A COMPARATIVE STUDY OF INTRATHECAL BUPIVACAINE HYDROCHLORIDE WITH DEXMEDETOMIDINE AND BUPIVACAINE HYDROCHLORIDE WITH CLONIDINE FOR PROLONGATION OF ANALGESIA IN MAJOR ORTHOPAEDIC SURGERIES

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ABSTRACT

BACKGROUND
Though spinal anaesthesia is cost affective, rapid onset of action, its short duration is a disadvantage. To overcome this adding adjuvants to local anaesthetics intrathecally has become common these days.

AIM
The purpose of this study is to compare the onset and duration of sensory and motor block, as well as the hemodynamic changes following intrathecal Bupivacaine supplemented with a low dose of either Dexmedetomidine or Clonidine.

DESIGN
A randomized controlled study of patients undergoing major orthopaedic surgery.

MATERIALS & METHODS
The study includes 100 patients, divided into 2 groups of 50 each. In Group C patients received Clonidine with Bupivacaine and in Group D patients received Dexmedetomidine with Bupivacaine intrathecally.

STATISTICAL ANALYSIS
Statistical analysis was done using SPSS (Statistical Package for the Social Sciences) 21 software**.** The demographic data were analyzed using either Student's t-test or Chi- square test. Quantitative data was analyzed by student's t test and qualitative data was analyzed by Chi-square test.

RESULTS & CONCLUSION
Bupivacaine spinal anaesthesia is prolonged by intrathecally administered Clonidine 37.5 µg and Dexmedetomidine 5µg, with minimal influence on haemodynamic parameters. Addition of 5 µg Dexmedetomidine significantly prolonged the duration of sensory blockade, motor blockade and post-operative analgesia as compared to the addition of 37.5 µg of Clonidine. The incidence of side effects was minimal in both the groups, and the difference between the groups was statistically insignificant.

KEYWORDS
Intrathecal, Bupivacaine Hydrochloride, Dexmedetomidine, Clonidine, Analgesia, Orthopaedic Surgeries.

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INTRODUCTION: Spinal anaesthesia was introduced into clinical practice by Karl August Bier in 1898. More than a century has passed and even to this day, it is one of the most popular techniques for both elective and emergency surgical procedures, particularly caesarean sections, lower abdominal surgeries, orthopaedic and urological surgeries. The advantages of spinal anaesthesia are, an awake patient, simple to perform, offers rapid onset of action, has minimal drug cost, relatively less side effects, and rapid patient turnover. These have made spinal anaesthesia the technique of choice of many surgical procedures.

These advantages are sometimes offset by the relatively short duration of action of intrathecal local anaesthetics, and an uncomfortable postoperative period when their action wears off. Other methods like epidural anaesthesia require technical expertise, a larger drug dose, and have a high rate of incomplete or patchy and unpredictable neuraxial block.

Therefore the ability to enhance and extend the sensory blockade of intrathecal neuraxial anaesthesia into the postoperative period forms a challenging forefront in clinical research. One can attempt to achieve this by combining the lowest possible doses of long acting local anaesthetic drugs with the least side effects, with adjuvant drugs that can extend the intraoperative analgesia into the post-operative period. A number of spinal adjuvants like opioids, Clonidine,

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Ketamine, and other drugs have been added to intrathecal Bupivacaine in an attempt to prolong or intensify the motor and sensory block and into the post-operative period also. However each of these drugs has its own limitations, and a need for alternative methods or drugs always exist.

The identification of opiate receptors in the central nervous system in 1971 by Goldstein and the isolation of endorphins in 1974 by Terenius et al, led to the use of intrathecal narcotic agonists for analgesia. In 1979 Wang et al[1] first reported the use of spinal intrathecal opioids in humans. He demonstrated that small doses of morphine administered intrathecally produced prolonged relief of chronic pain.[1] Buprenorphine is a synthetic analgesic of high potency and long duration of action. Capogna et al suggested that Buprenorphine can be administered safely in the subarachnoid space.[2] However, all these drugs may produce pruritus, urinary retention, nausea, vomiting or respiratory depression.

Clonidine's anti-nociceptive properties were first described in 1974 by Paalzow.[3] The rationale behind the intrathecal administration of Clonidine was to achieve a high drug concentration in the vicinity of the α_2-adrenoceptor in the spinal cord. Clinical trials of systemic, epidural or intrathecal administration of Clonidine show that less Clonidine is needed intrathecally than epidurally to produce a similar analgesic effect with fewer side effects.

Dexmedetomidine is new, highly selective $\alpha_2$adrenoceptor agonist that has been approved by the Food and Drug Administration (FDA) as an intravenous sedative and analgesic drug in intubated patients in the intensive care settings. Its α_2:α_1 selectivity is eight times higher than that of Clonidine. Therefore there has been a growing interest in the potential use for this drug as an adjuvant to intrathecal Bupivacaine. However, only a few studies are currently available in literature evaluating the efficacy of intrathecal Dexmedetomidine in prolonging the duration of spinal block.

On the basis of previous studies, our hypothesis is that intrathecal Dexmedetomidine 5 µg or Clonidine 60 µg would be equipotent and would produce a similar effect on the characteristics of Bupivacaine spinal anaesthesia.

AIMS AND OBJECTIVES: The objective of the present study is to evaluate and compare the onset and duration of sensory and motor block, as well as the haemodynamic changes following intrathecal Bupivacaine supplemented with a low dose of either Dexmedetomidine or Clonidine.

MATERIAL AND METHODS: The study was conducted in the Department of Anaesthesia, MediCiti Institute of Medical Sciences, after obtaining approval by the ethics committee and after informed consent. It was conducted over a period of 12 months. Patients were randomly divided into two groups of 50 each.

Study Design: A randomized controlled study of patients undergoing surgery undergoing spinal anaesthesia for elective orthopaedic surgeries.

Sample Size: A total sample size of 100 cases.

Inclusion Criteria: 1. Informed consent from all patients. 2. Age 18yrs-60yrs, both male and female. 3. Physical status ASA I and II. 4. Patients undergoing elective orthopaedic surgeries under spinal anaesthesia.

Exclusion Criteria: 1. Patients refusal. 2. Emergency cases. 3. Physical status ASA 3, 4, 5. 4. Distortion of Spinal anatomy. 5. Superficial lumbar site infection. 6. Pregnant women. 7. Patients with coagulopathy.

Pre Anaesthetic Check-Up: Was carried out with a detailed history, general physical examination and systemic examination. Airway assessment and spinal column examination were done.

METHODOLOGY: 100 patients were randomly divided into two groups of 50 each. After shifting the patient to the operating table, IV access was obtained on the forearm with an 18 Gauge IV cannula and preloading with Lactated Ringer's solution 500mL was infused intravenously before the block. The monitors connected to the patient included non-invasive blood pressure, oxygen saturation using pulse oximeter and ECG. Baseline HR, BP, RR, and SpO2 were recorded.

Group "C" Clonidine Group: Receiving Intrathecal 0.5% hyperbaric Bupivacaine hydrochloride 15 mg (3 mL) +37.5 µg Clonidine in 0.5 mL normal saline (Total 3.5mL).

Group "D" Dexmedetomidine Group: Receiving Intrathecal 0.5% hyperbaric Bupivacaine hydrochloride 15 mg (3 m) + 5 µg Dexmedetomidine in 0.5 mL normal saline (Total 3.5mL).

OBSERVATIONS:

Sensory and Motor Blockade: Onset, time to peak sensory blockade, highest level of sensory block, and duration of sensory block. The level of sensory block was tested every 5 min by pin-prick method using a hypodermic needle till the peak level had been established. The time of onset was taken from the time of injection of drug into subarachnoid space to loss of pin prick sensation. The highest level of sensory block and time required to achieve was noted. Motor block of the lower extremities was assessed according to the Modified Bromage Scale, every 5 min until achievement of Modified Bromage Score of 3 or up to a maximum of 15 min, whichever was earlier.

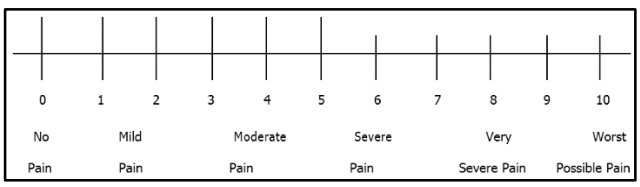
Modified Bromage Scale[4]:

- Grade 0: Full flexion of knees and feet.
- Grade 1: Just able to flex knees, full flexion of feet.
- Grade 2: Unable to flex knees, but some flexion of feet possible.
- Grade 3: Unable to move legs or feet.

Recovery Parameters: Time to regression of sensory blockade to T 12 dermatome, and time to motor recovery. The duration of sensory blockade was documented by

assessing the level of sensory block every 30min, as the time from onset to the time of return of pinprick sensation to T 12 dermatomal level.

Analgesia: Duration of complete and effective analgesia, and time to first pain medication. Pain was assessed by Visual Analogue Self Rating Method (Visual Analog Scale).



Patients were assessed for pain every 30 min after surgery until they complained of moderate pain requiring supplemental analgesia. Duration of effective analgesia was measured as the time from intrathecal drug administration to the patient's first request for analgesic administration, recorded in minutes.

Hemodynamic Changes, and Complications: HR, BP and SpO2 were noted every 5 minutes till 30 minutes, then every 15 mins, till the end of surgery. Hypotension is treated with a bolus administration of 300 ml of Ringer's solution over 5 min and 6 mg of intravenous ephedrine. Bradycardia is treated with 0.6 mg of intravenous atropine.

Statistical Analysis: Statistical analysis was done using SPSS (Statistical Package for the Social Sciences) 21 software. Data was expressed as either mean±standard deviation or numbers and percentages. The demographic data of patients were studied for both the groups. The means of the continuous variables were compared between the two groups using analysis of variance ANOVA. The demographic data were analyzed using either Student's t-test or Chi-square test. Quantitative data was analyzed by student's t test and qualitative data was analyzed by Chi-square test. The P

RESULTS:

Group	Range	Mean	SD
C	18-60	37.96	13.99
D	18-60	38.88	12.09
P-value	0.362		

Table 1: Age distribution of subjects (years)

On statistical analysis there was no significant difference between the two groups with respect to the age of the patient.

Group	Male		Female	
	No.	%	No.	%
C	38	76	12	24
D	38	76	12	24
P- value	N. A.			

Table 2: Sex distribution of subjects

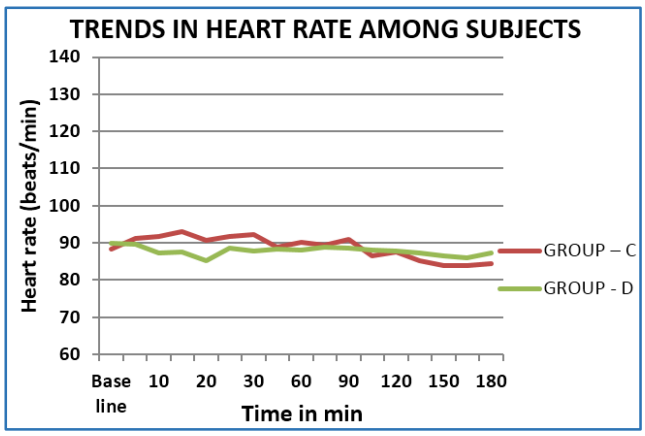


Fig. 1

- In Group C, the mean baseline heart rate was 88.36 with a standard deviation of 12.46.
- In Group D, the mean baseline heart rate was 89.86 with a standard deviation of 13.92.
- On comparing the two groups there was no statistically significant difference (p value >0.05) between the groups.

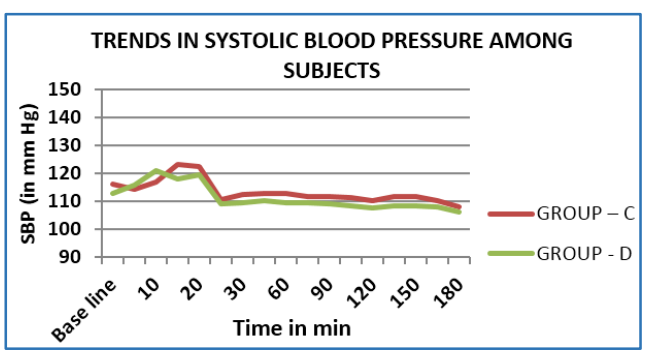


Fig. 2

In Group C, the mean baseline systolic blood pressure was 116.14 with a standard deviation of 9.35. A fall in systolic blood pressure was recorded in Group C intra operatively, from 5mins up to 180mins, which was statistically significant (p value <0.05). In Group D, the mean baseline systolic blood pressure was 113.02 with a standard deviation of 8.78. A fall in systolic blood pressure was noted in Group D intra operatively, form 25mins up to 180mins, which was statistically significant (p value < 0.05). On comparing the two groups, the fall in systolic blood pressure was not statistically significant (p value >0.05).

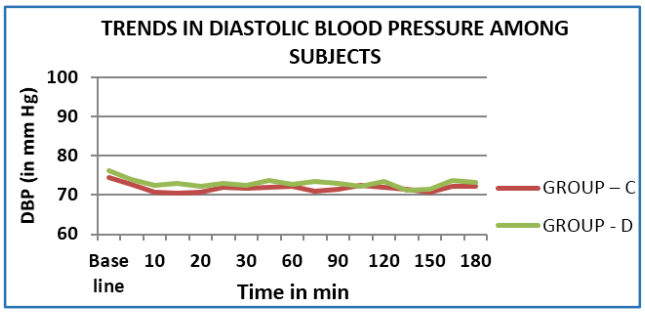


Fig. 3

In Group C, the mean baseline diastolic blood pressure was 74.46 with a standard deviation of 7.31. A fall in diastolic blood pressure was recorded from 5mins up to 180mins, which was statistically significant (p value <0.05). In Group D, the mean baseline diastolic blood pressure was 76.14 with a standard deviation of 5.7. A fall in diastolic blood pressure was noted from 5mins up to 180mins, which was statistically significant (p value <0.05). On comparing the two groups, the fall in diastolic blood pressure was not statistically significant.

(p value>0.05).

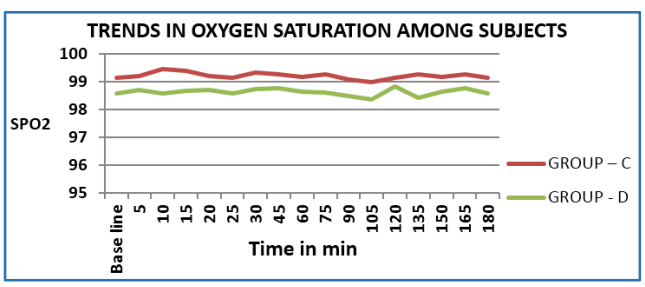


Fig. 4

- In Group C, the mean baseline oxygen saturation was 99.16 with a standard deviation of 2.235.
- In Group D, the mean baseline oxygen saturation was 98.58 with a standard deviation of 2.081.

On comparing the two groups there was no statistically significant difference (p value>0.05) between the groups.

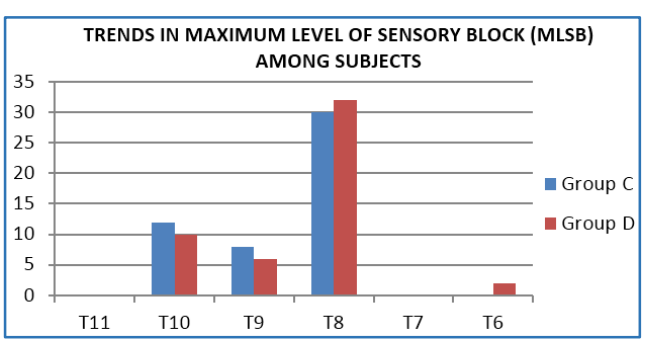


Fig. 5

- In Group C, 30 patients (60%) had a peak sensory block level of T8, 8 patients (16%) had a level of T9, and 12 patients (24%) had a level of T10.In Group D, 32 patients (64%) had a peak sensory block level of T8, 6 patients (12%) had a level of T9, 10 patients (20%) had a level of T10, and Two (4%) had level of T6.
- There was no statistically significant difference between the groups (p value >0.05) in the height of the peak sensory block achieved.

Group	Mean	Range	SD
C	**8-15**	**11.14**	1.807
D	10-15	12.66	1.520
P -value	0.00001		

Table 3: Time taken to attain maximum level of sensory block (in minutes)

- In Group C, the mean time taken to attain maximum level of sensory block was 11.14 minutes with a standard deviation of 1.807. In Group D, the mean time taken to attain maximum level of sensory block was 12.66 minutes with a standard deviation of 1.520.
- On comparing the two groups, the time taken to attain maximum level of sensory block was longer in Group D, which was statistically significant (p value <0.05).

Group	**Mean**	**Range**	**SD**
C	4-10	6.1	1.515
D	2-5	3.68	1.077
P- value	0.00001		

Table 4: Time taken to achieve complete motor blockade (in minutes)

- In Group C, the mean time taken to achieve complete motor blockade in minutes was 6.1with a standard deviation of 1.515. In Group D, the mean time to achieve complete motor blockade was 3.68 minutes with a standard deviation of 1.077.
- On comparing the two groups, patients in Group D took statistically significant (p value <0.05) less time to achieve complete motor blockade.

Side Effect	**Group C**		**Group D**		**P value (Two –tailed)**
	No.	**%**	**No.**	**%**	
Nausea	1	2.0	2	4.0	0.5591
Vomiting	1	2.0	2	4.0	0.5591
Hypotension	2	4.0	3	6.0	0.6474
Bradycardia	1	2.0	2	4.0	0.5591

Table 5: Distribution of subjects according to side effects

Nausea: One patient (2%) in Group C and2 patients (4%) in Group D complained of nausea. The difference was not statistically significant (p value > 0.05).

Vomiting: 2 patients (4%) in Group D complained of vomiting, but one (2%) in Group C. The difference was not statistically significant (p value >0.05).

Hypotension: 2 patients in (4%) in Group C and 3 patients (6%) in Group D had hypotension.

The difference was not statistically significant (p value > 0.05)

Bradycardia: One patient (2%) in Group C and 2 patients (4%) in Group D had bradycardia. The difference was not statistically significant (p value >0.05)

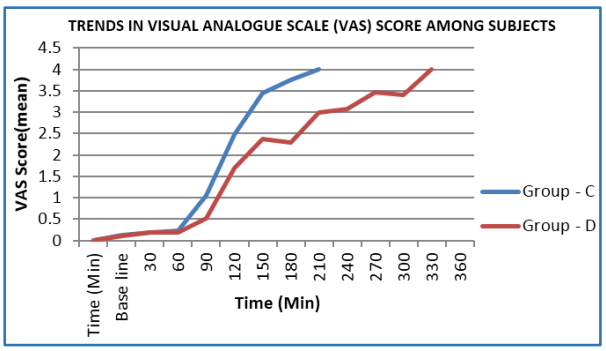


Fig. 6

Post operatively patient's pain was graded according to VAS score and rescue analgesia was given at a VAS score of 4.The mean baseline VAS score in Group C was 0.12 with a standard deviation of 0.44, whereas in Group D it was 0.10 with a standard deviation of 0.51.

- On statistical analysis there was significant difference between the two groups at 90 mins, 120 mins, 150 mins, 180 mins and 210 mins post operatively (p value < 0.05).
- The trend of increase in VAS score was earlier in Group C as compared to Group D.
- In Group C the maximum duration of analgesia, post operatively was 210 minutes where as in Group D it was 330 minutes.

Group	Range	Mean	SD
C	180-330	267.6	32.736
D	250-510	356.9	58.430
P-value	p<0.001		

Table 6: Duration of analgesia among subjects (in minutes)

This table depicts the duration of time elapsed in minutes, from the time of onset of analgesia to the time when the first dose of rescue analgesia was given, i.e. at VAS Score=4. In Group C the mean time was 267.6 minutes with a standard deviation of 32.736 minutes. In Group D the mean time was 356.9 minutes with a standard deviation of 58.430 minutes.

On comparing the two groups, Group D had a longer duration of analgesia which was statistically significant (p value <0.05).

Group	Range	Mean	SD
C	90-180	151.7	22.533
D	150-300	199.7	34.067
P-value	p<0.001		

Table 7: Time of regression to t12 among subjects (in minutes)

This table depicts the duration of time elapsed in minutes, from the time of onset of sensory blockade to the time when the sensory blockade level had regressed to T12 level. In Group C the mean time taken was 151.7 minutes with a standard deviation of 22.533 minutes. In Group D the mean time taken was 199.7 minutes with a standard deviation of 34.067 minutes.

On comparing the two groups, Group D had a longer duration of sensory block, and the difference was found to be statistically significant (p value <0.05).

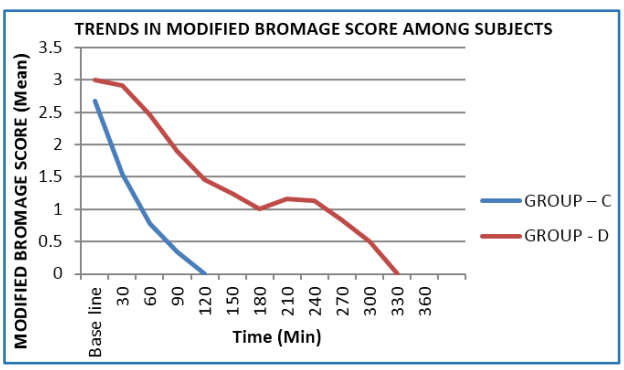


Fig. 7

Motor blockade was assessed post operatively using the Modified Bromage Scale scoring system every 30 minutes until full return of lower extremity motor function i.e. score =0.At '0' minutes post-operatively, i.e. at baseline, 50 patients in Group C had a mean Modified Bromage Score of 2.68 with a standard deviation of 0.512, whereas the 50 patients in Group D had a mean score of 3.0 with a standard deviation of 0.285. On statistical analysis, there was significant difference between the two groups at 0 min, 30 mins, 60 mins, 90 mins and 120 minutes post operatively. (p value <0.05).The trend to return of Modified Bromage Score to 0 was earlier in Group C as compared to Group D. In Group C the maximum duration of motor blockade post-operatively was 120 minutes, whereas in Group D it was 330 minutes.

Group	Range	Mean	SD
C	150-270	197.5	25.659
D	195-510	290.9	50.21
P-value	p<0.001		

Table 8: Time until full return of motor function (in minutes)

This table depicts the duration of time elapsed in minutes, from the time of onset of motor blockade to the time when motor function is completely recovered in the lower extremities (Modified Bromage Score=0). In Group C, the mean time taken was 197.5 minutes with a standard deviation of 25.659, whereas in Group D it was 290.9 minutes with a standard deviation of 50.21. On comparing the two groups, Group D had a longer duration of motor blockade, which was statistically significant. (p value <0.05).

DISCUSSION: Spinal anaesthesia is a very popular anaesthetic technique, which has stood the test of time, since its introduction. It requires small dose of anaesthetic agent, simple to perform, offers rapid onset of action, provides reliable surgical anaesthesia, and good muscle relaxation. Various drugs such as epinephrine, phenylephrine, adenosine, magnesium sulfate, Neostigmine and Clonidine, have been used as adjuvants in an effort to decrease the onset time, improve the quality of the block, prolong the duration of spinal anaesthesia, and extend the analgesic effect in to the immediate post-operative period.

Clonidine, an imidazoline compound is a selective agonist for α_2-adrenoreceptors with an α_2:α_1 selectivity ratio of approximately 220:1. The rationale behind the intrathecal administration of Clonidine was to achieve a high drug concentration in the vicinity of the α_2-adrenoceptors in the spinal cord. Therefore, spinal Clonidine is being evaluated as an alternative to spinal opioids for the control of pain and has been proven a potent analgesic free of some opioid-related, but not all, side effects.

Dexmedetomidine is a newer α_2 agonist drug that has been approved by the FDA as an intravenous sedative and analgesic drug in intubated patients in the intensive care settings. Its α2:α1 selectivity that is higher than that of Clonidine. Therefore there has been a growing interest in the potential use for this drug as an adjuvant to intrathecal Bupivacaine. However, only a few studies are currently available in literature evaluating the efficacy of intrathecal Dexmedetomidine in prolonging the duration of spinal block. In Kanazi et al[5] study of low dose intrathecal Dexmedetomidine and Clonidine as adjuvants to intrathecal Bupivacaine, found that 3 µg of Dexmedetomidine intrathecally was not associated with anyonset of back, buttock or leg pain, or weakness, two weeks post-operatively, and produce a shorter onset time for motor block and a prolongation in the duration of motor and sensory block with haemodynamic stability without sedation.

Niemi et al,[6] In this study, the analgesic and circulatory effects of intrathecal Clonidine were studied in patients undergoing knee arthroscopy under spinal anaesthesia. Forty ASA I–II patients were randomly divided to two groups. One group received Clonidine 3µg/kg mixed with 15mg 0.5% Bupivacaine and the other group an identical saline volume mixed with Bupivacaine as above, in a double–blind fashion. Sensory analgesia, blood pressure, heart rate and sedation were followed during and after the operation. The study concluded that duration of sensory analgesia and motor blockade was longer in the Clonidine group than in the control group.

Gupta R, Bogra J, Verma R, Kohli M, et al[7] Evaluated the efficacy and safety of intrathecal Dexmedetomidine added to ropivacaine with ropivacaine alone, in 60 patients, in a randomized double blinded trial. Data regarding the highest dermatomal level of sensory blockade, the time to reach this level from the time of injection, time to S2 sensory regression and incidence of side effects were collected. Sedation was assessed with a four-point verbal rating scale (1=no sedation, 2=light sedation, 3=somnolence, 4=deep sedation). Postoperatively, pain scores were recorded by using VAS between 0 and 10. They concluded that the addition of Dexmedetomidine to ropivacaine intrathecally produces a prolongation in the duration of the motor and sensory block.

Al–Ghanem et al[8] study concluded that 5 µg of dexmedetomidine seems to be alternative as adjuvant to spinal Bupivacaine in surgical procedures, especially in those requiring a long duration of block with minimal side effects and an excellent quality of analgesia.

De Kock et al[9] used Clonidine with ropivacaine intrathecally in three different doses of 15, 45, and 75µg for ambulatory knee arthroscopy, observed that a small 15µg dose of Clonidine significantly improves the quality of anaesthesia without delaying sensory and motor recovery. They also noted that a 45µg dose of Clonidine prolongs the sensory blockade without any influence on motor blockade, but a dose of 75µg is associated with delayed sensory and motor recovery as well as detectable side effects such as hypotension and sedation. From these studies, we concluded that a 30µg dose of Clonidine, and a 5 µg dose of Dexmedetomidine intrathecally, would be safe and appropriate for our study.

The present study was conducted at MediCiti Institute of Medical Sciences, Ghanpur on 100 patients of ASA Grade I or II of either sex, undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia. The patients were randomly allocated into two groups C and D. Group C consisted of 50 patients who received 3ml of 0.5% hyperbaric Bupivacaine+37.5µg of Clonidine in 0.5ml normal saline (Total of 3.5 ml), and Group D consisted of 50 patients who received 3ml of 0.5% hyperbaric Bupivacaine+ 5 µg of Dexmedetomidine in 0.5 ml of normal saline (Total of 3.5 ml) intrathecally. Various parameters, as per the protocol were noted.

The aims and objectives of this study were to evaluate the efficacy, in terms of time to onset of action, time to peak sensory and complete motor blockade, time to regression to T 12 dermatome, and duration of analgesia. We also compared the two groups for hemodynamic changes and side effects.

Demographic profile across the group: In our study, majority of the patients in both groups were middle aged, with patients in Group C having a mean age of 37.96 years and those in Group D having a mean age of 38.88years. There was no statistically significant difference between the mean ages of the two groups. In both Groups C and D, 76% of the patients were male and 24% were female, and there was no statistically significant difference. The mean height and the mean weight in either group were also identical. The type of surgeries performed were also identical in both the groups. These parameters were kept identical in both the groups to avoid variations in intraoperative and postoperative outcome of patients.

Sensory blockade: Maximum level of sensory block (MSL): In our study there was no statistically significant differences in the maximum sensory level achieved, between the groups. In Group C, 30 patients (60%) had maximum sensory level till T8, 8 patients (16%) had till T9, and 12 of then (24%) had till T10. In Group D, 32 patients (64%) had maximum sensory level till T8, 6patients (12%) had till T9, 10 patients (20%) had till T19 and 2 patients (4%) had till T6.

Strebel et al (2004)[10] reported that the range of upper level of sensory blockade was similar in all groups: T1–T10 in Group 1 (Bupivacaine+ saline), T1–L1 in Group 2 (Bupivacaine+ Clonidine 37.5 mcg), T1-T10 in Group 3 (Bupivacaine+ Clonidine 75 mcg) and T1–T12 in Group 4 (Bupivacaine+ Clonidine 150 mcg).

Time to reach peak level of sensory blockade: In Group C, the mean time taken to attain peak level of sensory block was 11.14 minutes whereas in Group D it was 12.66 minutes. In our study, the longer time taken by Group D to attain maximum level of sensory block could be due to the fact that there were more patients in Group D who had a slightly higher maximum level of sensory blockade.

Time taken for regression of sensory blockade to T12 Dermatomal level: In our study, the rate of regression of sensory blockade to T12 level was faster in Group C as compared to Group D. In Group C the mean time taken for the sensory block to regress to T12 from the time of onset of sensory blockade was 151.7 minutes as compared to the mean time of 199.7 minutes in Group D. On comparing the two groups, Group D had a longer duration of sensory block, and the difference was found to be statistically significant (p value < 0.05).

Kanazi GE. et al[5] (2006) in their study on the effect of low-dose Dexmedetomidine (30 µg) or Clonidine (3 µg) on the characteristics of Bupivacaine spinal block, with that of Bupivacaine alone reported that: the difference between the groups in the mean times to reach T10 sensory block and the peak sensory level did not reach statistical significance. The sensory block regression times of the two dermatomes and to the S1 dermatome were significantly different between the Bupivacaine group and that of the of Clonidine and Dexmedetomidine groups. However, the sensory regression times were similar between the Clonidine and Dexmedetomidine group.

Al Mustafa MM et al[11] (2009) in their study of the effect of two different doses of Dexmedetomidine (5 and 10 µg) added to spinal Bupivacaine for urological procedures, reported that the mean time of sensory block to reach the T10 dermatome was 4.7±2.0 minutes in D10 group, 6.3±2.7 minutes in D5, and 9.5±3.0 minutes in group N (plain Bupivacaine). The regression time to reach S1 dermatome was 338.9±44.8 minutes in group D10, 277.1±23.2 minutes in D5, and 165.5±32.9 minutes in group N. They concluded that the onset and regression of sensory and motor block were highly significant (N versus D5, N versus D10, and D5 versus D10, p<0.001).

The results from our study are comparable to the results in the studies described above in regards to the peak level of sensory block achieved and the time taken to achieve it. The duration of sensory block was longer in the Dexmedetomidine group in comparison to the Clonidine group in our study, which could be attributed to the fact that we used a higher dose of Dexmedetomidine than Kanazi GE. et al.[5]

Motor Blockade: Time taken to achieve complete motor blockade: In our study, the mean time to achieve complete motor blockade was 6.1+1.515min in Group C and in Group D it was 3.68+1.077 min. Based on statistical analysis, we found that Group D took statistically significant (p <0.05) less time to achieve complete motor blockade than Group C.

Trends in modified bromage score among subjects: In our study motor blockade was assessed post operatively using Modified Bromage Score (MBS) every 30 minutes till full return of motor function, i.e. score=0. On statistical analysis, there was significant difference of MBS between the two groups at 0 minutes, 30 minutes, 60 minutes, 90 minutes and 120 minutes post operatively. The trend of return of Modified Bromage Score to 0 was earlier in Group C as compared to D.

Time until full return of motor function: In our study, the time to full return of motor function was assessed as the time elapsed from the onset of motor blockade to the return of full motor function, i.e. MBS=0. Group D had a statistically significant longer duration of motor blockade. In Group C, the mean time taken was 197.5 minutes with a standard deviation of 25.659, whereas in Group D it was 290.9 minutes with a standard deviation of 50.21.

In Kanazi GE. et al[5] (2006) study, they found that the time taken to reach Bromage 3 motor block was significantly shorter, and the time taken for motor block regression to Bromage 0 was significantly longer in both the Dexmedetomidine (250+76 min) and Clonidine (216+35 min) groups in comparison to the Bupivacaine only group. However, there was no significant difference between the Dexmedetomidine and Clonidine groups. Our findings were different compared to this study probably due to the higher dose of Dexmedetomidine (5 µg) used in our study. In the study conducted by Al Mustafa MM et al[11] (2009), that compared the effects of varying doses of intrathecal Dexmedetomidine on Bupivacaine spinal anaesthesia, the mean time to reach Bromage 3 scale was 10.4±3.4 minutes in group D10, 13.0±3.4 minutes in D5, and the regression time to Bromage 0 was 302.9±36.7 minutes in D10, 246.4±25.7 minutes in D5, and 140.1±32.3 minutes in group N. The findings in our study are consistent with the regression time to B 0 for Dexmedetomidine 5 µg group in this study.

The results from our study are comparable to those of the above studies with respect to the time taken to achieve complete motor blockade, and the time taken to return of

complete motor function when similar dosage groups are taken in to consideration.

Duration of analgesia: In our study, post-operative pain was graded according to VAS score. The duration of analgesia was assessed as the time taken from the onset of analgesia till the time the first dose of rescue analgesia was given i.e. at VAS score=4. The trend of increase in VAS score was earlier in Group C as compared to Group D. There was significant difference between the two groups at 90 minutes, 120 minutes, 150 minutes, 180 minutes and 210 minutes post-operatively. Group D (mean time 356.9 min) had a longer duration of analgesia than Group C (mean time 267.6 min), which was statistically significant ($p < 0.05$). This implies a better quality of analgesia and a greater reduction in the need for analgesics postoperatively, when 5 µg of Dexmedetomidine is used intrathecally, than when 37.5µg of Clonidine is used.

Most of the previous clinical studies involved in the use of intrathecal α2-adrenergic agonists have been described with Clonidine. The use of intrathecal Clonidine has a well-established synergistic effect with local anaesthetics. The mechanisms by which intrathecal α2-adrenergic agonists prolong the motor and sensory block of local anaesthetics is not clear. It may be an additive or synergistic effect secondary to the different mechanisms of action of the local anaesthetic and the α2-adrenergic agonist. The local anaesthetic acts by blocking sodium channels, whereas the α2-adrenergic agonist acts by binding to pre-synaptic C-fibers and post-synaptic dorsal horn neurons. Intrathecal α2-adrenergic agonists produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons. This antinociceptive effect may explain the prolongation of the sensory block when added to spinal anaesthetics. The prolongation of the motor block of spinal anaesthetics may result from the binding of α2-adrenergic agonists to motor neurons in the dorsal horn.

Strebel et al (2004)[10] in their study comparing 3 doses of Clonidine ie 37.5 µg, 75 µg, 150 µg with isobaric 0.5% Bupivacaine 18 mg intrathecally showed a dose-dependent prolongation of pain free interval i.e. the interval from spinal anaesthesia to the first request for supplemental analgesia. They also observed significant reduction of VAS score in patients receiving 150mcg Clonidine, but not smaller doses.

The results from our study are comparable to those of the above studies with respect to the duration of post-operative analgesia, when similar dosage groups are taken into consideration. Importantly, we found a significantly longer duration of post-operative analgesia and lower VAS scores in Group D, as compared to Group C.

Vital Parameters: Haemodynamics–Heart Rate & Blood Pressure:

Heart Rate: In our study, the two groups did not differ significantly with respect to heart rate at any interval. There were no episodes of bradycardia in either group.

Systolic Blood Pressure: In our study, in Group C there was a continuous fall in systolic blood pressure from 5 mins to 180 mins intra-operatively, and this fall was statistically significant. In Group D, there was a continuous fall in systolic blood pressure from 25 mins to 180 mins intra-operatively, and this fall was statistically significant. However, on comparing the two groups, the fall in systolic blood pressure was not statistically significant ($p > 0.05$).

Diastolic Blood Pressure: In our study, in Group C there was a continuous fall in diastolic blood pressure from 5 minutes to 180 minutes intra-operatively, and this fall was statistically significant. In Group D, there was a continuous fall in diastolic blood pressure from 5 mins to 180 minutes intra-operatively, which was statistically significant. However, on comparing the two groups, the fall in diastolic blood pressure was not statistically significant ($p > 0.05$).

In the study conducted by Strebel et al (2004)[10] 80 orthopaedic patients were randomly assigned to intrathecally receive isobaric 0.5% Bupivacaine 18mg, plus saline (Group 1), Clonidine 37.5mcg (Group 2), Clonidine 75mcg (group 3) and Clonidine 150mcg (group 4). A small but statistically significant decrease in diastolic blood pressure was observed in Group 2, 3 and 4. In addition, systolic blood pressure was decreased in Group 3 and 4. These findings demonstrated a decrease in arterial blood pressure with small doses and relative hemodynamic stability with administration of larger doses of Clonidine. Clonidine after neuraxial or systemic administration, affects arterial blood pressure in a complex manner because of opposing actions at multiple sites. Intrathecal Clonidine decreases blood pressure at lower doses, mediated by a spinal α2-adrenergic mechanism i.e. it produces sympatholysis through effects at specific brainstem nuclei and on sympathetic preganglionic neurons in the spinal cord, whereas at higher doses it increases blood pressure by action at peripheral α1 and α2 adrenoceptors which causes vasoconstriction Solomon RE.[12] As a result, the dose response for neuraxial Clonidine on arterial blood pressure in humans in generally considered to be U shaped; with peripheral vasoconstriction from circulating drug concentrations at high doses opposing central sympatholysis.

In their study of two doses of intrathecal Dexmedetomidine (5µg and 10µg) on spinal Bupivacaine block, Ashraf Amin Mohamed et al[13] reported the following findings. Regarding hemodynamic variables measured during the intraoperative period, there was a significant reduction in pulse rate starting at 20 minutes until 120 minutes in the Dexmedetomidine+ group and starting at 20 minutes until 60 minutes in the Dexmedetomidine group in comparison to the control group ($P < 0.05$). Systolic blood pressure showed a significant reduction starting at 5 minutes until 90 minutes intraoperatively in both the Dexmedetomidine and Dexmedetomidine+ groups in comparison to the control group ($P < 0.05$). There was a significant reduction in intraoperative diastolic blood pressure starting at 5 minutes until 20 minutes

intraoperatively in both the Dexmedetomidine and Dexmedetomidine+ groups in comparison to the control group (P <0.05).

Kanazi GE. et al,[5] in their study had administered equipotent small doses of spinal Dexmedetomidine (3 µg) and Clonidine (30 µg) intrathecally to spinal Bupivacaine block. They reported that, the mean values of MAP and HR were comparable between the three groups throughout the intra and post-operatively, and that there was no statistically significant difference amongst the two groups.

Our study findings regarding intra-operative hemodynamic changes are comparable to the findings of the above mentioned studies. Similar to the findings of Strebel et.[10] (2004) and Ashraf Amin Mohamed et al.[13] We found a statistically significant decline in the systolic and diastolic blood pressures intra-operatively within the Clonidine and Dexmedetomidine groups. However, when the two groups were compared, we found no statistically significant differences, which is similar to the findings of Kanazi GE et al,[5] despite using a slightly higher dose of Dexmedetomidine in our study.

OXYGEN SATURATION: In our study, there were no patients in either group who had a decrease in saturation (SpO_2< 96%) at the various recording times, and the mean SpO_2 was similar amongst the two groups, without any statistically significant difference. Similar results were obtained in the study conducted by Sethi et al[14] (2007), where no significant change in saturation was observed.

SIDE EFFECTS: In our study:

Nausea: Two patients (4%) in Group D complained of nausea but one patient (2%) in Group C. The difference was not statistically significant.

Vomiting: Two patients (4%) in Group D had vomiting but one (2%) in Group C. The difference was not statistically significant.

Hypotension: 2 patients (4%) in Group C and 3 patients (6%) in Group D had hypotension, and this difference in number was statistically insignificant (p >0.05). The fall in systolic and diastolic blood pressure between the two groups was not statistically significant.

Bradycardia: One patient (2%) in Group C and 2 patients (4%) in Group D had bradycardia, which was not statistically significant (p >0.05%).

Kaabachi et al[15] in their study concluded that intrathecal Clonidine at 1 µg/kg prolonged spinal anaesthesia without causing severe adverse effects. Al Mustafa et al[11] in their study reported no cases of nausea or vomiting in the 5µg intrathecal Dexmedetomidine group. They also found no cases of hypotension and one case of bradycardia in this group. In comparison, they reported 1 case of nausea and vomiting, 4 cases of hypotension, and 2 cases of bradycardia in the Bupivacaine only group. They also reported on case of nausea and vomiting and one case of hypotension in the 10 µg Dexmedetomidine group. However, these differences were not statistically significant.

The findings in our study are comparable to the findings in the above studies, allowing us to conclude that there is no statistically significant difference as regards to nausea and vomiting, or the incidence of hypotension and bradycardia between Group C and Group D.

SUMMARY: This study was designed to compare the duration of subarachnoid blockade of intrathecal Dexmedetomidine and Clonidine combined with 0.5% hyperbaric Bupivacaine. Patients involved in this study were randomly divided into two groups, Group C and Group D of 50 patients each.

Group C received intrathecal 0.5% hyperbaric Bupivacaine 15 mg (3 mL) +37.5 µg Clonidine in 0.5 mL normal saline (Total 3.5 mL).

Group D received intrathecal 0.5% hyperbaric Bupivacaine 15 mg (3 mL) +5 µg Dexmedetomidine in 0.5 mL normal saline (Total 3.5mL).

1. There was no statistically significant difference between the groups with respect to age and sex distribution of the patients. There was no statistically significant difference with respect to heart rate and oxygen saturation.
2. There was a statistically significant fall in systolic and diastolic blood pressure within Groups C and D from 5 minutes to 180 minutes. However, on comparing the two groups, this fall in blood pressure was not statistically significant.
3. There was no statistically significant difference between the groups with regard to the maximum level of sensory blockade achieved. The difference in the meantime taken to attain maximum level of sensory block was statistically significant (p value=0.00001).
4. The difference in mean time taken to achieve complete motor blockade was statistically significant (p value= 0.0001).
5. The trend in regression of sensory blockade to T12 level was earlier in Group C as compared to Group D. There was a statistically significant difference in the number of patients achieving T12 level at 0 min, 30mins and 60 minutes post operatively (p value <0.05).
6. The mean time taken from the onset of sensory blockade to regression to T12 level was longer in Group D (199.7±34.067 minutes) as compared to Group C (151.7±22.533 minutes). This difference was statistically significant (p value=0.003).
7. The trend in the return of full motor function was earlier in Group C as compared to Group D, which was statistically significant (p value <0.05).
8. The duration of motor blockade was longer in Group D as compared to Group C. This result was statistically significant (p value <0.001).
9. The trend of increase in VAS score was earlier in Group C as compared to Group D, which was statistically significant between 90 to 210 minutes post operatively (p value <0.05).

10. The duration of analgesia was longer in Group D as compared to Group C. This result was statistically significant (p value <0.001).
11. On comparing the side effects, there was no statistically significant difference between Group C and Group D in the incidence of nausea, vomiting, hypotension, or bradycardia (p >0.05).

CONCLUSION:

We can thus conclude from the present study that:

1. 5 µg of Dexmedetomidine given intrathecally along with 0.5% hyperbaric Bupivacaine has a faster onset of motor blockade as compared to 37.5µg of Clonidine.
2. 5 µg of Dexmedetomidine given intrathecally along with 0.5% hyperbaric Bupivacaine has a longer duration of sensory blockade, motor blockade and analgesia as compared to 37.5µg of Clonidine.
3. There was a statistically significant fall in systolic and diastolic blood pressure in both the groups. However, on comparing the two groups, there was no statistically significant difference in the fall in blood pressure between the groups.
4. The difference in the incidence of sedation between the two groups is not statistically significant.
5. The incidence of side effects was minimal in both the groups, and the difference between the groups was statistically insignificant.

BIBLIOGRAPHY:

1. Wang JK, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. Anaesthesiology 1979;50(2):149-51.
2. Capogna G, Celleno D, Tagariello V, et al. Intrathecal buprenorphine for postoperative analgesia in the elderly patient. Anaesthesia 1988;43(2):128-130.
3. Paalzow L. Analgesia produced by clonidine in mice and rats. J Pharm Pharmacology 1974;26(5):361-3.
4. Bromage PR. Epidural Analgesia. Philadelphia: WB Saunders 1978:P-144.
5. Kanazi GE, Aouad MT, Jabbour-Khoury SI, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiologica Scandinavia 2006;50(2):222-227.
6. Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, haemodynamic, and postoperative analgesia in patients undergoing knee arthroscopy. Acta Anaestesiological Scandinavica 1994;38(7):724–728.
7. Gupta R, Bogra J, Verma R, et al. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. Indian J Anaesth 2011;55(4):347-51.
8. Al-Ghanem SM, Massad IM, Al-Mustafa MM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures. Am JAppl Sci 2009;6(5):882-7.
9. De Kock M, Gautier P, Fanard L, et al. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia intrathecal ropivacaine and clonidine for ambulatory knee arthroscopy. A dose response study. Anesthesiology 2001;94:574-8.
10. Strebel S, Jürg A. Gurzeler, et al. Small- dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: a dose response study. Anesth Analg 2004;99(4):1231-1238.
11. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J 2009;30(3):365-70.
12. Solomon RE, Brody MJ, Gebhart GF. Pharmacological characterization of alpha adrenoceptors involved in the antinociceptive and cardiovascular effects of intrathecally administered Clonidine. J Pharmacol Exp Ther 1989;251(1):27-38.
13. Ashraf Amin Mohamed, Khaled Mohamed Fares, Sahar Abd-Elbaky Mohamed. Efficacy of intrathecally administered dexmedetomidine versus dexmedetomidine with fentanyl in patients undergoing major abdominal cancer surgery. Pain Physician 2012;15(4):339-348.
14. Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low dose intrathecal clonidine as adjuvant to bupivacaine. Indian J Anaesth 2007;51(5):415–419.
15. Kaabachi O, Zarghouni A, Ouezini R, et al. Clonidine 1µg/kg is a safe and effective adjuvant to plain bupivacaine in spinal anaesthesia in adolescents. Anaesth analg 2007;105:516-519.