Original Research Article

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Comparision of Analgesic Efficacy of Two Dissferent Doses of Intrathecal Buprenrphine

Vidhya Prakash S.[1], Subha R.[2]

[1, 2]Assistant Professor, Department of Anesthesia, Karpagam Faculty of Medical Sciences & Research, Coimbatore – 641032, Tamilnadu, India.

Abstract

Pain is the most common symptom that brings the patient to a health care provider. The fear of pain during and after surgery affects the psychological state of the patient immensely. The technical skills and the extensive pharmacological knowledge on pain relief places the anesthesiologist in an ideal position to treat pain in the perioperative setting. Comparisonof analgesic efficacy and safety of two different doses of intrathecal buprenorphine (30 µg and 60 µg) along with bupivacaine (2.2 ml) in geriatric patients 60-80 years undergoing hemiarthroplasty.

Keywords: Inthtraecal; Hemiarthroplasty; Buprenorhine.

Introduction

Neuraxial blockade is the preferred method of anaesthesia for surgeries on the lower half of the body. It provides effective pain relief in the initial postoperative period. But additional analgesics are required as the effect of neuraxial blockade wears off. Additives added to the local anaesthetics while producing block not only improves the quality of analgesia but also prolong the analgesia compared to local anaesthetics alone, thus decreasing the need for frequent rescue analgesics.

Related Works

In 1900, matas discovered that the adverse effects of intrathecally administered cocaine could be mitigated with the addition of morphine. He used 1.5 mg of morphine intrathecally to reduce the CNS effects of cocaine. In 1901 a Japanese anaesthesiologist *Otojiro Kitagawa*, used 10 mg of morphine with local anaestheticeucaineintrathecally for cancer pain relief.

With the discovery of opioid receptors in the spinal cord, interathecal opioid administration quickly spread to perioperative care in a wide array of surgical procedures.

The pioneering animal studies conducted by *Yaksh and Rudy (1976)* showed spinal site of action. Thus, intrathecally administered opioids ushered in a new and exciting era in clinical pain therapy. Extension of this concept of intrathecal and epidural injection in man by *Behar et al (1979) and Wang et al (1979)* was subsequently followed by many clinical reports and scientific studies to determine the specific action, dose – response relations, pharmacokinetics and long-term effects of spinal opiate administration.

In recent years, studies have been done using buprenorphine, an opioid analgesic with agonist-antagonist properties, as an additive to spinal lignocaine or bupivacaine. Many studies have been done with intrathecal buprenorphine mostly in

Corresponding Author: Subha R., Assistant Professor, Department of Anesthesia, Karpagam Faculty of Medical Sciences & Research, Coimbatore – 641032, Tamilnadu, India.
E-mail: surendararavindhan@ieee.org

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adult patients. Only very few studies were done in elderly patients with intrathecal buprenorphine. Hence this study was done in geriatric patients undergoing elective hemiarthroplasty of hip surgery who usually suffer from pain postoperatively due to tissue damage.

A comparative study was done with two different doses of intrathecal buprenorphine 30µg and 60 µg along with bupivacaine (2.2 ml) with an intention of reducing the incidence of side effects and to study whether considerable post operative analgesia was provided with minimal dosage. This study was conducted in our hospital settings who presented for elective hemiarthroplasty of hip.

Objectives of the Study

Primary Objective

- To compare the post operative analgesic efficacy of Intrathecal buprenorphine in two different doses (30µg/60µg).

Secondary Objective

- To compare the hemodynamic Instability.
- To compare the incidence of side effects like Nausea, vomiting, shivering, pruritus and respiratory depression.

Opioids

The term opioid refers to all compounds related to opium derived from juice of opium poppy, papaver somniferum. Opiate is the term used for drugs derived from opium. Morphine is the prototype opioid. Opioid compounds can be classified as naturally occurring, semisynthetic and synthetic opioids. With the development of synthetic drugs with morphine like effects, the term opioid is now used to refer all exogenous substances natural and synthetic that bind to opioid receptors and produce some agonistic effect.

The presence of opioid binding sites in the nervous system was reported in the year 1973. Immunohistochemical studies have demonstrated opioid receptors in various areas of the central nervous system. These include the amygdala, the mesencephalic reticular formation, the periaqueductal gray matter, and the rostral ventral medulla.

Mechanism of Analgesic Action

Opioids act as agonists at stereo specific opioid receptors at presynaptic and postsynaptic sites in the central nervous system (CNS) and also outside the CNS in the peripheral tissues.

Opioid agonists bind with the opioid receptors, leading to activation of the G-protein. Activity of adenylatecyclases and the voltage-dependent Ca^{2+} channels is suppressed on the other hand, inward rectifier K^{+} channels and mitogen – activated protein kinase are activated.

Pain Pathways

The spinothalamic tract: the axons of most second order neurons cross the midline close to their level of origin (at the anterior commissure) to the contralateral side of the spinal cord before they form the spinothalamic tract and send their fibres to the thalamus, the reticular formation, the nucleus raphe magnus, and the periaqueductal gray matter.

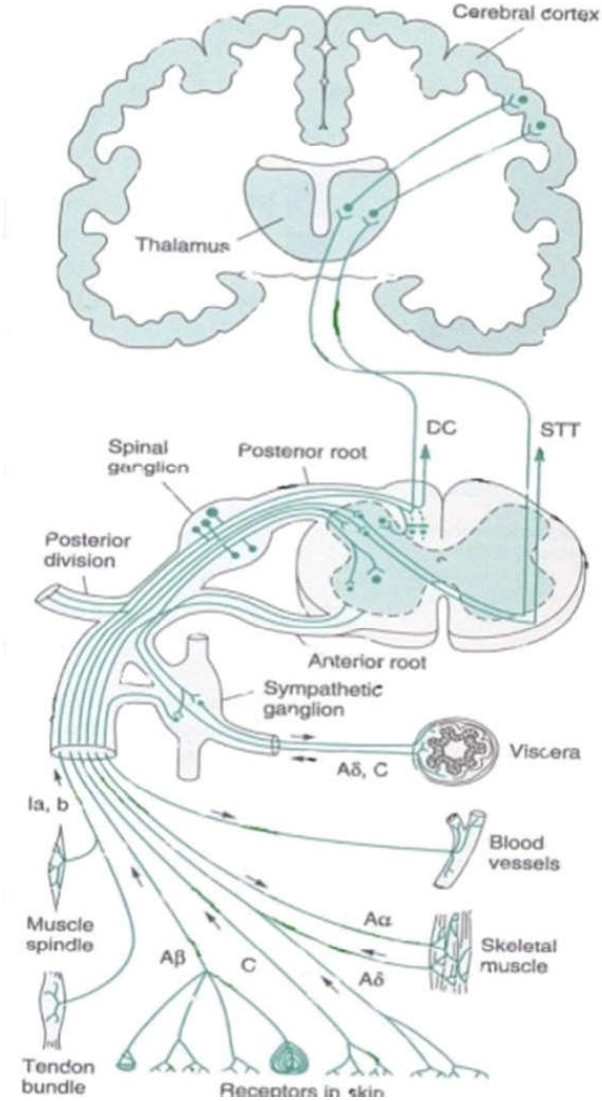


Fig. 1: Pain Pathways

Alternate Pain Pathways

These include the spinoreticular tract, the spinomesencephalic tract, the spinohypothalamic, the spinotelencephalic tract and the spinocervical tract.

Integration with symapathetic and motor systems: somatic and visceral afferents are fully integrated with the skeletal motor and the sympathetic systems in the spinal cord, brainstem and the higher centers. Afferent dorsal horn neurons synapse both directly and indirectly with anterior horn motor neurons.

Buprenorphine

Buprenorphine was first synthesised in 1966. It is an oripavine derivative of the alkaloid thebaine. It is a narcotic analgesic having powerful agonist and partial antagonistic action and low addiction potential. The antinociceptive effect of buprenorphine in mice is μ-opioid receptor-mediatedyet severely compromised by concomitant activation of opioid receptor like-1receptors.

Buprenorphine affects nociceptive processing by acting at both supraspinal and spinal μ and ORL1 receptors.In terms of spinal and supraspinal effects of buprenorphine, it is likely that buprenorphine facilitates the C-fiber reflex via a supraspinal mechanism that acts on sensory and/or motor components of the reflex arc although the depression of the reflex involves a spinal mechanism.

Observations and Results

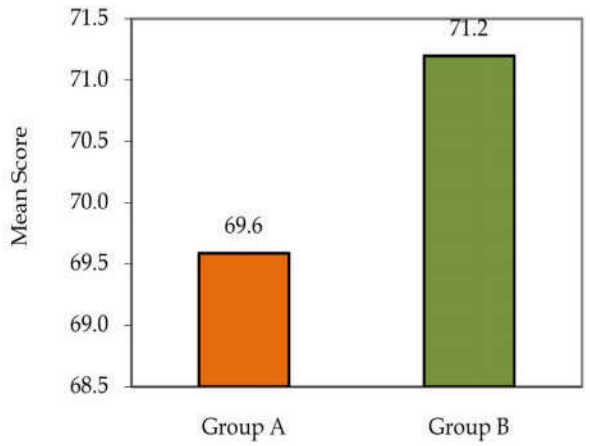
Demographic Data

The graph above clearly indicates that the mean age in Group A is 69.6±6.0 and the mean age in Group B is 71.2±5.4 No significant difference between the two groups with respect to age.

Table 1: Comparison of Age based on Group

Age	Group I		Group II	
	Count	Percent	Count	Percent
60-70	42	56.0	35	46.7
71-80	33	44.0	40	53.3
Mean ± SD	69.6 ± 6.0		71.2± 5.4	

t = 1.79, p > 0.05



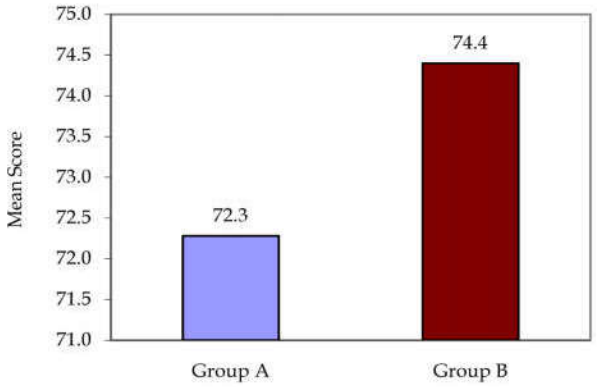
The graph clearly shows that the mean pulse rate in Group 1 is 72.3±13.2 and the mean pulse rate in Group 2 is 74.4±13.2. p value is 0.328>0.05. No significant difference between the two groups with respect to mean baseline pulse rate.

The graph shows that the mean baseline Respiratory rate in Group A is 14.9±0.9 And the mean Baseline Respiratory rate in Group B is 14.8 ±0.9. p value is 0.410 which is >0.05. The two groups are comparable with respect to mean baseline respiratory rate.

The graph above shows that the mean baseline BP in Group A is 104.3±5.3 and the mean baseline BP in Group B is 103.7± 5.5 . p value is 0.48 which is greater than 0.05. The two Groups are comparable with respect to mean baseline BP.

Table 2: Comparison of PR_Baseline based on Group

	Mean	SD	N	t	P
Group A	72.3	13.2	75	0.98	0.328
Group B	74.4	13.2	75		



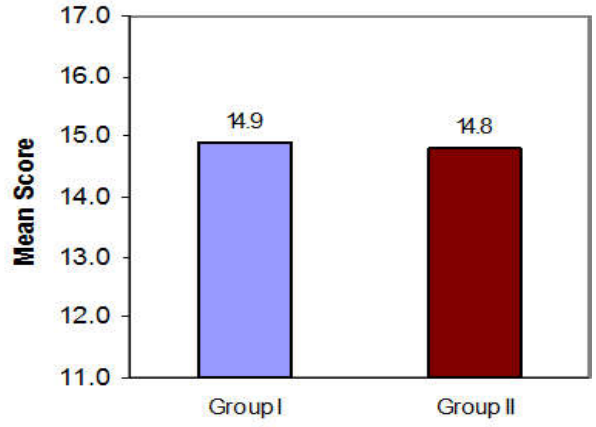
The above graph clearly tells that in Group A 61.6% were of female patients and in Group B 57.3% were of female patients whereas, male patients in Group A are 38.7 % and in Group B are 42.7%.

No significant difference was found between the two groups with respect to gender (p = 0.618).

The Graph shows that in Group A- 42.7% of Patients belongs to ASA 1 Grading and in Group B- 54.7% of patients belongs to ASA1 Grading.

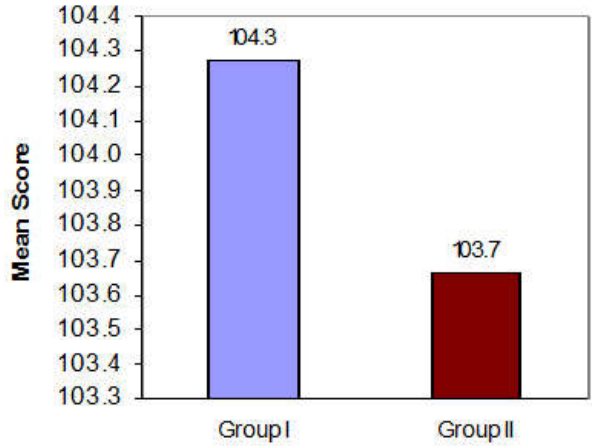
Table 3: Comparison of RR_Baseline based on Group

	Mean	SD	N	T	P
Group I	14.9	0.9	75	0.826	0.410
Group II	14.8	0.9	75		



Comparison of Mean Baseline BP based on Group

	Mean	SD	N	T	p
Group I	104.3	5.3	75	0.7	0.488
Group II	103.7	5.5	75		



Comparison of Gender Distribution based on Group

Gender	Group I		Group II		χ^2	p
	Count	Percent	Count	Percent		
Female	46	61.3	43	57.3	0.249	0.618
Male	29	38.7	32	42.7		

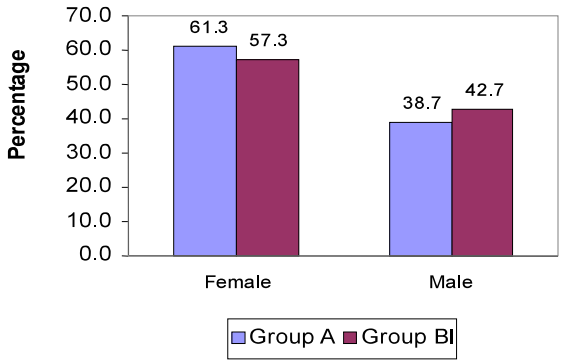


Table 4: Comparison of ASA Distribution based on Group

ASA	Group A		Group B		χ^2	p
	Count	Percent	Count	Percent		
Grade I	32	42.7	41	54.7	2.16	0.142
Grade II	43	57.3	34	45.3		

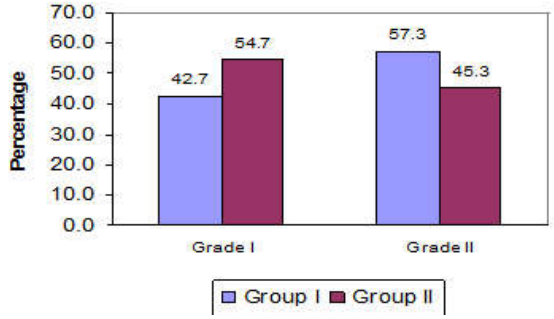
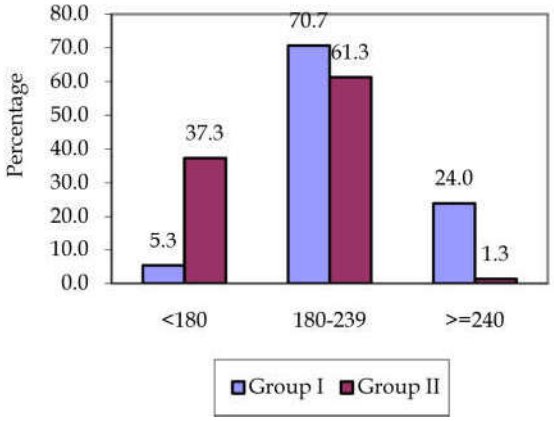
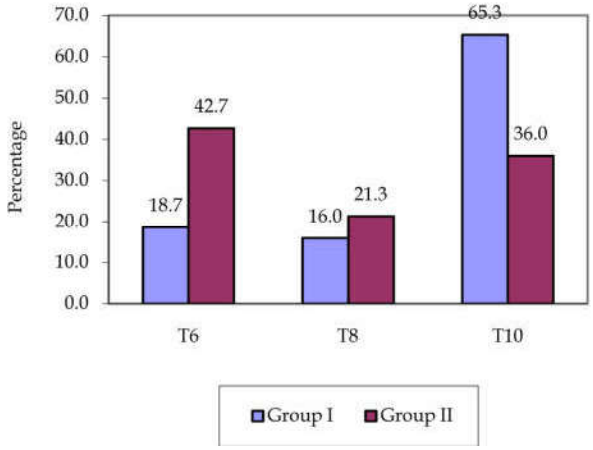


Table 5: Comparison of Time of Onset based on Group

Time of onset seconds	Group A		Group B	
	Count	Percent	Count	Percent
<180	4	5.3	28	37.3
180-239	53	70.7	46	61.3
>=240	18	24.0	1	1.3
Mean ± SD	211.9± 25.5		186.4± 24.0	

t = 6.3, p < 0.01





The graph also clearly depicts that in Group B 57.3% of patients belongs to ASA2 Grading and 45.3% of patients belongs to ASA2 Grading. p value is 0.142 which is greater than 0.05. The two groups were comparable with respect to ASA Grading.

Time of Onset.

The Time taken to reach the maximum level of sensory block.

Group A 211.9±25.5 Seconds

Group B 186.4±24.0 Seconds

The data was analysed using the 't' test and the p value was found to be <0.01 which is statistically significant between the two groups. Time taken to reach the maximum level of sensory block was shorter in Group B.

P value is 0.01 which is statistically significant

Maximum sensory block:

Group A

18.7 % of patients had maximum level of sensory block upto-T_6

16 % of patients had maximum level of sensory block upto-T_8

65.3% of patients had maximum level of sensory block upto-T_{10}

Group B

42.7% of patients had maximum level of sensory block upto-T_6

21.3% of patients had maximum level of sensory block upto-T_8

36% of patients had maximum level of sensory block upto-T_{10}

The data analysed using t test found p value to be 0.001 which is statistically highly significant.

Table 6: Comparison of Maximum Sensory Block based on Group

Max sensory	Group A		Group B		χ^2	p
	Count	Percent	Count	Percent		
T6	14	18.7	32	42.7	13.98**	0.001
T8	12	16.0	16	21.3		
T10	49	65.3	27	36.0		

**: - Significant at 0.01 level

Maximum level of sensory block was noted in Group B patients who were administered 60 µg of intrathecal buprenorphine.

The graph clearly states that,

Group A-

8% of patients had a sedation score of 1

62.7% of patients had a sedation score of 2

29.3% of patients had a sedation score of 3

Group B

4% of patients had a sedation score of 1

26.7% of patients had a sedation score of 2

69.3% of patients had a sedation score of 3

Patients in Group 2 had excellent intra operative sedation. But the p value is 0.220. Hence the two groups are comparable in terms of sedation score.

Mean Duration of Analgesia

Group A - 3.7± 0.41 hrs

Group B - 7.6± 1.1 hrs

p value is < 0.01 which is statistically significant between the two groups.

The graph clearly tells that mean duration of analgesia was prolonged in Group B.

P value>0.05. There was no statisticallysignificant side effects noted in either of the groups

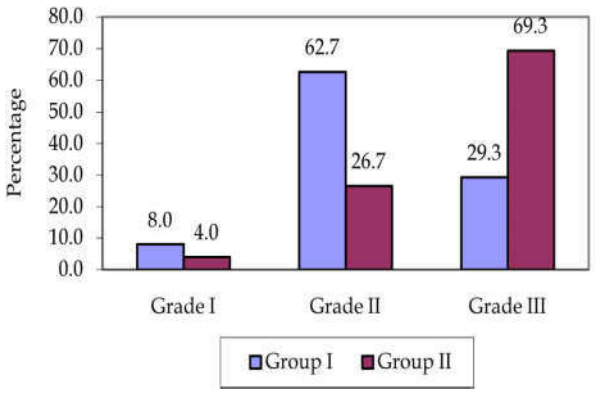
Table 7: Comparison of Sedation Score based on Group

Ng sedation	Group I		Group II		χ^2	p
	Count	Percent	Count	Percent		
Score 1	6	8.0	3	4.0	1.51	0.220
Score II	47	62.7	20	26.7		
Score III	22	29.3	52	69.3		

Table 8: Comparison of Duration of Analgesia based on Group

Duration of Analgesia	Group A		Group B	
	Count	Percent	Count	Percent
2-4 Hr	57	76.0	0	0.0
4-6 Hr	18	24.0	4	5.3
6-8 Hr	0	0.0	40	53.3
>8 Hr	0	0.0	31	41.3
Mean ± SD	3.7± 0.41		7.6± 1.1	

t = 26.1, p < 0.01



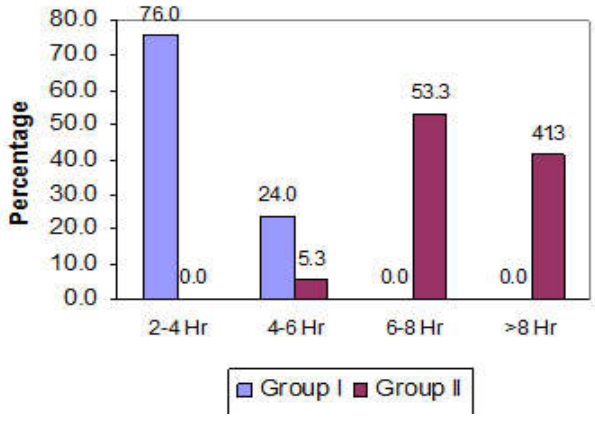
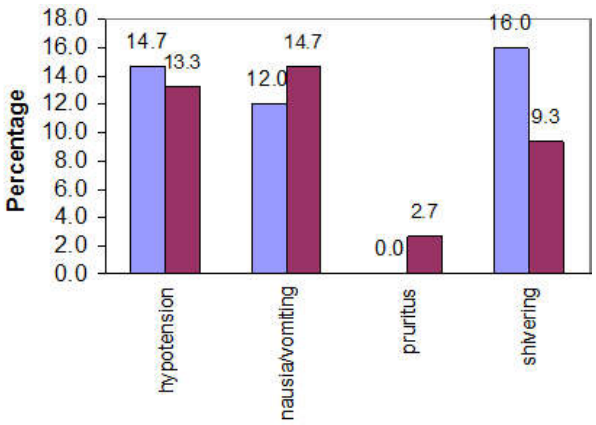


Table 9: Comparison of Side Effects based on Group

Hypotension	Group I		Group II		χ^2	p
	Count	Percent	Count	Percent		
Hypotension	11	14.7	10	13.3	0.05	0.814
nausea/vomiting	9	12.0	11	14.7	0.23	0.631
Pruritus	0	0.0	2	2.7	-	-
Shivering	12	16.0	7	9.3	2.03	0.155



Conclusion

The study done with the addition of two different doses of intrathecal buprenorphine, 30 µg and 60 µg along with bupivacaine 2.2ml (0.5%) clearly proves that,Post operative analgesia is prolonged with higher dosage of buprenorphine 60 µg given intrathecally along with bupivacaine. No increase in side effects were noted with the addition of buprenorphine in two different doses studied (30µg, 60µg). Use of 30µg of buprenorphine intrathecally also provideconsiderable prolongation of post operative analgesia. Since the side effects are incomparable between the two groups, 60µg of intrathecal buprenorphine can be safely administered to geriatric patients.

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