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ORIGINAL RESEARCH

A COMPARATIVE CLINICAL STUDY OF INTRATHECAL HYPERBARIC BUPIVACAINE WITH CLONIDINE AND BUPIVACAINE ALONE IN GYNAECOLOGIC SURGERIES

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ABSTRACT

Background: In this study, we wanted to evaluate the efficacy of intrathecal clonidine as an adjuvant to the hyperbaric bupivacaine (0.5%) providing better intraoperative and postoperative analgesia and hemodynamic stability.

Methods: This was a hospital based prospective randomised double-blinded study conducted among 100 patients of age group 30 to 65 years who underwent gynaecological surgeries under spinal anaesthesia categorized based on American Society of Anaesthesiologists (A.S.A.) physical status I – II to the Department of Anaesthesia, G.M.H / S.V.R.R.G.G.H., Tirupati after obtaining clearance from institutional ethics committee and written informed consent from the study participants.

Results: The mean time for the onset of sensory block in Group I was observed to be 4.21 minutes compared to 2.10 minutes in Group II, was statistically significant.

The mean time for the onset of motor block in Group I was observed to be 4.92±0.61 minutes compared to 2.23±0.51 minutes in Group II, was statistically significant.

The mean time was taken for the two-segment regression of sensory block in group I was 132.43 minutes varying from 107 to 173 minutes, while in Group II the time taken was 206.48 minutes with a minimum of 160 minutes to a maximum of 260 minutes, was statistically significant.

The mean duration of analgesia in Group I was 212.6±38.10 minutes, varying from 162 to 342 minutes and in Group II was 315.3±52.16 minutes, varying from 240 to 450 minutes, was statistically significant.

In Group II, 16% (8 patients) of study participants had dry mouth, 28% (14 patients) study participants had sedation and 14% (7 patients) study participants had both dry mouth and sedation while in n Group I none had these side effects, was statistically significant.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

Conclusion: In conclusion, the addition of clonidine 75 µg to hyperbaric bupivacaine, hastens the onset of sensory and motor blockade of bupivacaine, provides excellent surgical analgesia, prolongs the duration of postoperative analgesia and offers relative hemodynamic stability.
The 75µg of clonidine dose provides maximum benefit, and minimum side effects and these doses have an effect on sedation level, heart rate and mean arterial pressure which does not, however, require any therapeutic intervention and hence it can be an advocate as an adjuvant to bupivacaine in spinal anesthesia for gynecological surgeries.

Keywords: Intrathecal clonidine, hyperbaric bupivacaine (0.5%), intraoperative, postoperative analgesia, hemodynamic stability

INTRODUCTION

There has been growing interest in gynaecological anaesthesia, particularly in subarachnoid space, in the use of a combination of drugs that would reduce the individual dosages, thereby obtaining more significant analgesic effect with a lower incidence of side effects and various analgesic additives to local anaesthetics (L.A.) can improve the quality of analgesia both intra and postoperatively. Intrathecal clonidine is being extensively used as an alternative to neuraxial opioids. Intrathecal clonidine is free from opioid-related side effects.[1] It is known to increase both the sensory and the motor block of local anaesthesia.[2,3]

Various factors can influence the spread and action of the anaesthetic solution in vivo; those include a temperature of the solution, the patient position during and after the spinal injection, pH and density of the solution, the volume of the drug injected, and the height of the patient.[4] Commonly adjuvants are mixed with hyperbaric bupivacaine (H.B.) in a single syringe before injecting intrathecally because of its ease of administration, and this can alter the density of both the drugs and thus influencing their extent in the cerebrospinal fluid (CSF).[5]

Gynaecological surgeries are often associated with severe postoperative pain. The need of the hour is a minimally invasive technique that offers good intraoperative and postoperative analgesia using minimal concentration of a drug with minimal or no side effects. The task of medicine is to preserve the health and restore the health and to relieve the pain, and understanding pain is essential to both these goals.[6] The word pain was derived from the Latin word, poena that means penalty or punishment.[7]

Relief of pain during the operation and postoperative period is one of the mainstays of balanced anaesthesia, so any experience acquired in this field must be extended to the postoperative period also. In order to maximize postoperative analgesia, a number of adjuvants have been added to spinal local anaesthetics. Central neuraxial opioids like morphine, pethidine, fentanyl, sufentanil prolong the postoperative analgesia but are associated with side effects like nausea, vomiting, urinary retention, pruritis and in particular the potential of delayed respiratory depression. Intrathecal clonidine is being extensively evaluated as an alternative to neuraxial opioids for the control of pain and has been proven to be a potent analgesic, free of at least some of the opioid-related side effects'.[8]

The postoperative pain relief is a growing concern for anesthesiologist as an uneventful postoperative period makes surgery a comfortable proposition for surgical patients.[9] The use of spinal clonidine\ alpha 2 agonist has been in use since 1984. The alpha 2 agonist clonidine has a variety of different actions which includes the ability to potentiate the effects of local anaesthetics, and unlike spinal opioids, clonidine does not produce pruritis or respiratory depression, and it also prolongs the necessary blockade[10,11], and it reduces the amount or concentration of local anaesthetic required to produce postoperative analgesia.[12,13] The adjuvant given intrathecally along with a local anaesthetic like bupivacaine, can enhance the

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

postoperative analgesia by reducing the need for the NSAIDS in the immediate postoperative period will be beneficial.

There were very few studies conducted in this region to know the efficacy of the use of clonidine on spinal anaesthesia, especially gynaecological studies. Hence, the present study was initiated to evaluate the efficacy of intrathecal clonidine as an adjuvant to the hyperbaric bupivacaine (0.5%) providing better intraoperative and postoperative analgesia and hemodynamic stability.

Aim and Objectives

Aim

A comparative clinical study of intrathecal hyperbaric bupivacaine With clonidine and hyperbaric bupivacaine alone in gynaecological Surgeries.

Objectives

To compare the following parameters:

1. Assessment of sensory blockade:
   - The onset of sensory block
   - Maximum level reached
   - Duration of analgesia
2. Assessment of Onset of motor blockade
3. Assessment of intra-operative & postoperative complications.

Study of the duration of analgesia

MATERIALS & METHOD

Study Design: A prospective randomised double-blinded study.

Study Setting: Department of Anesthesia, G.M.H / S.V.R.R.G.G.H., Tirupati.

Study Population: Patients of age group 30-65 years who underwent gynaecological surgeries surgery under spinal anaesthesia categorized based on American Society of Anaesthesiologists (A.S.A.) physical status I - II and inclusion & exclusion criteria.

Exclusion Criteria

1. Known sensitivity to the drugs.
2. Peripheral neuropathy
3. Systemic infections
4. Coagulation disorders.

Sample Size

A total of 100 study participants were studied. The study population was divided into two groups of fifty each randomly.

Group I: Received 3.5ml of 0.5% bupivacaine (hyperbaric)

Group II: Received 3ml of 0.5% bupivacaine (hyperbaric) + 0.5ml of clonidine (75µg).

A lumbar subarachnoid block was performed under aseptic precautions in the L3 and L4 interspace, midline approach, using 25 gauze quincke's needle. The time of injection of the drug was recorded as zero minute. During surgery, all the patients were given intravenous fluids-isotonic saline and ringer's lactate for maintenance.

Intraoperative Monitoring

- N.I.B.P., E.C.G., Pulse oximeter were the intraoperative monitors used.

The following parameters were studied,

1. Assessment of sensory blockade:
   Sensory blockade was assessed by pinprick and time was noted for the block to reach different dermatomal levels.
   - The onset of sensory block
   - Maximum level reached

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

- Duration of analgesia

2. Assessment of Onset of motor blockade.
3. The patients were carefully monitored for any untoward effects like Inadequate block, hypotension, bradycardia, respiratory distress nausea, vomiting, shivering, restlessness, pruritis and anaphylactic reactions intraoperatively.
4. Patients were shifted to postoperative ward and observed till the administration of rescue analgesia and for the next 24 hours postoperatively for delayed complications or any side effects.

Ethical Considerations

The data was collected after taking ethical clearance from the Institutional Ethics Committee, and informed consent from study participants before administration of the questionnaire.

Statistical Analysis

Data entered in M.S. Excel and analyzed by using S.P.S.S. software. Qualitative data were represented as frequencies or percentages, and quantitative data were represented as means and standard deviation.

Terms and Definitions

The onset of Sensory Block - this was taken as the time 'from the deposition of a drug to the feeling of tingling sensation in the legs'.

The upper level of a sensory block - the highest dermatome of the block was assessed - taken as the time interval between the deposition of the drug and the loss of sensation at the highest dermatomal level.

The onset of motor block was noted. Time is taken from the onset of paresis to the loss of motor power (patient was not able to lift the legs).

Bromage scale: 0 = no motor blocked, 1 = hip blocked, 2 = hip and knee blocked, 3 = hip, knee and foot blocked.

Duration for 2 segment regression - time taken for recovery of the sensory level to 2 dermatomal segments below the highest level.

The total duration of analgesia — Time when the patient first complains of pain after spinal block (time for rescue analgesia)

Hypotension was treated with Oxygen, Rapid infusion of intravenous fluids, Mephentermine intravenously at 6mg increments, Injection atropine 0.6mg if associated with bradycar

Nausea and vomiting were treated with Inj. Ondansetron 4mg I.V.

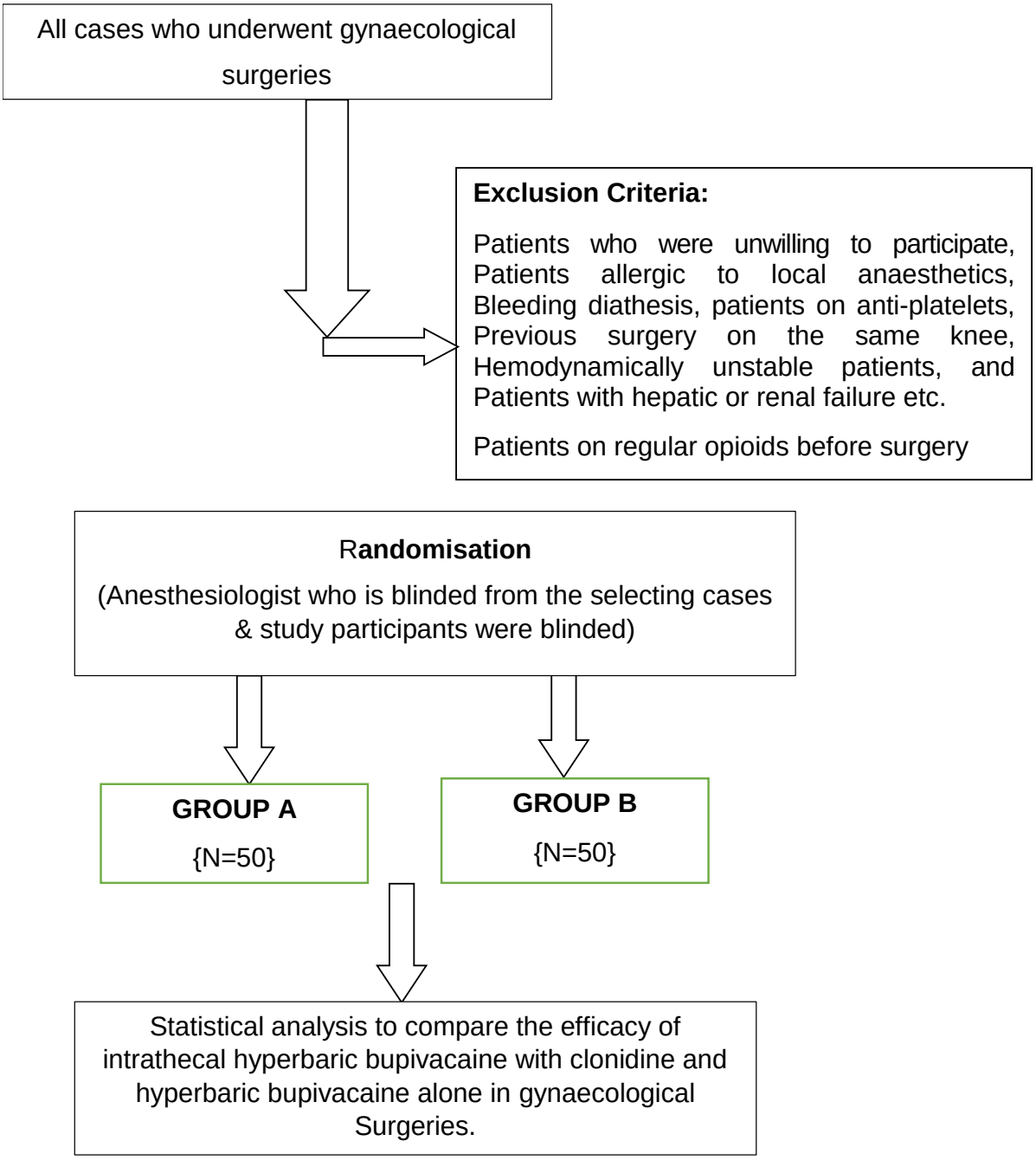
Delayed Complications

- Post dural puncture headache.
- Transient neurological symptoms
- Nausea
- Vomiting
- Shivering
- Respiratory depression
- Dry Mouth
- Drowsin

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

ALGORITHM OF THE STUDY

Flow Chart Showing the algorithm of the study



RESULTS

A total of 100 study participants were included, 50 from each group.

Chi-Square test was used to know the statistical significance between qualitative variables. Unpaired t-test was used to know the statistical significance between quantitative variables. P-value <0.05 was considered as statistically significant.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

The mean duration of surgery in Group I was 84±9.5 minutes and 85±7.2 minutes in Group II. The difference observed between the two groups with regard to the duration of surgery was statistically not significant.

The mean time for the onset of sensory block in Group I was observed to be 4.21 minutes compared to 2.10 minutes in Group II, with a P-value of <0.0001 which was found to be statistically significant.

The mean time for the onset of motor block in Group I was observed to be 4.92±0.61 minutes compared to 2.23±0.51 minutes in Group II, with a p-value of <0.000, which was found to be statistically significant.

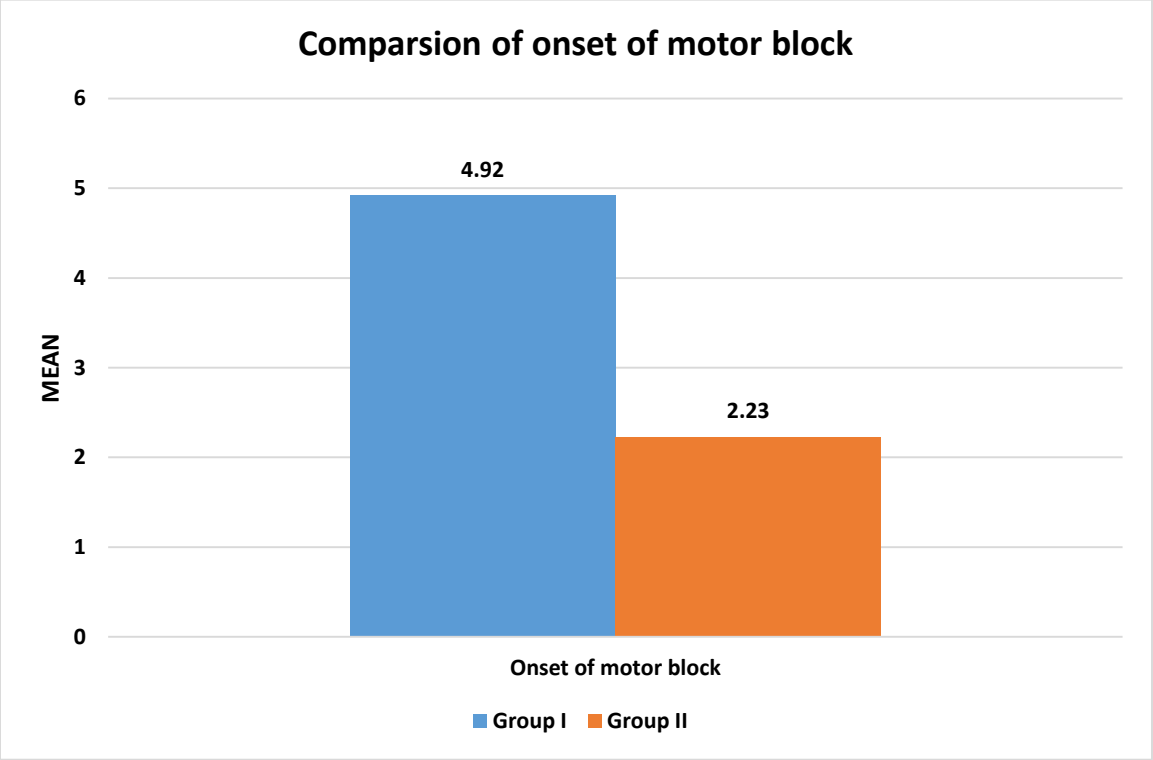


Figure 1: Comparison of study participants based on onset of motor block

The mean time is taken for the two-segment regression of sensory block in group I was 132.43 minutes varying from 107 to 173 minutes, while in Group II the time taken was 206.48 minutes with a minimum of 160 minutes to a maximum of 260 minutes and found to be statistically significant between the two groups with a P-value of <0.001

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

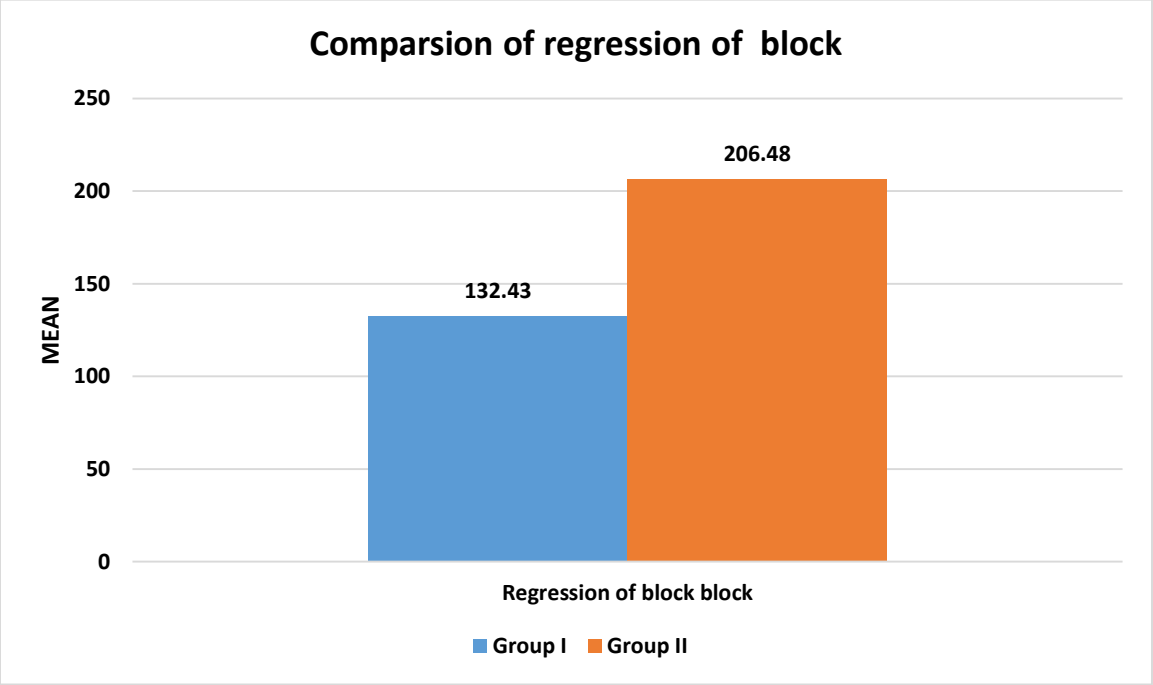


Figure 2: Comparison of study participants based on regression of block

In most cases, the maximum level reached was T6 (64% in Group I and 66% in Group II). There was no statistically significant difference between the two groups (p>0.05).

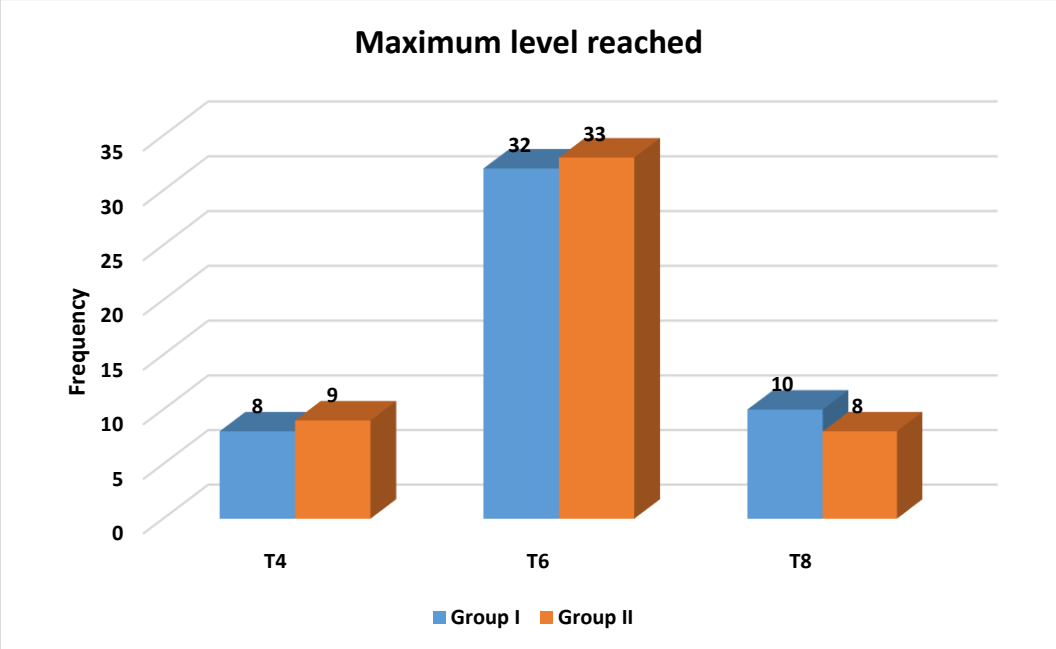


Figure 3: Comparison of study participants based on maximum level block reached

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

Table 1: Comparison of study participants based on the duration of analgesia

Variable	Group I (Mean ± S.D.)	Group II (Mean ± S.D.)
Duration of analgesia	212.6 ±38.10	315.3 ± 52.16
Inference	Unpaired t-test, p=0.001 (highly significant	

The mean duration of analgesia in Group I was 212.6±38.10 minutes, varying from 162 to 342 minutes and in Group II was 315.3±52.16 minutes, varying from 240 to 450 minutes and found to be statistically significant between the two groups with a P-value of <0.000.

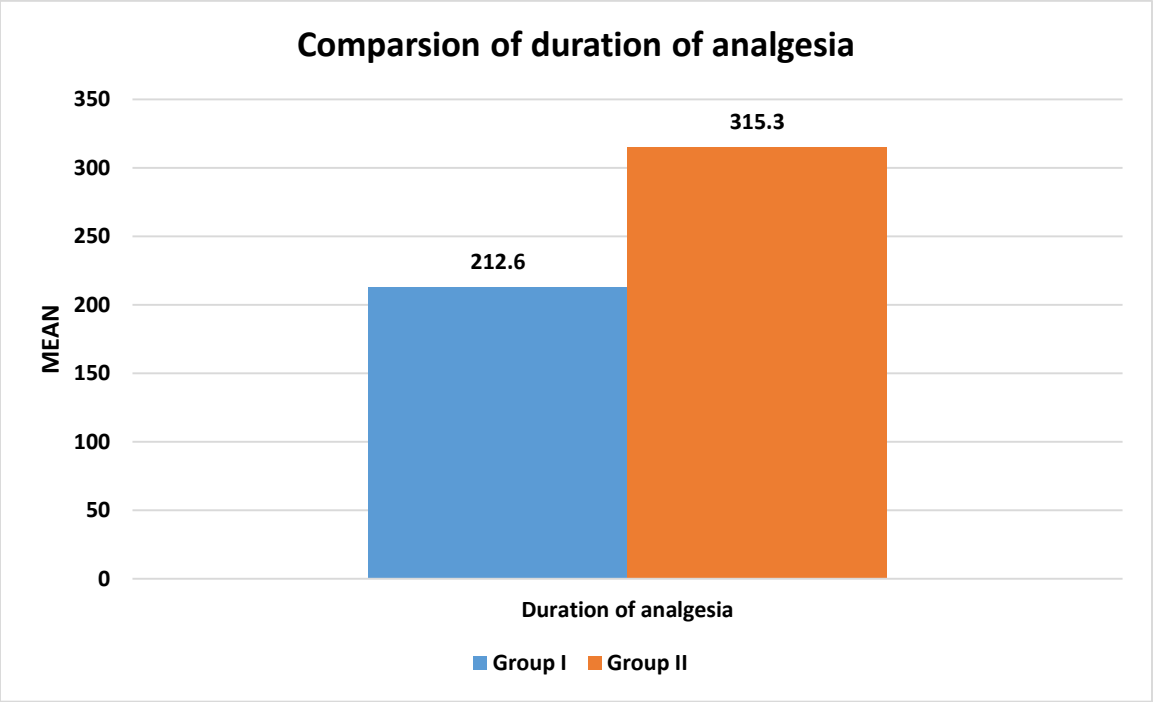


Figure 4: Comparison of study participants based on the duration of analgesia

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

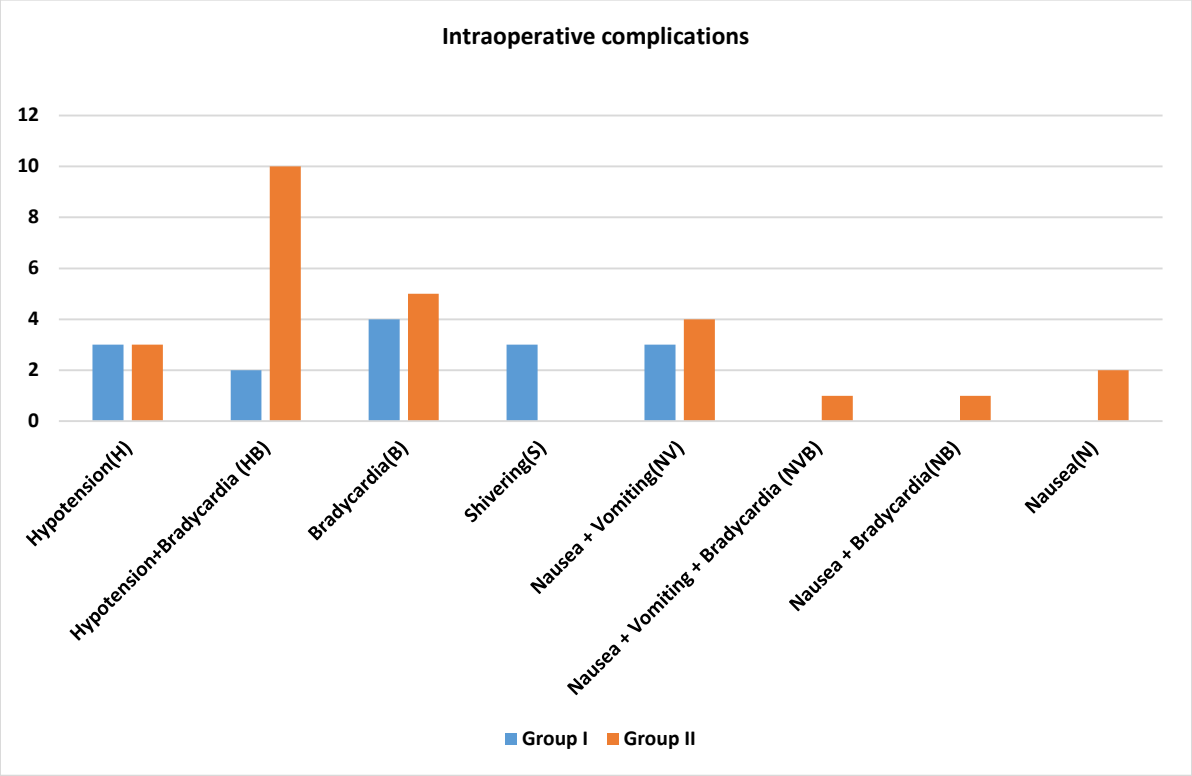


Figure 5: Comparison of intraoperative complications between groups

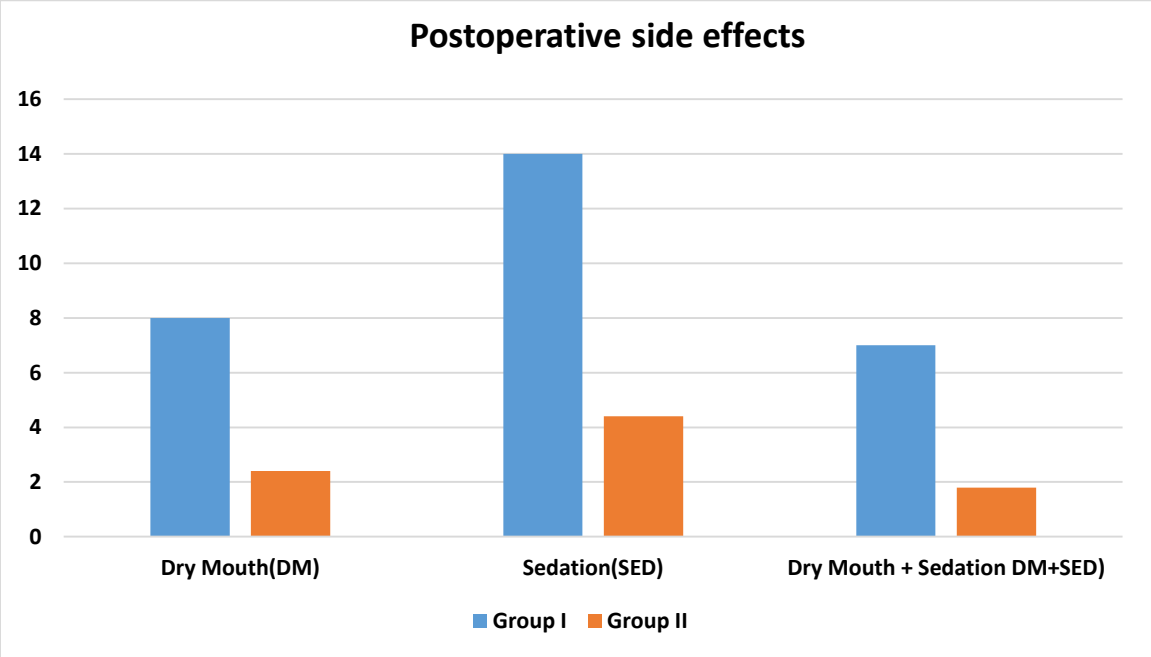


Figure 6 : Comparison of Postoperative side effects between groups

In Group II, 16% (8 patients) of study participants had dry mouth, 28% (14 patients)study participants had sedation and 14% (7 patients) study participants had both dry mouth and sedation while in n Group I none had these side effects. It was statistically significant which had a P-value of <0.000.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

DISCUSSION

A comparative clinical study of intrathecal hyperbaric bupivacaine with clonidine and hyperbaric bupivacaine alone in gynaecological Surgeries was done in 100 patients which are randomly allocated into two groups 50 in each group.

- Group I: Received 3.5ml of 0.5% bupivacaine (hyperbaric)
- Group II: Received 3ml of 0.5% bupivacaine (hyperbaric) + 0.5ml of clonidine (75µg).

Age:

In the present study, there were no statistically significant differences between the groups with regard to age.

A.S.A. status:

In this study, 66% of the patients in Group I and 78% of patients in Group II belong to A.S.A. Grade I, while 34% in Group I and 22% in Group II belong to A.S.A. Grade II. This difference between the groups with regard to the distribution of A.S.A. physical status is not significant.

Haemodynamic changes:

Heart rate:

There was no statistically significant difference observed in the mean Heart Rate, Blood pressure in the present study between two groups.

The onset of sensory block:

In the present study onset of sensory block was faster in group II, i.e. clonidine group (2.10±0.81 mins) than group I (4.21±0.92 mins) and this difference was found to be statistically significant.

Table 2: Comparison of Onset of sensory block findings of the present study with other studies

Studies	The onset of sensory block		P-value
	Clonidine Group (Mean±S.D.)	Other Group (Mean±S.D.)	
Present	2.10±0.81 mins	4.21±0.92 mins	<0.05

Highest level of the block:

In this study, the median and range of the highest sensory level recorded were T6 in both the groups.

Regression of sensory block:

The present study time for two-segment regression of sensory block was 206.48± 21.17 min in Group II and 132.43±10.70 min Group I and this difference was found to be statistically significant.

The onset of motor block:

In this study, the meantime taken for the onset of motor blockade was 4.92±0.61 minutes in Group I and 2.23±0.51 minutes in Group II and this difference were statistically significant. It indicates that the onset of motor block was faster in the clonidine group.

Table 3: Comparison of Onset of motor block findings of the present study

Studies	The Onset of Motor Block		P-value
	Clonidine group (Mean±S.D.)	Other group (Mean±S.D.)	
Present	2.23±0.51 minutes	4.92±0.61 minutes	<0.05

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

Duration of analgesia:

The mean duration of analgesia in Group I was 212.6±38.10 minutes while in Group II, it was 315.3±52.16 minutes, and this difference was statistically significant between the two groups.

Table 4: Comparison of duration of analgesia findings of the present study

Studies	Duration of analgesia		P-value
	Clonidine group (Mean±S.D.)	Other group (Mean±S.D.)	
Present	315.3±52.16 mins	212.6±38.10 mins	<0.05

Complications

In the present study, intraoperative complications were seen in both groups. In Group I, hypotension was observed in 3 patients, both groups, and in Group II 3 patients had hypotension. Bradycardia was observed in 4 patients Group I and in 5 patients in Group II. The shivering was noted in three patients in Group I, and none was observed in Group II. Nausea and vomiting were recorded in 3 patients in Group I and in 4 patients in Group II.

In the present study, the postoperative complications observed were in Group II 8 patients had dry mouth, 14 patients had sedation, and 7 patients had both (dry mouth and sedation) while in Group I none had these side effects.

CONCLUSION

The acute pain following surgical procedures is common to the clinical practice of the pain medicine, and it is one of the few opportunities in which the cause of pain is known before its occurrence, the pain is reliably expected to occur, and can be annulled effectively.

In conclusion, this study shows that the addition of clonidine 75 µg to hyperbaric bupivacaine, hastens the onset of sensory and motor blockade of bupivacaine, provides excellent surgical analgesia, prolongs the duration of postoperative analgesia and offers relative hemodynamic stability.

The 75µg of clonidine dose provides maximum benefit, and minimum side effects and these doses have an effect on sedation level, heart rate and mean arterial pressure which does not, however, require any therapeutic intervention and hence it can be an advocate as an adjuvant to bupivacaine in spinal anaesthesia for gynaecological surgeries.

This approach to pain therapy may give favourable outcomes such as successful analgesia may be achieved with minimal side effects.

- The addition of 75 µg of clonidine to hyperbaric bupivacaine resulted in a faster onset of sensory block and this difference was found to be statistically significant.
- In the present study, statistically significant faster onset motor blockade in group II was observed.
- The maximum level of sensory block was comparable in both groups.
- The duration of analgesia was significantly prolonged in Clonidine group was found to be statistically significant.
- In the present study, intraoperative complications were seen in both groups. Hypotension, Bradycardia, Shivering, Nausea and vomiting were recorded in both groups.
- In the present study, the postoperative complications observed were dry mouth, sedation, and both (dry mouth and sedation). In the Group I none had these side effects.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 5, 2023

The above findings show that the use of 75µg of intrathecal clonidine as an adjuvant to the hyperbaric bupivacaine in gynaecological surgeries is beneficial in several aspects and scored over the use of the hyperbaric bupivacaine alone with minimal side effects.

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