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NALBUPHINE AS A SUPPLEMENT TO BALANCED ANESTHESIA IN OFF PUMP CORONARY ARTERY BYPASS SURGERY

Anaesthesiology

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ABSTRACT

Nalbuphine is known as a potent analgesic.It is a synthetic partial kappa agonist and mu antagonist opoid of the phenanthrene series.It has less side effects like nausea,vomiting and respiratory depression.The onset of action of nalbuphine is 5-10 minutes and duration of action is 3–6 hours. It has minimal side effects with the dosage of 0.2-0.4 mg/kg. Accordingly, we compiled this study using nalbuphine as a supplement to balanced anesthesia and postoperative analgesia in off pump coronary artery bypass (OPCAB) patients.Nalbuphine was used as an adjuvant during induction and maintenance of anesthesia and evaluation of hemodynamics and postoperative analgesia was done.

KEYWORDS

Analgesic, Postoperative, Off Pump Coronary Artery Bypass, Nalbuphine, Balanced Anesthesia.

Introduction –

The concept of 'balanced' anesthesia requires a potent analgesic, albeit to achieve the proper balance between the potency and safety of these drugs is still a challenge.[1]The opioids come with a clause,they have side effects like respiratory depression,nausea, vomiting and few are under the restriction of narcotic laws.[2,3]

Nalbuphine provides robust analgesia, less respiratory depression, has less risk of chest wall rigidity and apnea.[3]The features such as cardiovascular stability,longer duration of action,minimal postoperative nausea vomiting and potential safety in overdosage makes it an agent of choice in balanced anesthesia.[4]

Materials and Methods –

We studied 60 patients by dividing randomly in 2 groups of 30 each.Patients receiving nalbuphine were in Group N and patients who received pentazocine plus midazolam were in Group PM. Randomization was done with sealed opaque envelope technique. We considered the average visual analogue score (VAS) score to decrease by 1.5 as an important goal. These data suggested that a power of 90% for detecting a difference in VAS by 1.5 and a level of 0.05 would be obtained with 28 patients in each group. Inclusion criteria was patients posted for OPCAB surgery with single vessel disease or double vessel disease.Exclusion criteria were patients with respiratory problems, deranged liver and renal function tests, patients with EF <30%, hemodynamically unstable, on intraaortic balloon pump(IABP), associated valvular heart diseases, acute myocardial infarction, on temporary pacemaker, intraoperative conversion to on pump coronary artery bypass grafting(CABG).Parameters were monitored from premedication time to start of coronary grafting. Later the hemodynamics are influenced during grafting by factors like myocardial ischemia during anastomosis and mobilization, positioning or stabilization of the heart and also inotrope usage. After attaching all standard American Society of Anesthesiologist(ASA) monitors drugs were given by the anesthesiologist who was unaware of the premedicant drug.

Study group (Group N) was given Inj Nalbuphine 0.2 mg/kg intravenous(iv) slow for induction alongwith Inj Etomidate 0.2–0.3 mg/kg and Inj Rocuronium 0.6 mg/kg iv. Control group (Group PM) received Inj Pentazocine 0.3mg/kg and Inj Midazolam 0.05 mg/kg iv instead of Inj Nalbuphine, rest all drugs were same. Maintenance of anesthesia was done with Inj Propofol upto 50 mg was given whenever required and Inj Fentanyl 50 mcg was given only once at the start of grafting. Inj Atracurium iv was given intermittently. Sevoflurane 1-2% was administered throughout the procedure till completion of sternal wiring. Parameters studied were hemodynamics during induction and postoperative period, sedation score, VAS prior to postoperative analgesia, duration of postoperative analgesia.Comparison of period from extubation to administration of postoperative analgesia was also done.Side effects likehyper tension,hypotension,tachycardia, bradycardia,respiratory depression,nausea vomiting,shivering, psychomimetic effects and pruritus were monitored.

- The four point sedation score was followed
- 0- Awake and alert
- 1- Mildly sedated,easily aroused
- 2- Moderately sedated, aroused by shaking
- 3- Deeply sedated, difficult to be aroused by physical stimulation

Vomiting was defined as forcible expulsion of gastric contents orally. The magnitude of pruritus was defined on treatment either with reassurance or medications like tablet fexofenadine 120mg once daily.[1]Pain was assessed by VAS using 10 cm horizontal scale with no pain (0), mild pain (1-3), moderate pain (4-6) and severe pain (7-10).Duration of analgesia was noted.Sedation was assessed using sedation score.

Results –

The homogeneity of two groups was verified by lack of significant differences with respect to demographic data.The mean age was comparable 55.00±8.59 in group N and 59.00±7.40 in group PM.The mean weight was comparable 56.47±6.16 in group N and 55.97±5.93 in group PM.

Group N showed lesser tachycardia(Table 1), better maintenance of systolic blood pressure(SBP)(Table 2), diastolic blood pressure (DBP)(Table 3) as compared to Group PM. Sedation score(Table 4) and VAS(Table 5) were better in group N. VAS Score in Group N is 6.367±0.809 in Group N and 6.567±0.817 in Group PM with p value 0.345 not significant.

The duration of post-operative analgesia was longer in group N than group PM. It was 291.7±29.5 in Group-N and 179.0±26.4 in Group-PM with significant p value (0.000).Comparison of period from extubation to administration of postoperative analgesia in minutes was group-N 62.0±20.0 and in group-PM was 36.5±19.6 with significant p value (0.000).

Side effects like pruritus,shivering,nausea vomiting and psychomimetic effects were not significant statistically.Awareness during anaesthesia was not reported in any of our patient in both the groups. Side effects like hypotension in group-N was in 1patient (3.33%) and nil in group-PM and hypertension in group-PM was in 1 patient (3.33%) and nil in group-N and tachycardia, nausea/vomiting in 2 patients (6.66%) in group-PM and nil in group-N. Shivering in group-N was in 1 patient (3.33%) and nil in group-PM.No incidence of psychotomimetic effects and bradycardia occurred in any patient in both the groups.The sedation score, VAS score are described in detail in tables.

All Statistical analysis was done by using Minitab 15.Descriptive statistics were summarized as mean and standard deviation(SD) when the results were normally distributed and as median and range when they were not. Student's t-test was used to determine the significance of normally distributed parametric values and Mann-Whitney test for nonnormally distributed data. Categorical variables were presented using percentage. Statistical significance was accepted at $P<0.05$.

The abbreviations used in the table are -

A-PM – One minute after premedication, AF-N – Five minute after

Nalbuphine, A-IND – After Induction, AT INT – At Intubation, AF EXT – After Extubation.

Table 1 -

Heart Rate Beat/min	Group-N	Group-PM	t-Test	P-value
	Mean±SD	Mean±SD		
Baseline	74.80±7.19	74.03±7.50	0.40	0.688 NS
A-PM	77.00±7.02	74.33±6.89	1.48	0.143 NS
AF-N	76.20±5.64	80.27±7.08	-2.46	0.017 S
A-IND	73.87±5.30	76.87±8.54	-1.63	0.109 NS
AT INT	96.33±6.13	104.40±7.23	-4.66	0.000 S
1 min	92.77±5.33	103.40±6.28	-7.07	0.000 S
2 min	89.97±5.39	100.07±6.38	-6.63	0.000 S
3 min	87.03±5.98	94.27±7.35	-4.18	0.000 S
4 min	84.33±5.80	88.80±7.00	-2.69	0.009 S
5 min	81.40±5.99	87.20±6.29	-3.66	0.001S
10 min	78.13±5.63	84.07±7.78	-3.38	0.001 S
15 min	74.67±5.05	78.00±5.99	-2.33	0.023S
30 min	86.60±3.49	74.80±7.19	8.08	0.000 S
60 min	88.27±7.04	77.00±7.02	6.21	0.000 S
90 min	78.4±10.7	76.20±5.64	0.99	0.326 NS
120min	88.87±1.94	73.87±5.30	14.55	0.000 S

Table 2 -

SBP at	Group-N	Group-PM	t-Test	P-value
	Mean±SD	Mean±SD		
Baseline	115.67±7.47	114.93±9.96	0.32	0.748 NS
A-PM	118.20±6.81	115.17±9.56	1.42	0.163NS
AF-N	117.00±6.76	118.60±9.25	-0.76	0.448 NS
A-IND	111.00±5.48	116.67±9.73	-2.78	0.008 NS
AT INT	136.83±4.80	145.00±6.41	-5.59	0.000 S
1 min	132.27±4.69	139.00±7.89	-4.02	0.000 S
2 min	127.80±5.29	137.33±5.90	-6.59	0.000 S
3 min	124.13±4.93	132.07±6.01	-5.54	0.000 S
4 min	121.87±4.90	128.87±7.48	-4.29	0.000 S
5 min	119.80±5.18	123.87±7.26	-2.50	0.016 S
10 min	115.60±4.97	121.47±7.89	-3.45	0.001S
15 min	110.67±3.21	120.13±6.47	-7.18	0.000 S
30 min	132.33±2.35	115.67±7.47	11.66	0.000 S
60 min	128.67±4.01	118.20±6.81	7.25	0.000 S
90 min	129.40±9.01	117.00±6.76	6.03	0.000 S
120min	128.67±4.01	111.00±5.48	14.25	0.000 S

Table 3 -

DBP at	Group-N	Group-PM	t-Test	P-value
	Mean±SD	Mean±SD		
Baseline	73.00± 7.59	75.70± 8.83	-1.27	0.209 NS
A-PM	75.20± 6.68	76.03± 6.94	-0.47	0.637 NS
AF-N	75.13± 4.45	77.53± 7.57	-1.50	0.141NS
A-IND	71.70± 4.95	77.00± 8.80	-2.88	0.006 S
AT INT	87.13± 5.37	91.7±10.1	-2.20	0.033 S
1 min	83.53± 4.92	88.4±11.1	-2.19	0.034 S
2 min	80.00± 4.61	84.73± 8.25	-2.74	0.009S
3 min	76.60± 4.96	85.07± 9.18	-4.44	0.000S
4 min	75.27±4.65	83.07± 8.96	-4.23	0.000S
5 min	73.13± 5.16	77.47±7.37	-2.64	0.011S
10 min	70.60± 5.18	76.20± 8.01	-3.22	0.002S
15 min	70.00± 4.61	76.20± 7.54	-3.84	0.000S
30 min	87.47± 3.15	73.00±7.59	9.64	0.000S
60 min	85.33± 3.98	75.20± 6.68	7.14	0.000S
90 min	86.93± 6.76	75.13±4.45	7.99	0.000S
120min	76.53± 5.85	71.70±4.95	3.46	0.001S

Table 4 -

Sedation Score				Mean Rank		Mann-Whitney	
		Group-N	Group-MP	Group 1	Group 2	Z	p-Value
AE	Range	2-4	2-4	24.37	36.63	-2.982	0.003 S
	Median (IQR)	2(1)	3(0.5)				
5 min	Range	2-3	1-4	25.4	35.6	-2.545	0.011 S
	Median (IQR)	2(1)	3(1)				
30 min	Range	1-4	1-5	25.67	35.33	-2.652	0.008 S
	Median (IQR)	2(0)	2(1)				
60 min	Range	1-4	2-5	20.87	40.13	-4.517	0.000 S
	Median (IQR)	2(1)	4(1)				
90 min	Range	1-4	3-5	24.03	36.97	-3.172	0.002 S
	Median (IQR)	3(1)	4(1)				
120 min	Range	2-4	3-4	26.6	34.4	-1.989	0.047 S
	Median (IQR)	3(0.250)	3(1)				
3 hrs	Range	2-4	2-4	28.22	32.78	-1.287	0.198
	Median (IQR)	3(1)	3(0)				
4 hrs	Range	1-3	2-3	26.55	34.45	-2.153	0.031 S
	Median (IQR)	2(0)	2(1)				
6 hrs	Range	1-3	2-3	26.03	34.97	-2.685	0.007 S
	Median (IQR)	2(0)	2(1)				
8 hrs	Range	1-3	1-3	30.47	30.53	-0.23	0.982 NS

Table 5 -

VAS Score				Mean Rank		Mann-Whitney Test	
		Group-N	Group-MP	Group 1	Group 2	Z	p-Value
AE	Range	1-3	2-3	27.27	33.73	-2.311	0.021 S
	Median (IQR)	2(0)	2(0)				
5 min	Range	1-4	2-8	21.33	39.67	-4.440	0.000 S
	Median (IQR)	2(1)	3(1)				
30 min	Range	1-7	0-7	25.65	35.35	-2.245	0.025 S
	Median (IQR)	4(1)	4(2)				
60 min	Range	0-8	0-7	36.43	24.57	-2.681	0.007 S
	Median (IQR)	6(2.250)	1(6)				
90 min	Range	0-7	0-2	24.7	36.3	-2.827	0.005 S
	Median (IQR)	0(0)	1(1)				
120 min	Range	0-2	1-4	17.25	43.75	-6.172	0.000 S
	Median (IQR)	0(0)	2(2)				
3 hrs	Range	0-2	2-6	15.7	45.3	-6.799	0.000 S
	Median (IQR)	0(0.250)	3(2)				
4 hrs	Range	0-4	2-6	20.87	40.13	-4.620	0.000 S
	Median (IQR)	2(1)	5(4)				
6 hrs	Range	1-6	2-4	40.87	20.13	-4.896	0.000 S
	Median (IQR)	4.5(2)	2(0)				
8 hrs	Range	2-3	1-5	25.1	35.9	-2.872	0.004 S
	Median (IQR)	2(0)	2.5(1)				

Discussion –

The analgesic potency of nalbuphine is equivalent to that of morphine on a milligram basis. Also, the side effects like nausea,vomiting and respiratory depression are less owing to its antagonistic effects of mu receptors.[5]Fentanyl is associated with increased risk of hypoxemia and apnea which is undesirable in patients with compromised cardiac status whereas nalbuphine has a safety profile with minimal effects on cardiovascular function.[6]Moreover, it causes no significant histamine release.[7] Further convenience lies in the fact that nalbuphine is not subject to restriction of narcotic laws and is freely available.[2,3]

OPCAB surgery requires maintenance of hemodynamic parameters. Tachycardia or hypertension increases the myocardial oxygen consumption hence are not permissible during OPCAB. According to literature nalbuphine prevents marked rise in heart rate and mean blood pressure associated with laryngoscopy and intubation.[4]Perhaps,sedation is a recognized feature of nalbu phine treatment.[8] Both analgesia and sedative actions of nalbuphine were exploited in our study during induction of anesthesia and postoperative analgesia.

Nalbuphine has a better safety profile than morphine regarding pruritus and respiratory depression.[9]Interestingly,it is as effective as naloxone in reversing postoperative opoid induced respiratory depression.[10]Also, the efficacy of nalbuphine is similar to fentanyl as intravenous analgesic during surgery with longer duration of postoperative analgesia with less respiratory depression.[3] The other advantage of nalbuphine is it has ceiling effect for respiratory depression and causes less nausea,vomiting compared to morphine, pethidine or pentazocine.[11,12]Furthermore,Januzzi RG have concluded that nalbuphine can be used as a first line treatment of opoid induced pruritus.[13]

Conclusion - Nalbuphine can be used to supplement anesthesia in OPCAB surgery during induction of anesthesia to help maintain hemodynamic stability and it also provides robust postoperative analgesia.

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