesis is percentage over column total. Values are expressed significant if p<0.05 (CI 95%).
* = Significant ;
** = Highly significant.

Base line Mean pulse rate per minute in group L was 76 ± 8.06 and in group LK was 76.76 ± 9.83; p<0.742(Table-04,Fig-05). Mean values of the pulse rate of group L varies from 72.66 ± 5.28 to 82.86 ± 7.80/min. Mean values in group LK varies from 75.86 ± 5.89 to 84.53 ± 6.86/min. There were significant difference in pulse rate between two groups after 30 minutes from starting anaesthesia (p<0.009)

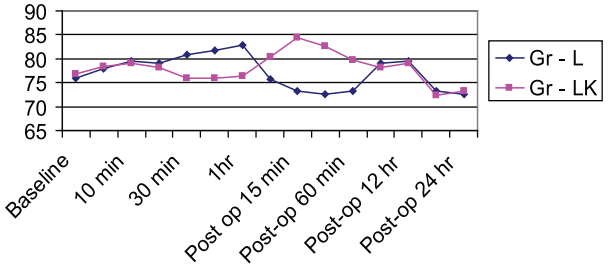

Fig 5 *Changes of pulse rate in different times (mean ± SD)*

The baseline mean arterial pressure in group L was 83.60 ± 9.90 and in group LK was 86.09 ± 10.45; p<0.348(Table-05,Fig-06). Mean values of the mean arterial pressure of group L varies from 82.03 ± 8.88 to 88.36 ± 9.68mmHg. Mean values in group LK varies from 86.09 10.45 to 96.66 ± 10.78mmHg. There were significant difference in mean arterial pressure between two groups in post operative period i.e. 05 minutes after release of the tourniquet (p<0.012).

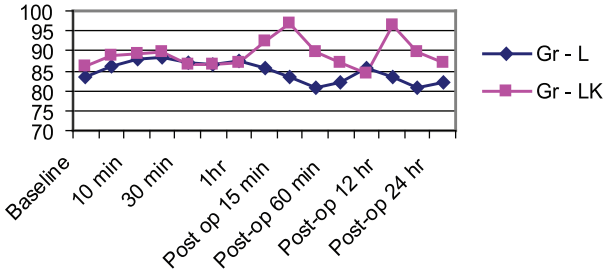

Fig 6 *Changes of mean arterial pressure in different time (mean ± SD)*

The time noted for first analgesic demand in post operative period. It was 27.30 ± 8.18 minutes in group L and 76.40 ± 11.78 minutes for the group LK. The result shows the first analgesic damand is significantly (p<0.000) higher in Group LK than Group L (Table-06,Fig-07).

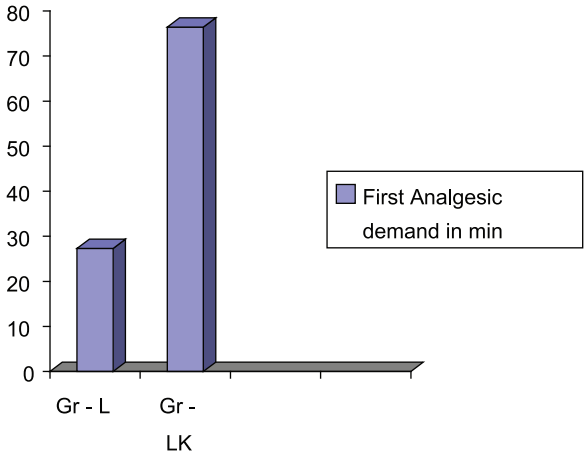

Fig-7 *Comparison of firs analgesic demand in post-operative period.*

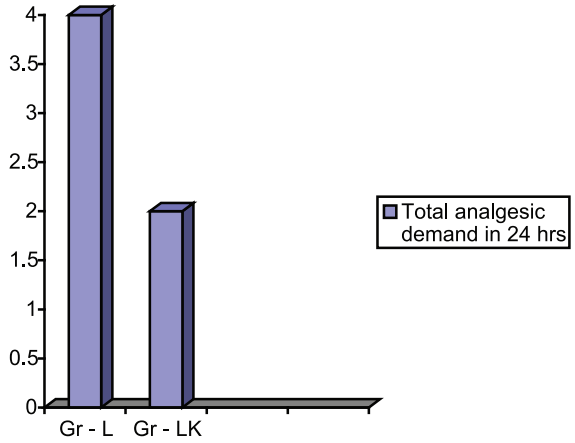

Fig 8 *Comparison of total analgesic demand in 24 hrs*

No patient complaints of moderate or severe pain due to tourniquet or surgery during operation. The mild tourniquet pain was in 07 (23.3%) patients of group L and 18 (60%) patients of group LK in 05 minutes, and 5 (16.7%) patients of group L and 15(50%) patients of group LK in 10 minutes, which is significantly higher, (p<0.003) and (p<0.002) respectively in group LK (Fig.-09). The complaints of mild operative (incision) pain during surgery were 5(16.7%) of group L and 12(40%) of group LK in 00 min, which was significantly (p<0.000) higher in group-LK. There were also complaints of mild operative pain during surgery in 1(3.3%) patients of group L and 09 (30%) patients of group LK in 45 min, and 3(10%) patients of group L versus 13(43.3%) patients of group LK in 60 minutes respectively. These results are also significantly (p<0.005) and (p<0.003) higher in group LK (Fig.-10).

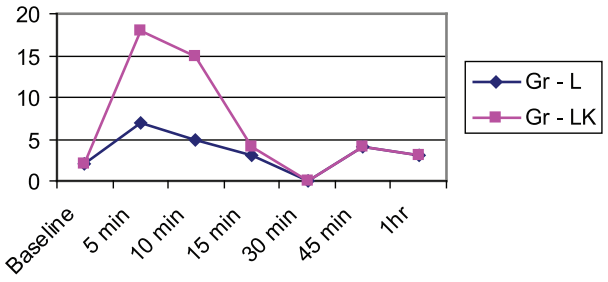

Fig-9 *Incidence of tourniquet pain with the time between the groups*

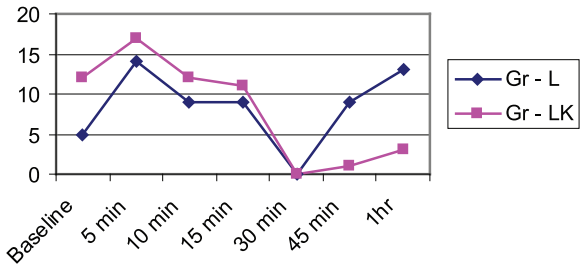

Fig.-10: *Incidence of operative (incision) pain with the time between the groups.*

Discussion

Regional anaesthesia provides several advantages including avoidance of general anaesthesia and associated complications such as cardiopulmonary depression and the need for tracheal intubation. In addition, patients with associated cervical spine injury, regional anaesthesia should reduce the possibility of complications that might occur during tracheal intubation.[17] Furthermore, regional anaesthesia avoids the side effects associated with opioid and non-opioid analgesics, decreases the incidence of postoperative nausea and vomiting (PONV) and provides excellent postoperative pain relief.[18] Adquate postoperative analgesia improves pulmonary function and reduces the incidence of postoperative pulmonary complications.[19] Adequate pain management should reduce the stress response and hypercoagulable state that may result in vaso-occlusive and thromboembolic complications.[20] Furthermore, the sympathetic blockade associated with regional anaesthesia improves regional blood flow, which may decrease thromboembolic complications. A reduced stress response may also improve the myocardial oxygen demand and supply balance and reduce myocardial ischemia, particularly in patients with coronary artery disease and in those with cardiac contusion caused by thoracic trauma. These advantages facilitate recovery, allow early mobilization, and reduce hospital stay, which may decrease overall healthcare costs.[20]

A survey in 1997[21] found that the five most commonly used regional anaesthesia techniques in United States were intravenous regional anaesthesia (80%), axillary, spinal epidural and ankle blocks. Lignocaine 0.5% (3 mg/kg) remains the local anaesthetic of choice for IVRA because of its lower potential of systemic toxicity. In spite of its longer duration of action, Bupivacaine is not recommended for IVRA because of its cardiovascular toxicity. Ropivacaine is a new long-acting amide local anaesthetic with physiochemical properties similar to those of bupivacaine. Unlike bupivacaine, ropivacaine may have a lower potential for systemic toxicity. Chan et al.[22] compared ropivacaine 1.2 mg/kg and 1.8 mg/kg (maximum dose 180 mg) with lidocaine 3 mg/kg for IVRA. They found that compared with lignocaine, IVRA with ropivacaine had similar times to onset of complete sensory and motor block, but produced longer-lasting residual analgesia. Although they did not observe any complications with the use of ropivacaine, the safety of ropivacaine for IVRA remains to be determined.[22]

In an attempt to improve the quality of the block, various adjuvants including opioids (e.g., fentanyl, meperidine, and morphine), nonsteroidal anti-inflammatory drugs (e.g., ketorolac), a_2-adrenergic agonists (e.g., clonidine), sodium bicarbonate, and muscle relaxants (e.g., atracurium and pancuronium) have been added to the local anaesthetic solution with varying degree of success. Although combination of meperidine with lidocaine for IVRA provides a dose-dependent improvement in postoperative analgesia, the incidence of opioid-related side effects is increased.[23] The addition of ketorolac (20 mg) to 0.5% lignocaine for IVRA results in prolonged postoperative analgesia and a reduced need for supplemental analgesics. Increasing the ketorolac dose to 30 or 60 mg does not provide further improvement in the duration of postoperative analgesia or analgesic requirment.[24] The combination of clonidine (150 mg) and lignocaine improves tourniquet tolerance during IVRA but does not improve postoperative analgesia.

However, this combination may result in hypotension and sedation following tourniquet release, particularly if the duration of tourniquet inflation is short.[25]

Malik et. al studied that adding Ketorolac-30 mg to Lignocaine in IVRA, increases the degree of anaesthesia and also provides prolonged post-operative analgesia.[21]

Rivera et al studied that using of Ketorolac (20mg) as an adjunct to the Bier block reduces the need of post-operative analgesia following non-trammatic hand and wrist surgery under Bier's block.[22]

This study was done to see the effect of Ketorolac 30 mg in Bier's block whether it prolongs the duration of block and whether it decreases post operative analgesic demand both in traumatic and non-traumatic hand and wrist surgery.

Though there was no complaints of moderate to severe tourniquet pain or surgical(operative) pain in any group at any time but significant number of patients complaints of mild tourniquet pain at 05 minutes($p<0.003$) and at 10 minutes($p<0.002$) may be due to delayed onset of action by low concentration of drugs in Gr-LK.[23] In the subsequent time the tourniquet tolerance pattern was similar in both groups. Though the significant number of patients ($p<0.046$) of Gr-LK complaints of mild incision pain 00 minute was absolutely vague, as the operation does not starts at 00 minute.[27] But significant number of Gr-L patients ($p<0.005$) at 45 min and ($p<0.003$) at 60 min complaints of mild pain during surgery, which was tolerable and no supplementation of systemic analgesic (pethidine / ketorolac) required.[28] The time noted for first analgesic demand in post-operative period was 27.30± 8.18 min inGr-L and 76.40±11.78min in Gr- LK(Table-06,Fig-07), which shows that the time of first analgesic demand significantly($p<0.000$) higher in Gr-LK than Gr-L. Moreover the total analgesic demand in post-operative 24-hours is also significantly reduced ($p<0.000$) (Figure-08).

Conclusion

Bier's block is most commonly used in hand and wrist surgery of short duration. The use of Ketorolac with Lignocaine as an anaesthetic agent produces significant anaesthesia during the procedure as well as it provides significant post-operative analgesia. The mixture also reduces the tourniquet pain, increases the time of first analgesic demand and reduces the amount of total analgesic demand in post-operative 24 hours period. So these patients required less post-operative analgesic demand, shorter hospital stay and ultimately satisfactory patient outcome.

References:

1. Lundell JC, Silverman DG, Nrull SJ, Reduction of post-burn hyperalgesia after local injection of ketorolac in healthy volunteer. Anaesthesiology, 1996; 84 : 502 – 9.
2. Ruben SS, Steinberg RB, Moclolek H, An evaluation of Analgesic efficacy of IVRA with lignocaine & ketorolac using fore-arm Vs Upper-arm Torniquet Anaesth Analgesia, August, 2002, 95(2), 457-460.
3. Teinbage et al, professional Med. J. Mar, 2008; 15(1): 1 – 4.
4. Malik Jamil, Muhammad Nasir, Khawar Latif, Bier's block: comparison of lignocaine vs lignocane + ketorolc, the professionals. com/v15n1/prof.1157.pdf
5. Rivera JJ, Villecco DJ, Dehner BK, the efficacy of ketorotac as an adjunct to the Bier block for controlling post-operative pain following non-traumatic hand and wrist surgery. AANA J, 2008 Oct; 76(5): 341 – 5.
6. Merskey II,Classification of chronic pain. Pain 1986;S1,5225.
7. Bonica JJ.The management of pain.Lea and Febriger,Philadelphia 1953.
8. Reven SS, Dupart KM. Intravenous regional anaesthesia using lidocaine and Ketorolac. Anaes Analg 1995;81:110-13.
9. Spencer AA. Relieving acute pain. Br J Anaes 1980;52:245-46.
10. Souter AJ, Freedman B. Controversies in the perioperative use of non steroidal anti-inflammatory drugs. Anaes Analg 1994; 79:1178-90.
11. Wolf CJ, Chong MS. Treating postoperative pain by preventing the establishment of central sensitization. Anaes Analg 1999; 77:362.

12. Ruben SS, Steriburg RB. Intravenous regional anaesthesia using lidocaine and Ketorolac. Anaes Analg 1995; 81:110-13.

13. Rice et el, A double blind study of speed of onset of analgesia following intramuscular administration of Ketorolac in comparison to intramuscular morphine and placebo. Anaes 1995; 46;541-44.

14. Salim M. Clinical management of pain. 1994; 23:2631-34.

15. Abdulla and Fadhil.The use of 0.25% Lignocaine with fentanyl and pancuronium for I/V regional anaesthesia. Anaesth Analg 1997; 84:200.

16. Reuben SS, Duprt KM. Comparison of wound infiltration with Ketorolac versus intravenous regional anaesthesia with Ketorolac for postoperative analgesia following ambulatory hand surgery. Reg Anaesth 1996; 21:545-68.

17. Thierbach AR, Lipp MDW: Airway management in trauma patients. Anesthesiol Clin N Am 1999; 17:62-82

18. Pavlin DJ, Rapp SE, Polissar NL, Malmgren JA, Koerschgen M, Keyes H: Factors affecting discharge time in adult outpatients. Anesth Analg 1998; 87:816-26.

19. Ballantyne, JC, Carr DB, deFerranti S, et al: The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. Anesth Analg 1998; 86:598-612.

20. Kehler H: The surgical stress response: should it be prevented? Can J Surg 1991; 34:565-7.

21. Hadzic A, Vloka JD, Koorn R et al: The use of regional anesthesia in ambulatory anesthetic practice. Results of a national survery. Anesthesiology 1997;87:A22.

22. Chan VWS, Weisbrod MJ, Kaszas Z, Dragomir C: Comparison of ropivacaine and lidocaine for intravenous regional anesthesia in volunteers. Anesthesiology 1999; 90: 1602-8.

23. Reuben SS, Steinbrg RB, Lurie SD, Gibson CS: A dose-response study of intravenous regional anesthesia with meperidine. Anesth Analg 1999;88:831-5.

24. Steinberg RB, Reuben SS, Gardner G: The dose? response relationship of ketorolac as a component of intravenous regional anesthesia with lidocaine. Anesth Analg 1998; 86:791-3.

25. Gentili M, Bernard J-M, Bonnet F:Adding clonidine to lidocaine for intravenous regional anesthesia prevents tourniquet pain. Anesth Analg 1999; 88:1327-30.

26. A Choyce, P Peng,; A systematic review of adjuncts for intravenous regional anesthesia for surgical procedures; *Canadian Journal of Anesthesia* 2002 ; 49:32-45

27. J.F. Amito, et. al; Intravenous regional anaesthesia with ketamine; Anaesthesia, 1985 ; 40 : 899-901.

28. Rawal, N; Analgesia for day case surgery; British journal of Anaesthesia 2001; 87 : 73 - 87.