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Comparison Of 0.5%Bupivacaine And 0.5% Bupivacaine Plus Buprenorphine in Brachial Plexus Block

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Abstract:
Introduction*: Opioids are well studied adjuncts although the evidence regarding the analgesic benefit of opioid adjuncts remains equivocal. The effectiveness of 0.5%Bupivacine and 0.5% Bupivacaine plus Buprenorphine into brachial plexus sheath was evaluated.*
Materials and methods*: The study was a comparative study carried out at GGH, Guntur. 60 ASA I and II patients undergoing elective upper limb surgeries, aged between16-70 years were randomly allocated into two groups of 30 each. All patients received 0.5% of Bupivacaine at 2mg/kg bodyweight. In addition, 30 patients in group B received Buprenorphine hydrochloride (2µg/kg) .Using VAS score the analgesia was evaluated every hourly for six hours, every two hours for next twelve hours and then every sixth hourly till 48 hours.*
Results: *A significant difference in the duration of analgesia was found between the groups. The duration of analgesia was longer in Bupivacaine plus Buprenorphine group than Bupivacaine group (22.18+/-12.13 hrs versus 14.13+/-8.41 hrs).*
Conclusion: *We conclude that Buprenorphine as an adjunct administered with local anesthetics into brachial plexus sheath is an efficient way to prolong the duration of analgesia in the peri-operative period for upper limb surgeries.*
Key Words: *Analgesics, Buprenorphine, Bupivacaine; pain, peri-operative, anaesthesia, conduction: brachial plexus.*

I. Introduction

General anaesthesia was one of the most common methods employed to provide anaesthesia for upper limb surgeries. With the introduction of newer and safer local anaesthetics and better advantages, regional anaesthesia has taken over as the principal technique for upper limb surgeries. There are many advantages of brachial plexus block for upper limb surgeries over general anaesthesia, namely effective analgesia with good motor blockade, awake patient, extended post operative analgesia, and early ambulation. Supraclavicular and Infraclavicular techniques are more effective in producing complete anaesthesia of all the branches of the brachialplexus as the narrowest part of the plexus is encountered by these techniques.

II. Objectives:

To compare between 0.5% Bupivacaine with 0.5% Bupivacaine plus Buprenorphine with respect to –
Onset of Sensory and motor blockade
Duration of sensory and motor blockade
Duration of analgesia
Untoward side effects.

III. Methodology

Source Of Data:

60 patients admitted to GGH, Guntur undergoing upper limb surgery lasting more than thirty minutes were included in the study. The elective surgical interventions were internal fixation of bones with plates and screws, excision of bone cysts, reconstructive and other surgeries involving upper limb.

Inclusion Criteria:

1. Patients with ASA1 and II physical status,
2. The age group of 16 to 70 years,
3. Both sexes
4. Undergoing elective surgeries

Exclusion Criteria:
1.Patients with age less than 16 and greater than 70 years.
2.Patients with coagulopathy or on anti coagulants.
3.Patients with peripheral neuropathy.
4.Patients who had received opioid in the past twelve hours.
5.Patients with history of substance abuse.
6.Local cutaneous infections.
7.Pregnant patients.
8.Patients with allergy to local anaesthetics and Buprenorphine.
9. ASA class III and IV patients;
10.Patients undergoing emergency surgical procedures.

Preoperative Preparation:

The study protocol was approved by the hospital ethical committee. All the patients underwent thorough preanaesthetic evaluation on the day prior to surgery. The anaesthetic procedure to be carried out was explained. They were informed about the development of paresthesia. Patients were reassured to alleviate their anxieties. A written informed consent was taken. They were educated regarding the visual analogue scale.

Method Of Collection Of Data:

Supraclavicular brachial plexus block was carried out as an elective procedure on the patients undergoing upper limb surgery. Sixty patients were randomly allocated into two groups (group A, n=30and group B, n=30). All drugs solutions were prepared by an anaesthesiologist involved in the administration of anaesthesia, patient care and data collection.

Group A (n=30): Received brachial plexus block with 0.5% Bupivacaine at the dose of 2mg/kg body weight.
Group B (n=30): Received brachial plexus block with 0.5 % Bupivacaine plus Buprenorphine 2 µg/kg into the solution.

All the necessary equipments and drugs needed for administration of general anaesthesia and for resuscitation were kept ready in order to manage in case of failed block or toxic reactions occurring during the procedure.

Procedure

Under aseptic precautions brachial plexus block was performed by Supraclavicular approach (classical / perivascular) with patients placed in supine position. Paresthesia in the forearm or hand was elicited. After negative aspiration for air or blood appropriate drugs were injected. Group A received 0.5% Bupivacaine at the dose of 2mg/kg body weight.Group B received 0.5% Bupivacaine at the dose of 2mg/kg body weight plus Buprenorphine 2 µg/kg .A separate 5 ml injection of 1% lidocaine plain was made for an intercostobrachial nerve block in the axilla to provide anaesthesia for application of tourniquet.
The effects of anaesthetics on the following parameters were observed;
1. The **time of onset** for sensory blockade, defined as time between injection and total abolition of pinprick response, was evaluated in four nerve areas (radial, ulnar, median and musculocutaneous) at every 3 minutes until 45 minutes after the injection. The block was judged to be failed if anaesthesia was not present in 2 or more peripheral nerve distribution and such patients were excluded from the study.
2. The **duration of sensory blockade,** defined as the time between onset of action and return of pinprick response, was assessed every 30 minutes in at least 3 major nerve territories.
3. The **duration of analgesia,** defined as the time between the onset of action and the onset of pain, was the time when the patients received the first dose of analgesic. Supplemental analgesia was given in the form of intramuscular inj Diclofenac sodium 50 to 75 mg, when visual analogue scale score was more than 4.
4. The **duration of motor blockade,** was assessed every 30 minutes till the return of complete muscle power in at least 2 major nerve distributions.

Post Operative Assessment

Patients would be evaluated post operatively, every hourly for first six hours, second hourly for next twelve hours, for the following parameters intensity of pain ,motor and sensory recovery. Patients were also monitored for the side effects of opioids. The intensity of pain was assessed using visual analogue scale (vas) score. The supplemental analgesia was given in the form of Inj.diclofenac 50-75mg IM, when VAS score was more than forty mm or four.

IV. Observations And Results

The average age was 33.37+/-10.97 yrs in-group A and 35.07+/-10.98 yrs in-group B. The average weights of the patients were 60.40+/-8.62 kgs in-group A and 63.33+/-9.48 kgs in-group B respectively. Both groups had predominantly male patients, accounting for nearly 2/3 of the total study population in each group. There was no significant difference in age, weight and sex distribution.

Comparison Of Heart Rate Between Two Groups

Study Period	Heart rate beats/min				P value
	Group A (n=30)		Group B (n=30)		
	Mean	SD	Mean	SD	
Baseline	91.27	12.01	90.47	9.59	0.7766
5th minute	101.53	14.54	101.00	14.92	0.8890
10th minute	106.33	13.56	101.07	13.65	0.1392
15th minute	104.70	12.50	101.10	14.56	0.3085
20th minute	101.63	12.31	101.47	13.50	0.9603
25th minute	100.07	10.90	99.23	13.02	0.7890
30th minute	97.87	12.58	96.37	12.00	0.6383
45th minute	95.33	12.20	94.53	11.62	0.7957
60th minute	92.93	8.86	93.30	10.39	0.8836
75th minute	91.23	8.72	90.33	9.79	0.7082
90th minute	89.00	10.04	88.80	9.23	0.9363
2nd hour	88.23	8.24	88.07	10.19	0.9447
3rd hour	84.93	8.30	84.90	8.88	0.9881
4th hour	83.20	9.29	85.33	8.41	0.3548
5th hour	82.60	8.68	84.43	7.75	0.3918
6th hour	82.23	8.56	84.20	6.84	0.3297
7th hour	82.00	9.07	83.93	7.49	0.3717
8th hour	84.47	9.36	83.87	8.06	0.7912
9th hour	87.13	10.55	82.47	7.55	0.0536
10th hour	89.50	10.31	81.93	7.42	0.0018**
11th hour	91.07	9.72	80.53	6.77	0.0000**
12th hour	91.53	10.25	82.80	7.23	0.0003**
13th hour	89.40	10.42	82.53	8.48	0.0070**
14th hour	88.07	9.66	84.00	8.37	0.0868
15th hour	86.33	10.04	85.53	11.22	0.7721
16th hour	85.60	9.98	88.00	10.73	0.3734
18th hour	83.53	9.00	86.93	9.98	0.1710
20th hour	82.30	8.00	85.07	10.28	0.2492
24th hour	81.23	7.96	83.67	9.47	0.2857
28th hour	80.70	8.09	79.47	7.18	0.5348
32nd hour	80.47	8.80	79.27	7.11	0.5636
38th hour	79.40	8.87	78.80	6.57	0.7670
42nd hour	78.93	7.62	78.60	6.56	0.8566
48th hour	78.80	7.06	78.07	7.04	0.6884

** Highly significant

This chart comparing the heart rate pattern of both groups show statistical significance at 10th to 13 th hour of the study period although they are within an acceptable clinical range.

Comparison Of Systolic BP Between Two Groups

Study Period	Systolic BP in mm Hg				P value
	Group A (n=30)		Group B (n=30)		
	Mean	SD	Mean	SD	
Baseline	134.07	6.54	135.60	5.64	0.3350
5th minute	134.67	4.99	136.87	5.77	0.1197
10th minute	135.53	4.26	138.20	5.10	0.0319
15th minute	134.67	5.69	136.67	4.15	0.1251
20th minute	134.40	5.39	135.07	4.26	0.5971
25th minute	133.07	6.27	135.53	4.32	0.0814
30th minute	132.13	5.53	134.00	4.36	0.1521
45th minute	131.60	7.40	132.73	5.00	0.4896
60th minute	131.20	5.79	132.80	5.60	0.2811
75th minute	130.80	5.50	131.87	4.81	0.4272
90th minute	129.27	5.24	131.93	5.24	0.0534
2nd hour	128.40	5.83	130.53	4.17	0.1086
3rd hour	129.20	6.36	130.30	4.66	0.4479
4th hour	128.60	6.46	129.67	5.04	0.4786
5th hour	128.13	6.30	129.27	4.25	0.4174
6th hour	127.60	6.61	128.40	4.38	0.5826
7th hour	129.93	6.42	128.37	4.44	0.2764
8th hour	131.40	6.91	128.43	5.72	0.0752
9th hour	134.13	7.88	129.10	5.61	0.0060**
10th hour	135.73	7.94	127.93	5.32	0.0000**
11th hour	135.53	7.33	129.60	4.85	0.0005**
12th hour	135.00	8.25	131.30	4.59	0.0360
13th hour	131.40	7.81	132.40	5.26	0.5631
14th hour	129.60	6.51	133.93	6.46	0.0122*
15th hour	130.40	7.40	135.73	6.41	0.0041**
16th hour	128.67	8.83	135.93	7.34	0.0010**
18th hour	127.00	6.21	134.93	7.46	0.0000**
20th hour	126.93	6.86	131.13	4.95	0.0086**
24th hour	125.50	6.69	130.80	6.27	0.0025**
28th hour	125.60	5.49	127.73	5.58	0.1409
32nd hour	128.57	6.02	127.07	4.69	0.2862
38th hour	125.80	7.92	126.87	4.48	0.5233
42nd hour	124.73	7.44	124.07	3.17	0.653
48th hour	124.00	7.14	123.03	3.09	0.744

In this chart the compared systolic blood pressure changes between two groups show statistical significance between 9^{th} to 11^{th} and 14^{th} ,15^{th},16^{th},18^{th},20^{th} and 24^{th} hours

Comparison Of Diastolic BP Between Two Groups

Study Period	Diastolic BP in mm Hg				P value
	Group A (n=30)		Group B (n=30)		
	Mean	SD	Mean	SD	
Baseline	86.07	5.13	85.87	5.63	0.8862
5th minute	87.40	3.68	87.13	4.95	0.8136
10th minute	86.73	5.62	86.93	4.69	0.8816
15th minute	86.20	4.94	87.27	4.41	0.3811
20th minute	85.40	4.40	87.00	5.14	0.2003
25th minute	85.73	4.69	86.07	4.91	0.7890
30th minute	85.13	5.19	85.60	4.85	0.7204
45th minute	86.27	5.11	85.13	4.78	0.3786
60th minute	85.00	4.86	85.00	4.72	1.0000
75th minute	84.67	5.07	85.47	4.95	0.5390
90th minute	83.53	4.95	84.40	5.21	0.5114
2nd hour	83.20	4.29	84.27	5.25	0.3920
3rd hour	81.73	9.30	82.73	4.47	0.5977
4th hour	82.70	4.98	82.63	5.23	0.9598
5th hour	81.73	4.09	82.07	5.00	0.7784
6th hour	82.53	3.79	81.40	5.10	0.3322
7th hour	82.40	3.87	80.33	5.54	0.0992
8th hour	83.80	4.05	80.00	5.71	0.0043**
9th hour	85.67	5.63	80.53	5.06	0.0005**
10th hour	87.40	6.22	81.27	5.13	0.0001***
11th hour	88.07	5.62	82.00	5.85	0.0001**
12th hour	87.33	4.71	83.00	5.32	0.0015**
13th hour	86.33	4.90	84.07	5.16	0.0863
14th hour	83.60	4.31	84.47	4.92	0.4709
15th hour	83.73	5.14	85.33	6.27	0.2840
16th hour	83.27	5.21	84.87	7.29	0.3322
18th hour	81.13	5.55	85.13	6.30	0.0115*
20th hour	81.20	5.11	83.80	5.05	0.0500*
24th hour	81.00	5.80	83.87	5.56	0.0500*
28th hour	80.33	5.12	81.47	5.46	0.4102
32nd hour	80.33	6.06	80.13	5.38	0.8929
38th hour	80.07	5.21	80.07	4.65	1.0000
42nd hour	79.60	5.47	80.07	5.00	0.7313
48th hour	79.33	3.98	80.33	4.20	0.3479

The compared diastolic blood pressure between two groups show statistical significance between 8^{th} to 12^{th} hrs and 18^{th},20^{th} and 24^{th} hrs.

Comparison Of Respiratory Rate Between Two Groups

Study Period	Respiratory rate numbers/min				P value
	Group A (n=30)		Group B (n=30)		
	Mean	SD	Mean	SD	
Baseline	15.67	0.99	15.80	0.88	0.5860
5th minute	15.80	0.92	16.60	1.33	0.0089**
10th minute	16.07	1.57	17.30	1.47	0.0027**
15th minute	16.50	1.61	17.20	1.73	0.1105
20th minute	15.67	1.37	16.40	1.94	0.0964
25th minute	15.13	1.53	16.00	2.13	0.0755
30th minute	15.60	1.13	16.23	1.85	0.1154

45th minute	15.30	1.39	15.80	1.65	0.2096
60th minute	15.27	1.14	15.67	1.56	0.2621
75th minute	15.43	1.25	15.93	1.89	0.2322
90th minute	15.23	1.25	15.37	1.50	0.7095
2nd hour	14.97	0.89	15.60	1.13	0.0192*
3rd hour	14.97	0.76	15.67	1.49	0.0260*
4th hour	15.07	0.98	15.57	1.33	0.1030
5th hour	14.90	0.71	15.47	1.36	0.0475*
6th hour	14.90	0.99	15.20	1.47	0.3588
7th hour	15.17	1.18	15.50	1.50	0.3428
8th hour	15.27	1.31	15.27	1.34	1.0000
9th hour	15.73	1.36	15.83	1.64	0.7983
10th hour	15.73	1.62	15.80	1.67	0.8757
11th hour	15.97	1.67	15.23	1.70	0.0969
12th hour	15.53	1.59	15.23	1.94	0.5154
13th hour	15.73	1.72	15.67	1.54	0.8749
14th hour	14.80	1.42	15.80	1.95	0.0273*
15th hour	15.57	1.55	16.27	1.80	0.1115
16th hour	15.43	2.03	16.90	2.16	0.0087**
18th hour	15.33	1.54	16.80	2.35	0.0059**
20th hour	14.87	1.17	16.13	1.94	0.0033**
24th hour	14.97	1.03	15.70	1.95	0.0739
28th hour	14.70	0.79	15.33	1.47	0.0423*
32nd hour	15.60	1.22	15.33	1.47	0.4477
38th hour	15.47	1.07	15.37	0.93	0.7010
42nd hour	15.20	1.19	15.57	1.28	0.2541
48th hour	15.00	0.98	16.10	1.65	0.0026**

In the above table there is statistical significance with respect to respiratory rate at 2nd to 5th hr, 14th hr, 16th to 20th hr,28th hr and 48th hours.

Comparison Of VAS Score Between The Two Groups

Study Period	VAS score (0=No pain 10=Pain)				P value
	Group A (n=30)		Group B (n=30)		
	Mean	SD	Mean	SD	
1st hour	0.37	0.49	0.63	0.76	0.220
2nd hour	1.30	0.95	0.87	0.86	0.086
3rd hour	1.83	0.79	1.17	0.79	0.002**
4th hour	2.13	0.86	2.00	0.79	0.550
5th hour	2.50	0.90	2.33	0.80	0.330
6th hour	2.83	1.02	2.60	0.77	0.180
7th hour	3.27	0.91	3.03	0.81	0.335
8th hour	3.50	0.63	3.37	0.67	0.422
9th hour	3.97	1.07	3.40	0.62	0.036*

10th hour	4.00	0.83	3.57	0.63	0.065
11th hour	4.23	1.07	3.57	0.73	0.006**
12th hour	4.47	1.38	3.77	0.90	0.037*
13th hour	4.10	0.99	3.67	0.80	0.038*
14th hour	3.77	0.77	3.70	0.70	0.612
15th hour	3.60	1.00	4.07	1.36	0.141
16th hour	4.06	1.77	4.07	1.17	0.385
17th hour	3.53	0.97	3.97	0.96	0.050*
18th hour	3.17	0.70	3.90	1.03	0.003**
19-24 hour	3.60	1.13	3.87	0.90	0.160
25-30 hour	3.53	0.86	3.60	0.72	0.742
31-36 hour	3.63	0.96	3.37	0.76	0.422
37-42 hour	3.23	0.86	3.07	0.64	0.602
43-48 hour	2.83	0.65	2.77	0.43	0.775

The patients were assessed for postoperative pain using visual analogue scale score.

The above graph compares the VAS scores between the two groups with statistical significance at 3rd, 9th, 11th to 13th, 17th and 18th hrs of the study period.

Comparison Of Study Parameters Between Two Groups

Study parameters	Group A (n=30)		Group B (n=30)		P value
	Mean	SD	Mean	SD	
Time of onset (Minutes)	20.47	3.64	19.47	4.90	0.373
Duration of Surgery (minutes)	79.50	26.27	84.33	37.27	0.564
Duration of Sensory blockade (minutes)	385.67	66.67	380.50	80.15	0.787
Duration of motor blockade (minutes)	367.40	71.43	360.00	77.87	0.705
Duration of analgesia (hours)	14.13	8.41	22.18	12.13	0.004**

In the above chart the average time of onset was 20.47+/-3.64 min in-group A and 19.49+/-4.90 min in-group B .The average duration of surgeries were 79.50+/-26.27min and 84.33+/-37.27 min in groups A and B respectively. The observed average duration of sensory blockade was 385.67+/-66.67 min in group A and 380.50+/-80.15 min in group B. The average duration of motor blockade was 367.40+/-71.43 in group A and 360.0+/-77.87 min in group B respectively. There was no statistical significance in terms of onset, durations of surgery, sensory blockade and motor blockade between the two groups However the average duration of analgesia were 14.13+/-8.41 hrs and 22.18.+/-12.13 hrs in groups A and B respectively, showed statistical significance. The group B showed prolonged analgesia produced by addition of Buprenorphine to local anaesthetics.

Comparison Of Side Effects Between The Two Groups

Side Effects	Group A (n=30)	Group B (n=30)
Nausea	3 (10.0%)	3 (10.0%)
Vomiting	2 (6.7%)	1 (3.3%)
Numbness	1 (3.3%)	1 (3.3%)
No side effects	24 (80.0%)	25 (83.3%)
Inference	Side effects are statistically similar between the two groups with P=0.739.	

Statistical Methods: Chi-Square and Fisher Exact test has been used to find the homogeneity of sex distribution between the two groups and student t test has been used to find the homogeneity age and weight distribution between the two groups. Student t test (Two tailed) has been used to find significant difference of hemodynamics between the two groups and the study parameters namely, Time of onset, duration of surgery, duration of motor and sensory blockade and duration of analgesia between the two groups. Mann Whitney U test has been used to assess the significant difference of VAS score between the two groups. Chi-Square and Fisher Exact test has been used to find significant difference of incidence of side effects between the two groups. The statistical software used were SPSS.12.0.1 for windows and statiistica.

V. Discussion

Varieties of receptors mediate nociception in peripheral sensory nerve fibers. The knowledge of these receptors has been used in the form of various adjuncts administered along with local anaesthetics. These adjuncts may not only prolong the analgesic duration but also thought to reduce the systemic analgesic consumption as well as their side effects. To prolong perioperative analgesia various adjuncts such as opioids, clonidine, verapamil,neostigmine and tramadol have been tried. [1]The objective of this study was to compare the analgesic efficacy between Bupivacaine alone and Buprenorphine as an adjunct to local anaesthetics in brachial plexus block.

In our study we observed that there was no change in the time of onset of sensory blockade between two groups. This was similar to the observation done by Eric J.Veil [2], who found no change in onset time when morphine and buprenorphine were added to 0.5% bupivacaine into brachial plexus sheath. However Fletcher et al [3] had an early onset of block with fentanyl.

We observed that addition of buprenorphine to local anaesthetic solution produced much longer acting analgesia (22.18+/-12.13 hrs) than produced by plain 0.5% bupivacaine. (14.13+/-8.41 hrs). Bazin et al[4], had observed a similar duration of analgesia(median 20 hrs) on buprenorphine administration. In a similar way Candido et al has observed duration of analgesia produced with buprenorphine 3 times longer than that produced by local anaesthetics alone. wajima et al[5] has also found satisfactory and prolonged analgesia with butorphanol administered as continuous intrabrachial infusion. The prolonged analgesic duration [6] observed with buprenorphine may be attributed to its high affinity for the mu opioid receptor and high lipid solubility, which favors easy penetration through the axonal myelin and nerve membrane.

We found no significant difference with respect to side effects like nausea, vomiting, numbness between the two groups. At the same time there were no incidences of pruritus, respiratory depression or urinary retention.

The significant changes observed with respect to hemodynamic parameters were due to variability in the onset of pain between the two groups. The early rise of heart rate and blood pressure in group A were due to analgesic wear off. The same occurred in group B in the later period .On an average the number of supplemental Diclofenac sodium injections received were two in group A , where as patient's in group B received one supplement over 48 hrs.

VI. Summary And Conclusion.

We compared the analgesic effects of bupivacaine 0.5% and buprenorphine added to bupivacaine 0.5% solution into brachial plexus sheath in 60 patients undergoing upper extremity orthopedic and reconstructive surgeries. Patients were randomized into two groups of 30 each.

Onset of sensory blockade (time between injection and total abolition of pinprick response)was 20.47+/-3.64 min in group A and 19.49+/-4.90 min in group B. However there was no significant change in time of onset(p=0.373). Duration of sensory blockade (the time between injection and complete recovery from sensory disturbance) was comparable in both groups (group A 385.67+/-66.67 min, group B 380.50+/-80.15 min) without any statistical significance (p=0.787). The duration of motor blockade was also comparable in group A 367.40+/-71.43 min and group B 360.0+/-77.87 min without any statistical significance (p=0.705).The duration of analgesia was prolonged in group B 22.18.+/-12.13 hrs, when compared with group A 14.13+/-8.41 hrs.. This difference was statistically significant (p=0.004**). (**p<0.05 is statistically significant).

In conclusion, Buprenorphine (2 mcg/kg body weight) is superior as an adjunct to local anaesthetic solution when administered into brachialplexus sheath for perioperative analgesia during upper limb surgery.

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