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Original Research Article

Comparative Study of Intra-Articular Clonidine and Bupivacaine for Post-Operative Analgesia in Patients Undergoing Arthroscopic Knee Surgeries

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Conflict of interest: Nil

Abstract:

Background: This study was conducted to evaluate the postoperative analgesic effect of intraarticular clonidine, compare the postoperative analgesic effect of intraarticular clonidine alone and in combination with bupivacaine, study the duration and quality of postoperative analgesia, study side effects if any, and determine as to whether the combination of intraarticular clonidine and bupivacaine is better than clonidine alone.

Methods: This was a hospital-based prospective, randomised, double-blind and comparative study conducted among 60 patients of either sex scheduled to undergo elective arthroscopic knee surgery after obtaining clearance from the institutional ethics committee and written informed consent from the study participants. Patients were assigned to one of the three treatment groups, in double-blinded randomized manner of 20 each. Group I: received 30ml of 0.25% bupivacaine intraarticularly. Group II: received 30ml of 0.25% bupivacaine with 1 ug/kg of clonidine intraarticularl. Group III: received 1ug/kg of clonidine in 30ml of saline intraarticularly.

Results: There was a significant difference in the postoperative pain score between the three groups. The mean value of the VAS score at rest at 4 hours, 8 hours and 12 hours was significantly lower in Group I as compared to Group II and Group III. P-value <0.05. The mean value of the VAS score at movement at 2 hours, 4 hours and 12 hours was significantly lower in Group II as compared to Group I and Group III. P-value <0.05. The mean value of the postoperative sedation score at 1 hour, 2 hours and 8 hours of intraarticular drug administration was significantly higher in Group II as compared to Group I and Group III (p-value <0.05). The mean value of the duration of analgesia in Group II was 533.5 min, which was significantly higher as compared to Group I's 510.9 and Group III's 512.5. (p-value <0.05). The post-operative requirement for analgesics during the first 24 hours of surgery was lower in Group II as compared to Group I and Group III. The mean dose of rescue analgesic required was 3.4 in Group II as compared to 3.95 and 4.4 in Group I and Group III respectively (p-value <0.05). The patient in Group II showed good analgesia and an earlier postoperative discharge from the hospital. The mean time of discharge from the hospital in Group II was 25.35 hours as compared to 27.9 hours and 27.6 hours in Group I and Group III respectively (p-value <0.05).

Conclusion: There were no significant differences among the three treatment groups with respect to duration of surgery, or the time of discharge from OT recovery room. There was mild sedation in intraarticular clonidine group. Thus, the combination of intraarticular clonidine and bupivacaine provided longer duration of analgesia than either of the drug when used alone.

Keywords: Intra-Articular Clonidine, Bupivacaine, Post-Operative Analgesia, Arthroscopic Knee Surgeries.

Introduction

The use of non-opioid analgesics, such as local anaesthetics, ketamine, acetaminophen, and non-steroidal anti-inflammatory drugs (NSAIDs), in conjunction with multimodal or "balanced" analgesic techniques, such as using smaller doses of opioid analgesics, is becoming a more common method of reducing pain following surgery. This study will discuss recent evidence supporting the use of non-opioid analgesic drugs and techniques during the perioperative period to facilitate recovery. Local anaesthetics are frequently administered into joint spaces to offer analgesia throughout and following arthroscopic operations. The alpha-2-adrenergic agonists, clonidine is used as it is known to prolong the duration of action of local anaesthetics. Also, we hypothesised that intraarticular clonidine and bupivacaine would provide more significant analgesia than clonidine alone.

Aims and Objectives

- To study the postoperative analgesic effect of intraarticular clonidine.
- To compare the postoperative analgesic effect of intraarticular clonidine alone and in combination with bupivacaine.
- To study the duration and quality of postoperative analgesia.
- To study any side effects.
- To determine whether the combination of intraarticular clonidine and bupivacaine is better than clonidine alone.

Materials & Methods

This was a hospital-based prospective, randomised, double-blind and comparative study conducted among 60 patients of either sex scheduled to undergo elective arthroscopic knee surgery after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Patients were assigned to one of the three treatment groups, in double blinded randomized manner of 20 each. Group I: received 30ml of 0.25% bupivacaine intraarticularly. Group II: received 30ml of 0.25% bupivacaine with 1 ug/kg of clonidine intraarticularl. Group III: received 1ug/kg of clonidine in 30ml of saline intraarticularly.

Inclusion Criteria

1. Patients with ASA grades I and II.
2. Patients of age between 20 and 60 years.
3. Patients weighing between 40 and 70 kg.
4. Patients undergoing arthroscopic knee surgery.

Exclusion Criteria

1. Patients not willing to participate in the study.
2. Patients being medicated with narcotics pre-operatively or if they had a contra indication to the use of NSAIDS.
3. Patients receiving drugs that interact with clonidine.

Statistical Methods

The data was tabulated and statistically analysed by the Pearson chi-square test and the Kruskal-Wallis test. The p-value of < 0.05 was considered statistically significant.

Results

Table 1: Comparison of Postoperative Diastolic BP

Diastolic BP (mmHg)	Group I			Group II			Group III		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
1hr	71.70	5.16	70.00	82.25	5.31	82.00	81.15	8.51	82.00
2hr	74.35	3.86	73.00	81.60	5.95	83.00	81.50	5.84	82.50
4hr	72.75	4.44	72.00	81.85	7.86	81.50	84.15	4.27	85.00
8hr ^	76.20	4.49	75.00	81.35	7.98	81.00	85.15	4.33	84.50
12hr	74.40	5.34	73.00	82.50	7.00	82.00	87.20	4.12	88.50
24hr	75.50	5.42	73.00	84.95	4.56	86.00	85.50	4.50	86.50

Diastolic BP (mmHg)	One-Way ANOVA			Tukey HSD: P-Value < 0.05?		
	F-value	p-value	Difference is-	Gp I vs. GPII	Gp I vs. GP III	Gp II vs. GPIII
1hr ^	19.837	4.92	Significant	Yes	Yes	No
2hr ^	17.219	0.000182	Significant	Yes	Yes	No
4hr ^	24.129	5.76	Significant	Yes	Yes	No
8hr ^	18.934	7.74	Significant	Yes	Yes	No
12hr^	27.517	1.06	Significant	Yes	Yes	No
24hr	26.905	5.91	Significant	Yes	Yes	No

The mean value of 1-hour postoperative DBP recordings was as follows: Group I, 71.7; Group II, 82.25; and Group III, 81.15. The p-value was 4.92, which was statistically significant.

The mean value of 2-hour DBP recordings was as follows: Group II, 81.6; and Group III, 81.5. The p-value was 0.000182, which was statistically significant. The mean value of 4 hour DBP recordings was as follows: Group I, 72.75; Group II, 81.85; and Group III, 84.15. The p value was 5.76, which was statistically significant. The mean value of 8-hour DBP recordings was as follows: Group I, 76.2; Group II, 81.35; and Group III, 85.15. The p-value was 7.74, which was statistically significant. The mean value of 12-hour DBP recordings was as follows: Group I, 74.4; Group II, 82.5; and Group III, 87.2. The p-value was 1.06, which was statistically significant. The mean value of 24 hour DBP recordings was as follows: Group I: 75.5; Group II: 84.95; and Group III: 85.5. The p-value was 5.91, which was statistically significant.

Table 2: Comparison of Post-Operative VAS at Rest

Post-Operative VAS at Rest	Group I			Group II			Group III		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
1 hr.	0.20	0.41	0.00	0.20	0.41	0.00	0.15	0.37	0.00
2 hr.	0.95	0.76	1.00	1.05	0.89	1.00	1.50	0.51	1.50
4 hr.	2.20	0.52	2.00	2.85	0.49	3.00	2.60	0.50	3.00
8 hr.	3.45	0.61	3.50	3.70	0.47	4.00	4.00	0.65	4.00
12 hr.	4.25	0.44	4.00	5.00	0.65	5.00	5.20	0.77	5.00
24 hr.	0.50	0.51	0.50	0.30	0.47	0.00	0.50	0.61	0.00

Post-Operative VAS at Rest	Kruskal Wallis Test			Tukey HSD: P-Value < 0.05?		
	Chi-Square	P-Value	Difference is-	Gp I vs. GPII	Gp I vs. GP III	Gp II vs. GPIII
1 hr.	0.219	0.896	No Significant	No	No	No
2 hr.	5.408	0.067	No Significant	No	No	No
4 hr.	13.266	0.001316	Significant	Yes	No	No
8 hr.	7.094	0.028805	Significant	No	No	No
12 hr.	18.317	0.0001.5	Significant	Yes	Yes	No
24 hr.	1.808	0.405	No Significant	No	No	No

The comparative data of the VAS (visual analogue scale) at rest for 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, and 24 hours intervals in three groups VAS score at rest at 4 hours in Group I was 2.2, Group II was 2.85, and Group III was 2.6. The p-value was <0.05, which was significant. The VAS score at rest after 8 hours in Group I was 3.45, Group II was 3.7, and Group III was 4.0. The p-value was <0.05, which was significant. The VAS score at rest after 12 hours in Group I was 4.25, Group II was 5.0, and Group III was 5.2. The p-value was 0.000105, which was significant.

Table 3: Comparison of Post-Operative VAS at Movement

Post-Operative VAS at Movement	Group I			Group II			Group III		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
1 hr.	0.30	0.47	0.00	0.40	0.50	0.00	0.40	0.60	0.00
2 hr.	1.75	0.55	2.00	1.30	0.57	1.00	2.40	0.50	2.00
4 hr.	3.80	0.70	4.00	3.30	0.73	3.00	4.50	0.83	4.50
8 hr.	5.50	0.69	5.50	5.10	0.72	5.00	5.55	0.69	6.00
12 hr.	6.70	0.80	6.50	6.40	0.68	6.00	7.05	0.76	7.00
24 hr.	0.55	0.51	1.00	0.50	0.61	0.00	0.40	0.50	0.00

Post-Operative VAS at Movement	Kruskal Wallis Test			Tukey HSD: P-Value < 0.05?		
	Chi-Square	P--Value	Difference is-	Gp I vs. GPII	Gp I vs. GP III	Gp II vs. GP III
1 hr.	0.432	0.806	No Significant	No	Yes	No
2 hr.	25.158	.044	Significant	No	No	Yes
4 hr.	18.567	9.29	Significant	Yes	No	Yes
8 hr.	4.303	0.116	No Significant	No	No	No
12 hr.	6.672	0.035572	Significant	No	No	Yes
24 hr.	0.848	0.655	No Significant	No	No	No

The VAS score at movement at 1 hr, 2 hr, 4 hr, 8 hr, 12 hr, and 24 hr intervals of giving intraarticular drugs in all three groups. The mean value of the VAS score at movement at a 2-hour interval in three groups, Group I 1.75, Group II 1.3, and

Group III 2.4, was significantly variable. The p-value obtained was 3.44, which was statistically significant. The Tukey HSD value demonstrated that Group I's VAS score at movement was higher than Group II's and Group III's.

The mean values of the VAS score at movement at a 4-hour interval were Group I 3.8, Group II 3.3, and Group III 4.5. The p value obtained was 9.29, which was significant. Additionally, the Tukey HSD value demonstrated that the median value of the VAS score at movement in Group III was significantly higher than that of Group II.

The mean values of the VAS score at movement at a 12-hour interval were Group I 6.7, Group II 6.4, and Group III 7.05. The p-value obtained was 0.035572, which was very significant. Group III showed significantly higher vas scores at movement as compared to Group II. The VAS score at movement at 1 hour, 8 hours, and 24 hours is comparable in the three groups. (p-value > 0.05).

Table 4: Comparison of Post-Operative Sedation Score

Post-Operative Sedation Score	Group I			Group II			Group III		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
1 hr.	1.25	0.44	1.00	1.75	0.72	2.00	1.95	0.51	2.00
2 hr.	1.15	0.37	1.00	1.55	0.51	2.00	1.55	0.51	2.00
4 hr.	1.05	0.22	1.00	1.30	0.47	1.00	1.30	0.47	1.00
8 hr.	1.15	0.37	1.00	1.00	0.00	1.00	1.00	0.00	1.00
12 hr.	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00
24 hr.	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00

Post-Operative Sedation Score	Kruskal-Wallis Test			Tukey HSD: P-Value < 0.05?		
	Chi-Square	P-Value	Difference is-	Gp I vs. GP II	Gp I vs. GP III	Gp II vs. GP III
1 hr.	13.998	0.000913	**Significant**	**No**	**Yes**	No
2 hr.	8.631	0.013361	**Significant**	**No**	**No**	**No**
4 hr.	4.828	0.089	Not significant	No	No	No
8 hr.	6.211	0.045	**Significant**	**No**	**No**	**No**
12 hr.	0.000	1.000	Not significant	No	No	No
24 hr.	0.000	1.000	Not significant	**No**	No	**No**

The postoperative sedation scores (POSS) at 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, and 24 hours intervals after giving intraarticular drugs in the three groups The mean value of the post-op sedation score after a 1-hour interval is as follows: Group I: 1.25; Group II: 1.75; Group III: 1.95. The SD values of Gp I were 0.44, Gp II 0.72, and Gp III 0.51. The p-value of 0.000913 was statistically significant. Also, the POSS of Group I was significantly higher than that of Group III, as obtained by Tukey HSD. The mean value of POSS after a 2-hour interval was as follows: Group I 1.15, Group II 1.55, and Group III 1.55. The SD values were Gp I 0.37, Gp II 0.51, and Gp III 0.51. The p value of 0.013361 was statistically significant.

The mean value of POSS after an 8-hour interval was as follows: Group I 1.15, Group II 1.0, and Group III 1.0. The SD values are Gp I 0.37, Gp II 0.0, and Gp III 0.0. The p value of 0.045 was statistically significant. The mean value of POSS after 4 hours, 12 hours, and 24 hours was almost similar and comparable in all three groups. P-value >0.05.

Table 5: Comparison of Duration of Analgesia, No. of Rescue Analgesia and Discharge from Hospital

Variables	Group I			Group II			Group III		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Duration of analgesia (min)	510.9	56.7	481.00	533.5	44.1	540.00	512.50	38.92	505.00
No. of rescue analgesia required in 24 hr. (doses)	3.95	0.83	4.00	3.40	0.50	3.00	4.40	0.50	4.00
Discharge from hospital (hrs.)	27.90	1.89	28.00	25.35	1.27	25.50	27.60	1.98	28.00

Variables	Kruskal-Wallis Test			Tukey HSD: P-Value < 0.05?		
	Chi-Square	P-Value	Difference is-	Gp I vs. GP II	Gp I vs. GP III	Gp II vs. GP III
Duration of analgesia (min)	2.589	0.274	Not significant	**No**	No	**No**
No. of rescue analgesia required in 24 hr (doses)	18.394	0.000101	**Significant**	**No**	**No**	**Yes**
Discharge from hospital (hrs)	19.031	7.37	**Significant**	**Yes**	**No**	**Yes**

The statistical data on quality of analgesia in the form of duration of analgesia, number of rescue analgesics required in the first 24 hours, and time of discharge from the hospital. The mean value of duration of analgesia in the three groups was as follows: Group I: 510.9 min; Group II: 533.5 min; and Group III: 512.5 min. The SD values are Gp I 56.76, Gp II 44.16, and Gp III 38.92. The p-value obtained was 0.274, which was statistically significant.

The mean value of the number of rescue analgesia required in 24 hours in the three groups is Group I, 3.95; Group II, 3.4; and Group III, 4.4. The p-value obtained was 0.000101, which was statistically significant. Group II required significantly fewer rescue doses as compared to Group III.

The mean value of time of discharge from the hospital in Group I was 27.9 hours, Group II was 25.35 hours, and Group III was 27.6 hours. The p-value obtained was 7.37, which was statistically significant. Group II was discharged significantly earlier than Group I and Group III.

Discussion

The mean values of the time of study drug given after induction in Group I were 69.6±12.61 min, in Group II was 71.45±17.79 min, and in Group III was 68.75±16.62 min, which was comparable and the difference was statistically not significant.

The mean values of time of discharge from the recovery room in Group I were 144.5±7.81 min, in Group II 140.05±4.45, and in Group III was 140.35±5.58, which were comparable and the difference was statistically not significant.

The mean duration of surgery in Group I was 144.5±7.81 min., in Group II was 140.05±4.45min and in Group III 140.35±5.58 min which was comparable and the difference was statistically not significant.

The above results are in concurrence with the following studies.

Goodwin RC, [1] et al. 2005; Short-term analgesic effects of intra-articular injections after knee arthroscopy. Patients receiving the study medication preoperatively had significantly lower pain scores at the first measurement (t = 0) than those receiving the study medication postoperatively (p = .0343). There was no statistically significant effect of the timing of the treatment medication administration at either 60 or 120 minutes postoperatively.

In 1999, Reuben SS et al. [2] investigated the use of intraarticular clonidine for postoperative analgesia following outpatient arthroscopic knee surgery. 50 patients were divided into five groups at random and given either clonidine (subcutaneously or i.a. route) or a saline placebo with or without i.a. bupivacaine. Regarding the timing of study medication administration, the length of surgery, or the time required for recovery room release, there were no appreciable variations among the five treatment groups.

Postoperative Hemodynamic Characteristics of the Patients Heart Rate

- The mean post-operative heart rate 1 hour after giving intraarticular (IA) drug in Group I was 90.05±2.63, in Group II was 89.35±3.8 and in Group III was 87.95±3.41 was comparable and statistically not significant.
- The mean post-operative heart rate 2 hours after giving intraarticular (IA) drug in Group I was 88.2±4.53, in Group II was 87±4.02 and in Group III was 83.75±5.23. Group III, which received only intraarticular clonidine showed a decrease in heart rate (p-value < 0.05), as compared to Group I, which received only IA bupivacaine.
- The mean post-operative heart rate after 4 hours, 8 hours, 12 hours, and 24 hours of giving the IA drug in the three groups was comparable and statistically not significant.

Thus, it is seen that there was no episode of bradycardia after administration of intraarticular clonidine. We opted to use a lower dosage of clonidine (1 μg/kg), in contrast to the trial by Gentili et al. [3] where participants got 150 μg (about 2 μg/kg).

Blood Pressure

The mean postoperative systolic BP after 1 hour, 2 hours, 8 hours, 12 hours, and 24 hours was comparable in the three groups. Although the values of postoperative diastolic blood pressure in Group I were significantly lower than those in Group II and Group III, there was no episode of hypotension in any of the groups.

The above results are in agreement with the following studies:

In 1999, Wanda Joshi et al [4] investigated intraarticular clonidine and/or morphine for postoperative analgesia following outpatient arthroscopic knee surgery. They assessed 60 patients having arthroscopic repair of the meniscus in the knee while sedated and under local anaesthesia. No patient had bradycardia (heart rate ≤ 60 bpm), hypoxemia (SpO2 ≤ 90%), or hypotension (mean arterial pressure ≤ 20% baseline). [5]

Reuben SS. et al. 1999 studied postoperative analgesia for outpatient arthroscopic knee surgery with intrarticular clonidine. 50 patients were divided into five groups at random and given either clonidine (subcutaneously or i.a. route) or a saline

placebo with or without i.a. bupivacaine. No patient had bradycardia (heart rate 60 bpm) or hypotension (mean arterial pressure 20% of baseline).

Postoperative Pain Scores

Compared to Group I, Group II showed significantly higher VAS scores at rest. But the VAS score remained below 5, even 8 hours after intraarticular (IA) bupivacaine and clonidine. Thus, the combination of IA bupivacaine and clonidine provided efficient analgesia. [6]

Compared to Group II, Group III showed significantly higher VAS scores at rest. Thus, the combination of IA bupivacaine and clonidine is more effective than IA clonidine alone. VAS score remained below 5, even 8 hours after IA clonidine, which showed efficient analgesia of IA clonidine.

Comparison of Post-Operative VAS Score at Movement

Compared to Group I, Group II showed significantly lower values of the VAS score at movement. The VAS score at movement after 4 hours of giving IA clonidine remained less than 5. Thus, Group II that received a combination of IA bupivacaine and clonidine showed good analgesia as compared to Group I that received IA bupivacaine alone. [7]

Compared to Group III, Group II showed significantly lower values of the VAS score at movement. Thus, the analgesia provided by the combination of IA bupivacaine and clonidine is superior to that of only IA clonidine.

The above results prove that IA clonidine enhances the analgesic effect of bupivacaine and the combination is synergistic and superior.

The above results are in concurrence with the following studies:

A randomised, double-blind trial conducted by Chan ST. et al. in 1995[5] investigated the analgesic effects of morphine and bupivacaine intra-articular injections during therapeutic arthroscopic knee surgery. A visual analogue score was used to measure post-operative discomfort. From 4 hours onward during the 24-hour research period, the morphine group had a substantially reduced pain score compared to the control group ($p<0.05$ at 4 hours and $p<0.001$ at 24 hours). During the first four hours, the bupivacaine group scored less painfully than the control group ($p<0.001$ at one hour and p 0.05 at two hours). It had comparable analgesic effectiveness to morphine after 4 hours. For patients who received therapeutic arthroscopic knee surgery, the combination of the two medications produced adequate analgesia for the duration of the trial ($p<0.001$ at 1, 2, and 24 hours and $p<0.05$ at 4 hours), and it proved to be a straightforward, secure, and efficient analgesic approach.

Gentili M. et al., (1996) first studied the peripheral analgesic effect of intra-articular clonidine. At the conclusion of the surgical process, 40 ASA I–III patients scheduled for arthroscopic knee surgery under general anaesthetic were randomly divided into 4 groups of 10 patients each. Patients in Group 1's control group got 20 ml of intra-articular isotonic saline as a control. Patients in Group 2 got an injection of isotonic saline and 150 micrograms of clonidine diluted in 20 cc. Group 3 patients received 150 micrograms of clonidine subcutaneously together with 20 ml of intra-articular isotonic saline. In group 4, the knee joint received an injection of 1 mg of morphine diluted in 20 ml of isotonic saline. A visual analogue scale (VAS) was used to measure postoperative pain in a double-blind method at 1, 2, 3, 4, 6 and 24 hours following surgery. At 1 and 2 hours following surgery, VAS values in groups 2 and 4 were considerably lower than in groups 1 and 3.

Comparison of Post-Operative Sedation Score (POSS)

Postoperative sedation score (POSS) in Group II and Group III was higher as compared to Group I at 1 hr and 2 hr intervals after giving IA drugs. Thus, patients who received IA Clonidine showed mild sedation as compared to those who received only bupivacaine. The POSS remained below 2 even after 1 hour of giving the IA drug.

The above results are in concurrence with the following studies:

De Andres J. et al., 1998[6] carried out a study for the comparison of three different regimens in intra-articular analgesia after arthroscopic knee surgery. In a prospective study, 103 patients between the ages of 16 and 80 with ASA grades I to II who were scheduled for arthroscopic meniscectomy were divided into one of four groups at random: Group 1 (n = 25): 0.25% bupivacaine (50 mg) intra-articular (IA); Group 2 (n = 27); 1 mg of 0.1% preservative-free morphine chloride in saline; Group 3 (n = 26); and Group 4 (n = 25): normal saline (0.9%). There were no discernible sedation or side effect differences between groups in the multifactorial analysis.

Reuben SS. et al., (1999) studied postoperative analgesia for outpatient arthroscopic knee surgery with intrarticular clonidine. 50 patients were divided into five groups at random and given either clonidine (subcutaneously or i.a. route) or a saline placebo with or without i.a. bupivacaine. On a scale of 1 to 5, the degree of sedation was determined (1 = fully awake, 2 = awake but sleepy, 3 = asleep but awake to verbal orders, 4 = sleeping but awake to tactile stimulation, and 5 = asleep and not awake to any stimulus). Between one and two hours after surgery, there was no discernible variation in sedation levels.

Duration of Analgesia

In our study, the duration of analgesia was considered to be the time from the IA injection of the study drug to the first requirement for supplemental oral analgesics. The mean duration of analgesia in Group I was 510.9±56.76 min, in Group II it was 533±44.16 min, and in Group III it was 512±38.92 min. The difference was statistically significant ($p<0.05$).

Thus, Group II, which received a combination of IA Clonidine and bupivacaine, showed a significantly longer duration of analgesia as compared to Group I and Group III, which received only bupivacaine and Clonidine, respectively.

The above results are in concurrence with the following studies:

In a 1996 study, Gentili M. et al. evaluated the possible analgesic effects of clonidine following intra-articular injection. At the conclusion of the surgical process, 40 ASA I–III patients scheduled for arthroscopic knee surgery under general anaesthetic were randomly divided into 4 groups of 10 patients each. IA Clonidine group had a considerably longer interval (533 +/- 488 min) between intra-articular injection and subsequent postoperative analgesic treatment than did the control group and subcutaneous clonidine group (70 +/- 30 min and 132 +/- 90 min, respectively) (P 0.05). Group IA's morphine group (300 +/- 419 min) did not differ significantly from the other groups. They came to the conclusion that the analgesia produced by a modest dosage of intra-articular clonidine is unrelated to the drug's vascular uptake.

Yang et al, 1998, postoperative analgesia by intra-articular neostigmine in patients undergoing knee arthroscopy. 60 patients having arthroscopic meniscus repair during general anesthesia were randomized to receive, in a double-blind manner, after operation 125, 250, or 500 micro gram intra-articular neostigmine; 2 mg intra-articular morphine; or as control groups intra-articular saline or 500 micro gram neostigmine given subcutaneously (SC).Analgesia lasted longer after 500 micro gram intra-articular neostigmine (350 +/- 126 min) compared with intra-articular morphine (196 +/- 138 min; $P < 0.05$) or with the control groups (intra-articular saline, 51 +/- 11 min; SC neostigmine, 46 +/- 8 min; $P<0.05$).

Number (Doses) of Rescue Analgesia

Compared to Group I and Group III, Group II required fewer doses of rescue analgesia. Group II that received a combination of IA bupivacaine and clonidine showed superior quality of analgesia as compared to Group I and Group III that received only bupivacaine and clonidine, respectively.

The above results are in concurrence with the following studies:

After arthroscopic knee surgery, Christoph Stein[7] researched the analgesic impact of intraarticular morphine. They looked at 52 patients who had received one of four injections at the conclusion of surgery in a double-blind, random experiment. The patients in group 1 (n = 18) received 1 mg of morphine intraarticularly and saline intravenously; those in group 2 (n = 15), saline intraarticularly and 1 mg of morphine intravenously; The mean (±SD) consumption of supplemental analgesic medication per 24 hours was significantly lower in group 1 (36±51 mg of diclofenac and 1.2±3.4 mg of meperidine) than in group 2 (75±42 mg of diclofenac and 14±18 mg of meperidine, $P<0.05$).

Discharge from Hospital

Compared to Group I and Group III, Group II showed an earlier discharge from the hospital. Group II that received a combination of IA bupivacaine and clonidine had efficient analgesia, good patient satisfaction, and thus an earlier discharge from the hospital.

The above results are in concurrence with the following studies:

In 1999, Wanda Joshi et al. investigated intraarticular clonidine and/or morphine for postoperative analgesia following outpatient arthroscopic knee surgery. They assessed 60 patients having arthroscopic repair of the meniscus in the knee while sedated and under local anaesthesia. Patients were divided randomly into four IA groups following surgery. Compared to either group IA clonidine or IA morphine, patients in group IA clonidine or morphine had longer analgesic durations and less 24-hour analgesic usage. They were unable to show a difference in discharge times between the research groups despite this early postoperative improvement in pain management.

In 1999, Reuben SS. et al. investigated the use of intrarticular clonidine for postoperative analgesia following outpatient arthroscopic knee surgery. 50 patients were divided into five groups at random and given either clonidine (subcutaneously or i.a. route) or a saline placebo with or without i.a. bupivacaine.

Conclusion

There were no significant differences among the three treatment groups with respect to duration of surgery, or the time of discharge from OT recovery room. There was mild sedation in intraarticular clonidine group. Thus, the combination of intraarticular clonidine and bupivacaine provided longer duration of analgesia than either of the drug when used alone.

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