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DEXMEDITOMIDINE AS INTRATHECAL ADJUVANT TO ISOBARIC ROPIVACAINE IN SPINAL ANAESTHESIA FOR LOWER LIMB ORTHOPAEDIC SURGERIES – A RANDOMIZED DOUBLE BLIND CONTROLLED STUDY

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Abstract:

Knowledge & use of adjuvant drug therapy has rendered neuraxial analgesia more effective in the management of both acute and chronic pain conditions. α2 adrenergic agonist dexmeditomidine have both analgesic and sedative properties when used as adjuvant in regional anaesthesia.

Aim – to study the effect of intrathecal dexmeditomidine added to ropivaciane for lower limb surgeries except hip & knee replacement under spinal anaesthsia.

Material & methods – this research study was conducted on 60 patients 30 in each group of ASA class I & II age group of 18-60 years of either sex posted for elective lower limb orthopaedic surgeries under spinal anaesthesia after taking informed consent & obtaining approval of institutional research & ethical committee. Patients were divided in 2 groups: Group R & Group RD.

Results – Mean peak sensory level was 7.13±1.02 in group R and 7.17±1.34 in Group RD but both groups were statistically comparable regarding mean sensory level (P= 0.598). Mean bromage score was (2.87±0.50) in group R and (2.85±0.55) in group RD which was statistically comparable (P= 0.765).

Time to reach maximum bromage score is significantly shorter in group RD (8.63±1.37) min. as compare to Group R (10.17±1.8) min. (P=0.0). However maximum fall in pulse rate was 13.7% (77.33 at 5 minutes) in group RD and 11.4% (80.80 at 15 min.) in group R.

Maximum fall in diastolic blood pressure was 9.66 & 9 % in group RD (72.60 mm of Hg at 10 min.) and in group R (74.50 mm of Hg at 20 min) respectively

Keywords: Dexmeditomidine, Ropivacaine, intrathecal, spinal anaesthesia.

Introduction:

Quinke in 1891 demonstrated a state predictable means of performing lumber puncture.[1] In 1899 August, Bier used Quinkes technique to inject cocaine in order to produce operative anaesthesia, the first real spinal anaesthesia.[2] The first phase in history of spinal anaesthsia. In 1905, Heinrich Braun[3] a German Surgeon, reported the use of procaine for operative spinal anaesthesia, means for controlling levels of anaesthsia by making procaine solutions hyperbaric by adding glucose, was first reported by Barker[4] in 1907. Synthesis of Tetracaine in 1931 and its introduction in

clinical practice by Sise[5] in 1935, synthesis of Dibucaine and its introduction in to clinical practice by Jones[6] in 1930 popularized spinal anaesthesia.

By the mid 1940s, spinal anaesthesia had reached a peak of its popularity, which was soon followed by almost equally widespread avoidance and neglect. The pharmacological explosion in anaesthesia between 1945 and 1965 made spinal anaesthesia appear unnecessarily demanding, inconvenient and tedious, as well as medico-legally unsafe. Around 1965, spinal anaesthesia began a recovery that has persisted and even accelerated. Over the last 50 years due to its simplicity, minimum skill implementation, optimal operative condition, lowered risk of aspiration, low intra-operative blood loss, continued analgesia in the post-operative period and minimal postoperative morbidity.

In view of the wider application of regional anaesthetic procedure in modern anaesthesia practice, there is a need for local anaesthetic with desirable properties like longer duration of sensory blockade and lesser duration of motor paralysis. Ropivacaine is newer amide type of local anaesthetic having a lower potential for cardiac and central nervous system toxicity.

In ASA 'Practice guidelines for acute pain management in the peri-operative setting 'stresses on multimodal therapy with two or more analgesic agents or techniques used in combination for control of post operative pain. The final aim of this aspect of therapy would be seen as the complete relief of postoperative pain with no treatment related side effects. Various adjuvants that can be added to local anaesthetics and administered in central neuraxial blockade are opioid-Fantanyl, sufentanyl, α-2 agonists-dexmeditomidine, clonidine, benzodiazepines-midazolam, neostagimine and ketamine. Dexmeditomidine is a highly selective α-2 agonist with 8 times greater affinity than clonidine. There are fewer studies available for these drugs as adjuvants to 0.5% Ropivacaine. Dexmeditomidine reduces opioids and inhalatation anaesthetic requirement and have been widely used for intensive care unit sedation with hemodynamic stability. Intrathecal α2 receptor agonists have antinociceptive action for both somatic & visceral pain. We have conducted the research study on use of intrathecal combination of Dexmeditomidine with isobaric ropivacaine in lower limb surgery in orthopaedics except total hip & total knee replacement.

The aim of this study was to evaluate haemodynamic effects intraoperatively as well as to notify the duration of post operative analgesia.

Aims & objectives:

To study the effect of intrathecal Dexmeditomidine with ropivacaine in lower limb surgeries in orthopaedics.

Material & methods:

This study was conducted at RNT medical college Udaipur on 60 patients of ASA class I and Class II in the age group of 18-60 years of either sex posted for elective lower limb orthopaedic surgery under spinal anaesthesia after approval from institutional research and ethical committee and after valid informed written consent given by the patients.

Inclusion criteria:- ASA grade I and II patients, scheduled to undergo elective surgery under sub arachnoid block.

Randomization blindness of study and drug preparation:

This study was conducted in a randomized double blind fashion. All patients under study was subjected to a detailed pre-anaesthetic examination and investigation was carried out during this evaluation. Patients were randomly divided into two groups of 30 patients in each group using sealed envelop technique.

Group R:- patients were received 3 ml. 0.5% isobaric ropivacaine hydrochloride [Ropin 10ml. ampoule (50mg. ml) neon laboratories limited].

Group RD:- patients were received 3 ml. 0.5% isobaric ropivacaine with 5 µg Dexmeditomidine hydrochloride [DEXTOMID 1 ml. ampoule (100µg/ml) neon laboratories limited].

3ml (15mg) of isobaric ropivacaine was mixed with dexmeditomidine (5µg) according to randomly selected patient group R or RD (closed envelop method). Dexmeditomidine was drawn in a standard 1 ml BD syringe (100 parts = 100µg) with 5 parts for 5µg. Thus intrathecal volume was 3 ml in group R and 3.05 ml in Group RD

making no apparently significant volme difference.

The study solution was prepared in 5 ml. syringe by an anaesthesiologist who had performed subarachnoid block and was not involved further in study. Another anaesthesiologist who was conducting the study himself had recorded all the data and was not aware of group allocation.

Spinal anaesthesia technique:

After preparation PAC & preoperative medication, Lumbar puncture was performed at $L_3 - L_4$, $L_4 - L_5$ interspace under all aseptic precautions and drug was injected as per group allocation. The time of end of intrathecal injection was taken as time – 0 for further data recording. All further data was recorded as per proforma by anaesthesiologist who was not aware of group allocation.

Observations:

Table 1: Comparison of age (Year) in both group

Age	Group R (n=30)	Group RD (n=30)	P- Value
18-30	13(43.33%)	12(40%)	0.92
31-40	10(33.33%)	5(16.67%)	
41-60	7(23.33%)	13(43.33%)	
Range	20-55	22-55	
Mean±SD	36.56±12.95	36.33±11.70	

Test used: T-test

Table 2: Comparison of ASA status in both group

ASA	Group R (n=30)	Group RD (n=30)	P-value
Grade I	24(80%)	26(86.66%)	0.582
Grade II	6(20%)	4(13.33%)	

Test used: T-test

Table 3: Comparison of sex in both groups

Sex	Group R (n=30)	Group RD (n=30)	P value
Male	27(90%)	25(83.33%)	0.92
Female	3(10%)	5(16.66%)	

Test used: T-test

Table 4: Comparison of peak sensory level

		Group R (n=30)	Group RD (n=30)	P-value
Patients distribution according to peak sensory level n (%)	T6	4(13.33%)	5(16.66%)	0.488
	T7	13(43.33%)	15(50%)	
	T8	8(26.66%)	6(20%)	
	T9	5(16.66)	4(13.33%)	
Mean±SD		7.46±0.93	7.30±0.91	
Range		T6-T9	T6-T9	
Median		T7	T7	

Test used: T-test

Table 5: Motor block characteristics

Motor block characteristics	Maximum Bromage score (5 min after SAB)		
Patient distribution	Group R (n=30)	Group RD (n=30)	P value
0	0	0	0.561
1	0	0	
2	2(6.66%)	1(3.33%)	
3	28 (93.33%)	29(96.66%)	
Mean±SD	2.93±0.25	2.96±0.18	
Onset of motor block (min) mean	10.17±1.8	8.63±1.37	0.00
Range	8-14	6-10	
Return to max. Bromge score 0 (min)	143.67± 10.33	244.83±9.92	0.00
Range	130-160	240-250	

Test used: T-test

Table 6: Comparison of pulse rate in both groups

Pulse rate	Group R	Group RD	P-value
Pre op.	90.40±9.40	89.69±10.79	0.751
At 5 min	80.85±9.06	77.33±8.59*	0.134
10 min	80.86±7.95	80.73±8.62	0.975
15 min	80.80±9.38*	81.40±9.67	0.808
20 min	82.07±8.82	79.43±8.97	0.256
25 min	84.00±11.22	82.93±9.29	0.531
30 min	83.17±11.01	83.30±9.51	0.960
45 min	85.40±9.40	83.83±10.79	0.551
60 min	85.80±10.01	83.53±11.12	0.410
75 min	85.90±8.65	84.60±11.64	0.625
90min	86.53±9.54	85.87±11.65	0.809
120 min	85.73±11.06	85.20±10.80	0.851
150 min	84.27±9.83	85.53±11.62	0.650
180min	84.03±10.72	84.07±10.47	0.728
210min	83.10±9.92	83.37±10.95	0.922
240min	82.43±10.33	82.80±11.17	0.895
270min	81.20±7.69	82.43±10.33	0.602
300min	81.30±7.00	79.67±10.34	0.477
330min	83.17±11.01	83.30±9.51	0.960

Test used=T-test

Table 7: Comparison of diastolic blood pressure in both groups

Time	Group R	Group RD	P-value
Pre op.	81.00±4.98	80.27±5.84	0.60
At 5 min	77.00±6.04	75.73±5.87	0.40
10 min	75.13±7.60	72.60±7.59*	0.20
15 min	74.60±6.86	73.70±6.04	0.59
20 min	74.50±6.07*	75.80±6.24	0.41
25 min	74.83±5.46	76.03±4.95	0.37
30 min	75.93±4.53	76.03±5.22	0.93
45 min	75.70±4.81	77.20±5.21	0.25
60 min	75.83±4.56	77.50±4.53	0.16
75 min	76.70±4.72	77.57±5.41	0.51
90min	78.43±4.08	78.80±4.90	0.754
120 min	78.57±4.48	78.70±4.92	0.913
150 min	76.53±4.46	77.57±3.15	0.304
180min	76.50±3.43	77.07±3.00	0.499
210min	78.03±2.86	78.07±2.38	0.961
240min	77.30±3.14	78.07±2.60	0.307
270min	76.90±3.52	77.93±2.49	0.194
300min	78.73±5.10	79.00±4.57	0.832
330min	76.50±3.43	77.07±3.00	0.499

Test used=T-test

Results:

Mean peak sensory level was 7.13±1.02 in group R and 7.17±1.34 in Group RD but both groups were statistically comparable regarding mean sensory level (P= 0.598). Mean bromage score was (2.87±0.50) in group R and (2.85±0.55) in group RD which was statistically comparable (P= 0.765).

Time to reach maximum bromage score is significantly shorter in group RD (8.63±1.37) min. as compare to Group R (10.17±1.8) min. (P=0.0). However maximum fall in pulse rate was 13.7% (77.33 at 5 minutes) in group RD and 11.4% (80.80 at 15 min.) in group R.

Maximum fall in diastolic blood pressure was 9.66 & 9 % in group RD (72.60 mm of Hg at 10 min.) and in group R (74.50 mm of Hg at 20 min) respectively.

Discussion:

Spinal anaesthesia is most preferred technique for lower lib surgical procedures. Ropivacaine is a first single enantiomer specific compound, introduced to the clinical practice in 1996 with reduced risk of cardiac toxicity, neurotoxicity and rapid recovery of function.[7-11]

Ropivacaine was approved for a new route of administration, intrathecal route, in the European union in February 2004.[12]

Intrathecal α2 adrenoceptor agonist (Dexmeditomidine) produce analgesia by depressing the release of C-fibre transmitters and by hyperpolarization of post synaptic dorsal horn neurons.[13,14] This anti-nociceptive effect may explain the prolongation of the sensory block when added to spinal anaesthetics.

So we planned this study by using Dexmeditomidine as an adjuvant to ropivacaine in spinal anaesthesia and studied its effect on onset and duration of sensory and motor blockade, hemodynamic stability and incidence of side effects if any.

In our study 27 males, 3 females and 24 (80%) patients of ASA I and 6 (20%) patients of ASA II respectively in Group R, while in group RD males, 5 females and 26 (56.55%) patients of ASA I and 4 (13.33%) patients of ASA II respectively, and found that this data was statistically comparable between two groups (P>0.05).

It was in accordance with previous studies conducted by Gupta R et al[15], Shukla D et al[16] Mahendra et al and Al Mustfa MM et al[18]. In our study we used 3mg of 0.5% Ropivacaine with 5µg Dexmeditomidine.

Similarly Gupta R et al[15] used 3ml of 0.75% isobaric Ropivacaine plus 5µg Dexmeditomidine in patients undergoing lower limb surgery sensory block characteristics.

Onset of sensory block:

In our study sensory onset time was measured as time to reach to T_{10} sensory level and time to reach peak sensory level.

Time to reach peak sensory level ranged from T_6-T_9 with median value of T_7 in both groups. Mean peak sensory level was 7.46±0.93 in group R and 7.30±0.91 in group RD, which was statistically comparable (P=0.488).

Gupta R et al[15] conducted the study using 3ml of 0.75% isobaric ropivacaine and 3 ml of 0.75% isobaric ropivacaine plus 5 µg dexmeditomidine in patients undergoing lower limb surgery in spinal anaesthesia and found that peak sensory level was statistically comparable in both groups (P=>0.05).

Motor block:

Duration of Motor Block: in our study duration of motor block is defined as return of Bromage score to B^o, it was 143.67±10.33 min in group R and 244±9.92 min. in group RD, which was significantly prolonged in group RD (p=0.00).

Al-Mustafa MM etal[18] conducted the study using 12.5mg of hyperbaric bupivacaine plus 5µg dexmeditomidine in patients undergoing urological surgery in spinal anaesthesia and found that duration of motor block was 302.9±86.7 in group D_{10}, 246.4±25.7 min in group D_5 and 140.1±32.3 min in bupivacaine group which was significantly prolonged in group D_{10} and D_5 as compared to bupivacaine group (P=0.00).

Haemodynamic changes:

Haemodynamic changes, systolic blood pressure, diastolic blood pressure and heart rate were comparable with study conducted by Kanazi et al[19].

Side effects:

In our study only observed side effect was hypotension, nausea/vomiting & bradicaedia after spinal anaesthesia. These side effects were statistically comparable in both groups.

Conclusion:

Present study denotes that addition of dexmeditomidine (5µg) to ropivacaine 15mg (0.5% isobaric) was associated with early onset and prolonged duration of sensory and motor blockade with haemodynamically stability and long duration of postoperative analgesia without incidence of post operative complications as compare to ropivacaine alone intrathecally.

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