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RESEARCH ARTICLE

A PROSPECTIVE COMPARATIVE CLINICAL STUDY TO EVALUATE ORAL CLONIDINE AS A PREMEDICATION WITH 0.5% HYPERBARIC BUPIVACAINE & 0.5% HYPERBARIC BUPIVACAINE ALONE IN SPINAL ANAESTHESIA FOR PATIENTS UNDER GOING ELECTIVE LOWER ABDOMINAL AND LOWER LIMB SURGERIES.

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Abstract

BACKGROUND:-Spinal anesthesia is the most common technique used for lower abdominal surgeries. The concept of pre-emptive analgesia has been becoming popular and use of clonidine along with regional techniques is one of important milestones in post-operative pain management. Hyperbaric Bupivacaine has limited duration of action. Clonidine has been used to prolong duration of local anesthetic. Hence in our study, we studied effect of oral clonidine premedication on spinal anesthesia with hyperbaric bupivacaine with reference to onset and duration of sensory and motor block, duration of analgesia, sedation and including its effect on haemodynamic status.

METHODS:-Sixty patients of ASA grade I and II posted for elective surgeons under spinal anesthesia were selected. For this, prospective double blind study group received 150 microgram of oral clonidine, 90 minutes before spinal anesthesia. Spinal anesthesia was given with 3 ml of 0.5 % hyperbaric bupivacaine. Group P (control group) received sweetener tablet 90 minutes prior to spinal anesthesia.

RESULTS:-It was observed that clonidine as a premedication has no effect on the onset of sensory and motor block. Clonidine significantly prolonged duration of sensory and motor block ($p<0.001$). Duration of analgesia was also significantly prolonged in clonidine group ($p<0.001$). Clonidine at a dose of 150µcg is not associated with any major change in heart rate and blood pressure following spinal anesthesia. As compared to control group, Clonidine results in higher incidence of moderate sedation.

Conclusion:-We conclude that oral clonidine premedication in patients with hyperbaric bupivacaine prolong duration of sensory and motor block, also prolongs duration of analgesia and provides moderate sedation.

Introduction:-

Galen described pain as "A complex multidimensional human perception. It is divine to allay pain"

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Acute postoperative pain management is not only a human feeling, but it is a key aspect of postoperative care, as acute pain, regardless of its site, can adversely affect nearly every organ function, and so affects the postoperative morbidity and mortality (Morganet al., 2006)[1]

The Role of premedication, in ancient time, was to prevent the side effects of many anaesthetic agents example anticholinergic agent was given to prevent salivation and bradycardia produce by ether and cyclopropane. But with

development of newer anaesthetic with minimal side effects , the role of premedication has changed and now the goal of modern anaesthesia practice is to decrease anxiety and to make the experience of surgery less traumatic.

Prevention and treatment of post operative pain continues to be a major challenge in post operative care and plays an important role in early mobilization and well being of the surgical patients. Effective post-operative analgesia results in improvement of respiration and stress on cardiovascular system, early return of GIT motility, early ambulation and discharge from hospital. Earlier it was considered that the pathophysiology and management of postoperative pain and neuropathic pain were different and distinct entity but now they are regarded as same as far as management is concerned.

Oral therapy may include Opioids, NSAIDS or COX-2 inhibitors. Though none of the drug therapy is ideal for controlling acute pain, as opioids are inevitably associated with emesis, risk of respiratory depression and addiction. The use of NSAIDs and COX-2 inhibitors is limited by complications like dyspepsia, GI bleed, renal failure, etc. To overcome the problems of Opioid and NSAIDs, adjuvant drugs are being added to treatment, which significantly improves the quality of opioid analgesia, reduces opioid requirement, possibly prevents or reduces opioid tolerance and relieves anxiety.

The word "Pre-empt" is defined as 'to take action in order to prevent an attack or other anticipated event happening forestall'. Preemptive analgesia is defined as an antinociceptive treatment that prevents the establishment of altered central processing of afferent input, which amplifies postoperative pain.[2] The concept of preemptive analgesia to reduce postoperative pain was founded on a series of successful animal experimental studies that demonstrated central nervous system plasticity and sensitization after nociception. [3-5] A variety of interventions have been used to achieve a pronounced preemptive effect, such as epidural analgesia, peripheral local anesthetic infiltrations, systemic N-methyl d-aspartate receptor antagonists, systemic non-steroidal anti-inflammatory drugs and systemic opioids.[6,7] To hasten the onset of sensory and motor block and to improve quality and duration of post-operative analgesia, many adjuvants have been used along with local anaesthetics.

Alpha adrenergic agonist clonidine is now a days used currently as an adjuvant or as an premedication with local anaesthetics intrathecally to fasten onset & to prolong motor, sensory blockade; also to relieve post-operative pain.

There is a need for an adjuvant which increases the duration of analgesia with the duration of motor blockade, thus prolonging post operative analgesia, reducing post operative analgesic requirements.[8]

Intrathecal Bupivacaine is the most commonly used drug in day to day practice as it provides longer duration of anaesthesia and is four times more potent compared to its precursor lignocaine.[9]

Neuraxial adjuvants are used to improve blockade or prolong intra operative and post operative analgesia and decrease the adverse effects associated with high doses of a single local anaesthetic agent. In addition to their dose sparing effects, neuraxial adjuvants are also used to reduce the latency of onset, improve the quality and prolong the duration of neural blockade.

Common neuraxial adjuvants include opioids, sodium bicarbonate (NaHCO3), vasoconstrictors, alpha-2 adrenoceptor agonists, cholinergic agonists, N-methyl-d-aspartate (NMDA) antagonists and γ-aminobutyric acid (GABA) receptor agonists.[9]

Clonidine is a centrally acting partial alpha-2 adrenoceptor agonist. Its analgesic effect is said to be mediated by binding postsynaptic alpha-2 receptors (G-protein coupled inhibitory receptors) in the dorsal horn of the spinal cord, resulting in its antinociceptive action .

Clonidine has many routes of administration- intrathecal, oral, intramuscular, intradermal, intravenous and epidural.

When used as a neuraxial adjunct for pain relief after caesarean delivery, major abdominal and orthopaedic surgery, clonidine prolongs the duration of analgesia and anaesthesia, resulting in a longer period of post operative analgesia.[9]

Material and methods:-

This study was conducted in Dhiraj General Hospital in Department of Anaesthesiology for 1.5 years.

60 patients of American society of anaesthesiologists (ASA) Grade I –II, undergoing elective lower abdominal and lower limb surgeries under spinal anaesthesia were selected for this study. Patients were randomly allocated into two equal groups and this double blind study was conducted according to type of adjunct drug. The study was prospective and interventional in nature.

Methods of collection of the data:-

Data was collected in prescribed Performa meeting the objectives of the study**.** The study population was in 2 groups with 30 patients in each group (n=30).

Group P (P-Placebo): (n=30) received sweetener tablet 90 min before anaesthesia

Group C (C-Clonidine): (n=30) received Tablet clonidine 150µg 90 min before anaesthesia

Inclusion Criteria:-

- Adult patients aged between 18-65 years posted for elective lower abdominal and lower limb surgeries under spinal anaesthesia.
- Patients belonging to ASA Class I & II
- Patient willing to sign informed consent.

Exclusion Criteria:-

- Age <18 yrs and >65yrs.
- Patients belonging to ASA class III and above.
- Patients with hypertension, cardiac, renal, hepatic & cerebral diseases.
- obese patients.
- Patients posted for emergency surgeries.
- Pregnant females.
- Known allergy to the trials.
- Patient on beta blockers.

Pre-anaesthetic assessment:-

On the day prior to surgery, a preanaesthetic evaluation comprising of history of previous medical and surgical illnesses, previous anaesthesia exposures, and drug allergies was done. Thorough clinical examination including physical , systemic and back & spine examination was done. Any contraindication to spinal anaesthesia was ascertained.

Lab Investigations:-

Routine investigations were done. {CBC, Urine analysis, Serum creatinine, SGPT, Fasting blood sugar, ECG, Chest X-ray}No specific investigations were required pertaining to the study.

The patients were kept Nil per mouth for 6 hrs before surgery and informed written consent was taken. 60 packets of one tablet in each were made by an independent observer. Among these , 30 tablets were clonidine 150µcg (group C) and the remaining were placebo tablets (group P). All the packets were mixed and any packet was picked up by the investigator and given to the patient 90 min before spinal anaesthesia with sips of water. Baseline pulse rate ,systolic and diastolic blood pressure were recorded before premedication.

Half an hour before procedure, after taking intravenous line,preloading with Ringer lactate was started at 10ml/kg. In the operation theature ,noninvasive multipara monitor was attached and S_PO2, heart rate, blood pressure and sedation score was recorded.

After premedicated with Inj. Glycopyrrolate 0.2mg iv, Inj. Ondansetron 4mg iv under all aseptic and antiseptic precaution spinal block was administered in L3-L4 subarachnoid space in either sitting or lateral position using 25G Quincke Babcock spinal needle. After confirming free flow of CSF inj hyperbaric Bupivacaine 0.5% 3cc was injected over 10 sec. After spinal injection patient was returned to supine position .

Sensory block was evaluated by pinprick for every minute till T10 level achieved, then after sensory level was checked every 5 minute till two reading showed same level that was consider as highest sensory level.

Motor block was assessed using modified bromage scale.

Grade	Definition
0	Free movements of legs and feet , with ability to raise the extended leg.
1	Inability to raise extended leg and knee flexion is decreased, but flexion of feet and ankles is present.
2	Inability to raise leg or flex knees, flexion of ankle and feet present.
3	Inability to raise leg, flex knee or ankle , or move toes

Motor block was assessed every 2 min till bromage scale reached to grade 3.When sensory level T10 and bromage scale 3 achieved surgeon was allowed to start surgery. Through out surgery sensory and motor block was assessed every 10 min.

Intra operatively pulse, SBP , DBP and S_pO2, sedation score were recorded every 5min for first 30 min and then every 15 min till the end of surgery. Any complication like hypotension, bradycardia, nausea, vomiting, pruritus etc was noted and treated accordingly. Hypotension < 90 mmHg systolic blood pressure was treated with iv fluid & inj mephentermine 6 mg iv increments. Fall in heart rate < 50/min was treated with inj atropine 0.6 mg iv.

Sedation will be assessed by Ramsay's sedation score as written below

1- Anxious,agitated and restless.
2- Awake,cooperative,oriented,tranquil.
3- Semisleep responds only to verbal commands.
4- Asleep with brisk response to glabellar tap or loud auditory stimulus.
5- Asleep with sluggish response to glabellar tap or loud auditory stimulus
6- Non responsive.

At the end of surgery all patients were monitored in sicu for next 24 hours Sensory and motor block was assessed every 30 min till complete regression of both sensory and motor block. Duration of analgesia was assessed using visual Analogue scale and rescue analgesia in the form of Inj diclofenac 75mg iv was given when VAS >3.

VAS SCORE: 0-----1-----2------3-------4------5-----6-------7-------8------9------10

0- NO PAIN; 10-WORST IMAGINABLE PAIN.

Parameters to be recorded:-

1. **Onset of sensory block**: Time interval between completion of drug injection in subarachnoid space to achievement of T10 sensory level.
2. **Onset of motor block** : Time interval between completion of drug injection in subarachnoid space to achievement of bromage scale 3.
3. **Intraoperative haemodynamic parameters :** Pulse , Systolic blood pressure. Diastolic blood pressure.

4. **Sedation score:** intraoperative sedation score was recored at every 30 mins.
5. **Duration of sensory block:** Time interval between onset of sensory block to 2 segment regression of sensory level.
6. **Duration of motor block:** Time interval between onset of motor block to complete recovery of motor effect (bromage scale 0).
7. **Duration of post operative analgesia :** Time interval between onset of sensory block to vas score > 3.

Statistical Method Employed:-
Statistical analysis was done with non-paired (two tailed, independent) student t-test for continuous data.
Results were expressed as mean ± SD.
p-values :
p>0.05- Statistically not significant (NS)
p<0.05- Statistically significant (S)
p<0.01- Statistically highly significant (HS)
p<0.001- Very highly significant

The observation data were gathered from proforma, documented in the master chart and they were expressed in the form of charts and tables. These are mentioned in the chapter of observation and results.

Observations and results:-

Table 1: demographic data

Variables	Group – P	Group – C	p-value
Age (years)	46±11.095	43.67±11.167	0.420
Sex (M/F)	22/8	25/5	0.532
Height (cms)	164.7±2.97	165.7±3.54	0.241
Weight (kg)	51.63±4.28	50.8±3.86	0.432
DO Surgery	75±23.305	77.5±23.662	0.682
ASA (I/II)	13/17	20/10	0.119

The demographic data were comparable between two groups. (p >0.05)

The mean duration of surgery was 77.5±23.662 min and75±23.305 min in study and control group respectively.

There were 20 cases with ASA grade I and 10 with ASA grade II in group C. In group P, 13 cases with ASA grade I and 17 with ASA grade II.

Table 2: Age Distribution.

Age Group (years)	Group – P		Group – C	
	No	%	No	%
18-30	3	37.5	5	62.5
31-40	8	50.0	8	50.0
41-50	10	55.6	8	44.4
51-60	7	50.0	7	50.0
>60	2	50.0	2	50.0
Total	30	50.0	30	50.0

The mean age in group C, was 43.67±11.167 years and in group P it was 46±11.095 years. In both groups, maximum number of patients were between 41-50 years of age.

Table 3: Sex distribution.

Sex	Group – P	Group – C	p-value
Male	22 (73.33%)	25 (83.33%)	0.532
Female	8 (26.67%)	5 (16.67%)	
Total	30 (100%)	30 (100%)	

There were 25 (83.33%) males and 5 (16.67%) females in group C. And in group P, there were 22 (73.33%) males and 8 (26.67%) females.

Table 4: Types of surgery

Type Surgery	GROUP		Total
	Group-P	Group-C	
Gynecology	3	3	6
	10.0%	10.0%	10.0%
Orthopedic	14	18	32
	46.7%	60.0%	51.7%
Surgery	13	9	22
	43.3%	30.0%	38.3%
Total	30	30	60
	100.0%	100.0%	100.0%

Maximum number of patients from both groups, 46.7% from group P and 60% from group C had undergone orthopedic surgeries whereas 10% of patients from both group underwent gynecological surgeries.

In both study and control group, there were 3 (10.0%) gynecological surgeries in each group.

There were 18(60 %) and 14 (46.7 %) Orthopedic surgeries in study and control group respectively.

9 (30%) and 13 (43.3%) cases of general surgery were taken in group C and group P respectively.

Table 5 :Onset of Sensory & Motor Block

	Group – P	Group – C	p-value
Onset of Sensory Block (min)	3.60±0.498	3.57±0.568	0.810
Onset of Motor Block (min)	6.13±0.900	5.73±0.868	0.085

Mean duration of onset of sensory block in group P is 3.57±0.568 mins as compared to 3.60±0.498mins in group C. This was found to be statistically non-significant.($p>0.05$).

Mean duration of onset of motor block in group C is 5.73±0.868 mins as compared to 6.13±0.900 mins in group P. This is also found to be statistically non-significant.

Table 6 : duration of motor and sensory block and duration of analgesia

	Group – P	Group – C	p-value
Duration Of Sensory block (mins)	67.33±5.088	122.77±5.341	<0.001
Duration Of Motor block(mins)	112.27±12.929	209.2±16.666	<0.001
Duration Of Analgesia (mins)	133.37±27.001	221.23±44.049	<0.001

The mean duration of sensory block, in study group was 122.77±5.341 minutes and 67.33±5.088 minutes in control group. The data was statistically highly significant (P<0.001).

The mean duration of motor block , in group P was 209.2±16.666 minutes and 112.27±12.929 minutes in group C. The data was statistically highly significant (P<0.001).

In study group, mean duration of analgesia was 221.23±44.049 minutes and in control was 133.37±27.001 minutes.
The data was statistically highly significant
(P<0.001).

Table 7:Highest Sensory Block

Highest Sensory Block	Group – P		Group – C	
	No.	%	No.	%
8	16	53.3	17	56.7
10	14	46.7	13	43.3
Total	30	100	30	100

	Value	df	P-value
Pearson Chi-Square	0	1	1.000

16 patients out of 30 in group P achieved T-8 as the highest sensory level whereas 17 patients out of 30 in group C had highest sensory level at T8.

14 patients out of 30 in group P achieved T-10 as the highest sensory level whereas 13 patients out of 30 in group C had highest level at T10.

There was no significant difference among both the groups in achieving highest sensory level. (p>0.05)

Table 8:Mean of Highest Sensory Block

	Group – P	Group – C	p-value
Highest Sensory Block	9.13±1.358	8.87±1.008	0.391

Table 9: Mean pulse rate at different time intervals.

Time in mins	Group – P (pulse/min)	Group – C (pulse/min)	p-value
PR0	91.73±8.956	89.73±10.606	0.433
PR2	91.33±9.817	89.67±13.484	0.586
PR5	88.27±10.017	87.87±14.574	0.902
PR10	84.33±11.093	84.87±13.5	0.868
PR15	83.03±10.969	83.87±13.965	0.798
PR20	80.27±11.101	81.47±12.8	0.699
PR25	79.1±11.966	79.87±12.204	0.807
PR30	79.03±11.358	77.93±12.72	0.725
PR45	77.4±11.181	75.73±12.448	0.587
PR60	78.92±8.546	74.15±9.844	0.065
PR75	78.75±6.688	73.56±9.494	0.078
PR90	78.67±6.481	74.91±12.21	0.418
PR105	82.4±6.542	72±8.718	0.065
PR120	79±9.592	73±15.556	0.576

Difference in mean heart rate between two groups at any time interval throughout surgery was statistically insignificant. ($p > 0.05$)

Graph11: Chart representing comparison of mean pulse rate at different time intervals.

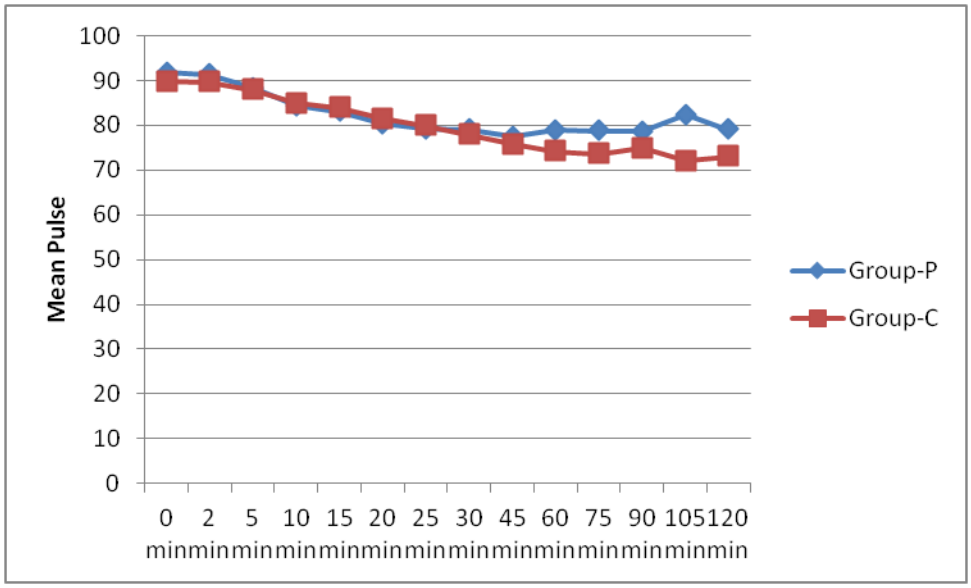

Table 10: Mean systolic Blood Pressure at different time intervals.

Time in min	Group – P (mm of Hg)	Group – C (mm of Hg)	p-value
SBP0	133.27±9.15	126.73±13.157	0.029
SBP2	130.07±10.11	123.6±13.619	0.041
SBP5	124.4±9.69	118.97±11.845	0.057
SBP10	117.93±7.343	115.13±8.846	0.187
SBP15	115.87±8.169	112.13±8.709	0.092
SBP20	113.53±8.955	111.07±8.94	0.290
SBP25	112.53±8.287	111.6±9.343	0.684
SBP30	112.87±8.299	110.53±10.464	0.343
SBP45	113.6±7.361	107.33±19.857	0.110
SBP60	113.31±7.693	111.41±11.078	0.473
SBP75	113.38±6.098	109.89±7.561	0.152
SBP90	116±4.796	110.67±7.28	0.085
SBP105	120±8.485	110.8±10.545	0.167
SBP120	120.5±5.745	105±4.243	0.030

Difference in mean systolic blood pressure between two groups at any time interval throughout surgery was statistically insignificant. ($p > 0.05$)

Graph12: Chart representing comparison of mean of systolic blood pressure at different time intervals.

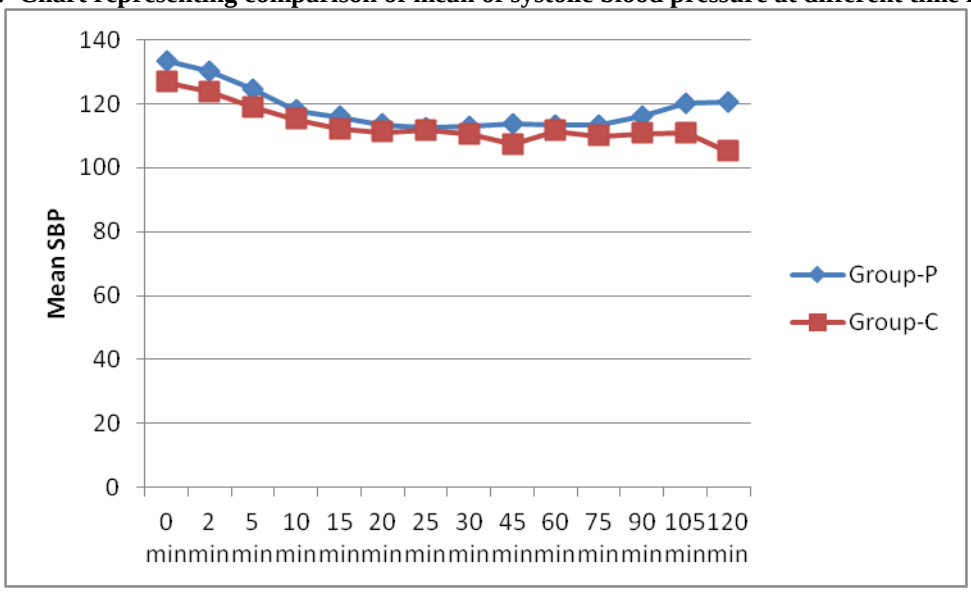

Table 11: Mean Diastolic Blood Pressure at different time intervals.

Time in min	Group – P (mm of Hg)	Group – C (mm of Hg)	p-value
DBP0	85.53±6.637	81.67±7.279	0.036
DBP2	83.8±7.36	82.4±7.304	0.463
DBP5	77.93±6.736	76.27±7.552	0.371
DBP10	74.53±7.736	74.47±7.533	0.973
DBP15	73.67±6.85	71.73±7.697	0.308
DBP20	72.8±7.383	71.07±8.013	0.387
DBP25	73.13±7.873	71.27±8.313	0.376
DBP30	72.67±6.712	71.6±8.144	0.582
DBP45	72.8±4.475	70.27±7.978	0.135
DBP60	73±5.993	70.81±10.172	0.348
DBP75	72.75±4.837	70.11±7.684	0.247
DBP90	71.56±4.333	70.89±4.91	0.764
DBP105	79.2±5.404	74.8±6.261	0.268
DBP120	80.5±8.226	79±4.243	0.149

Difference in mean diastolic blood pressure between two groups at any time interval throughout surgery was statistically insignificant. ($p > 0.05$)

Chart showing comparison of mean of diastolic blood pressure at different time intervals.

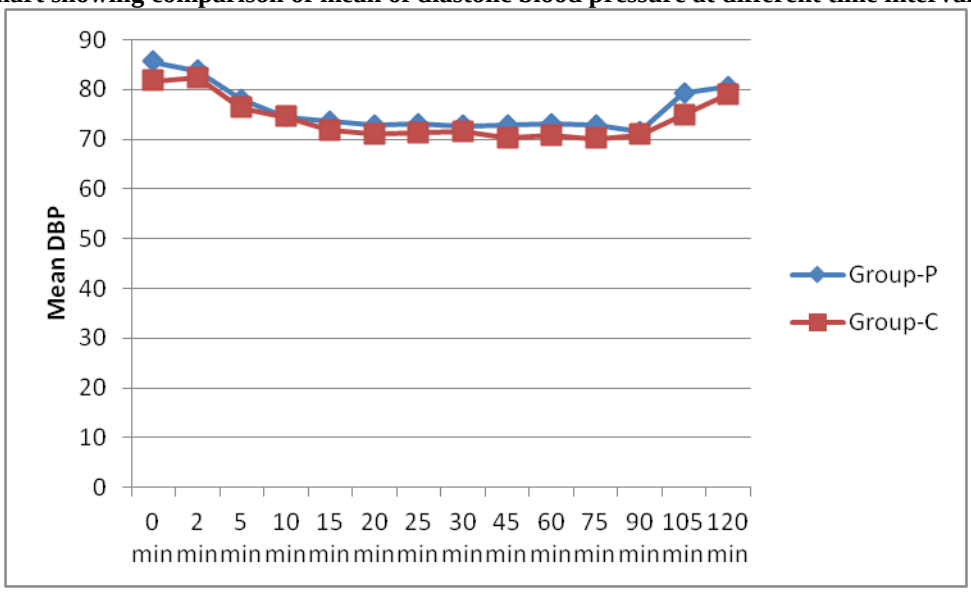

Table 12: Mean Respiratory Rate at different time intervals.

	Group – P (rate/min)	Group – C (rate/min)	p-value
RR0	16±0	16±0	NA
RR2	16±0	15.87±0.507	0.155
RR5	15.73±0.691	15.8±0.61	0.694
RR10	15.87±0.507	15.87±0.507	1.000
RR15	15.87±0.507	15.6±0.814	0.133
RR30	15.93±0.365	15.87±0.507	0.561
RR60	15.85±0.543	15.8±0.61	0.768
RR75	15.53±0.874	15.41±0.931	0.667
RR90	16±0	15.06±1.029	0.012
RR120	16±0	15.33±1.033	0.242

Chart showing comparison of mean of respiratory rate at different time intervals.

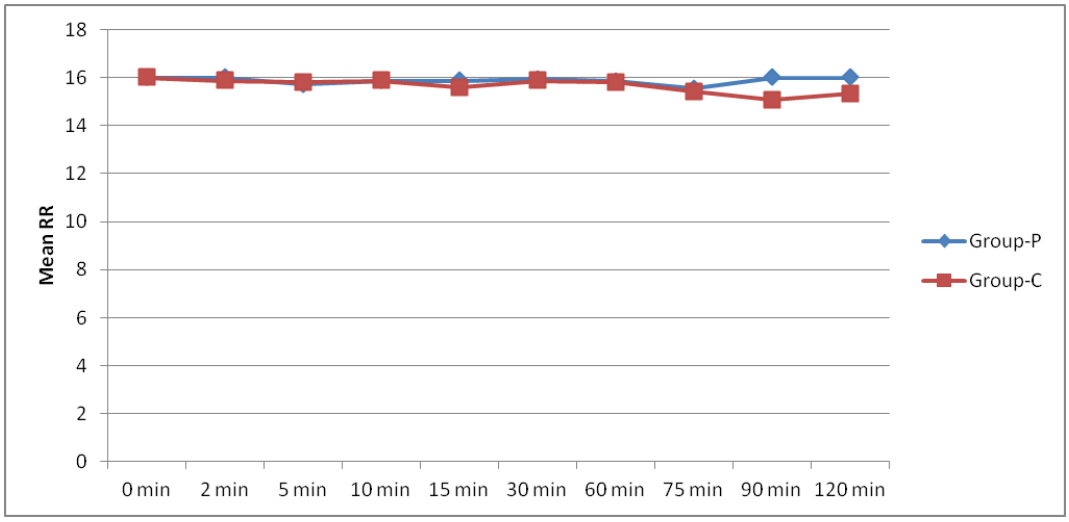

Table 13:sedation score

Average Sedation Score	Group – P		Group – C	
	No.	%	No.	%
2	30	100.0	11	36.7
3	0	0	19	63.3
Total	30	100	30	100

	Value	df	p-value
Pearson Chi-Square	27.805	1	<0.001

19 patients (63.3 %) from group C had average sedation score of 3 and 11 patients (36.7%) had average sedation score of 2 whereas 30 patients of group P had average sedation score of 2.

TABLE14: Side effects in control and study group.

Side Effect	Group – P		Group – C	
	No.	%	No.	%
BRADYCARDIA	1	3.33	2	6.67
Hypotension	0	0	2	6.67
Nausea	0	0	3	10

Two patients (6.67%) from group C had bradycardia compared to one patient (3.3%) of group P.
Two patients (6.6%) of group C had hypotension and 3 patients (10%) of group C had nausea.
None of the patients in group P had hypotension or nausea.

Discussion:-

The Role of premedication, in ancient time, was to prevent the side effects of many anaesthetic agents eg. anticholinergic agent was given to prevent salivation and bradycardia produce by ether and cyclopropane. But with development of newer anaesthetic with minimal side effects , the role of premedication has changed and now the goal of modern anaesthesia practice is to decrease anxiety and to make the experience of surgery less traumatic.[51]

Clonidine, an alpha-2 adrenergic agonist has sedative, anxiolytic and analgesic properties, thus it decreases the requirement of anaesthetic drug when use as an premedication[52].Besides performing the role of premedication oral clonidine can also potentiate the analgesic effect of local anaesthetics in regional anaesthesia[53,54]. Various studies are done with intrathecal clonidine but it will not act as an premedication, simultaneously main limitation of spinal anaesthesia is to provide longer duration of analgesia inspite of long acting local anaesthetic. So there is constant need for adjuvant which provide long duration of analgesia without significant side effects. Thus oral clonidine can work as a premedication and also as an adjuvant to local anaesthetic for intrathecal block.

Clonidine is an alpha2 agonist. and Imidazoline derivative, it is available as 100, 250, 300 µg tablets for oral administration, and injectable solution containing 150 µg/ml for I.v or i.m , local , regional use. It is a partial agonist with an alpha-2a to alpha-1 selectivity ratio of 39:1.

We evaluated 150µg Clonidine orally as a premedication on enhancing the effect of intrathecal Bupivacaine. **Anita Kumari et al** has compared two different doses of oral clonidine 150µg & 300µg and they concluded that " increasing the dose of clonidine does not prolong the duration of analgesia rather aggravate the side effects. **Spencer**

et al has used 200µg clonidine with lignocaine and they found significant hemodynamic depression with 200 µg clonidine[55]. Thus the dose response relationship has plateau effect at a dose of 150 µg.[56,57,58].

In our study oral clonidine was given 90 min before giving spinal anaesthesia similarly **Shruthi Jayaram** &**Anu Prasad** has used oral clonidine 90 min before spinal anaesthesia in their study and they found it effective. Orally administered clonidine completely gets absorbed and its peak effect occurs within 1-3 hours of administration. [59]

We studied 60 patients divided into two equal groups each having 30 patients to evaluate 150µg oral clonidine as an premedicantion for enhancing effects of intrathecal bupivacaine.. Group p was placebo group. Group c was clonidine group.

The demographic profile of the patients were comparable which provided an unbiased platform for statistical analysis. Various demographic variables such as age, gender, weight, height and duration of surgery were comparable in both groups and was found out to be statistically non-significant($p>0.05$). Duration of surgery in placebo group was 75.00±23.305 min and in clonidine group it was 77.50±23.662 min ($p>0.05$), which was also statistically insignificant.

Oral clonidine premedication did not result in any significant changes in initial block characteristics. There was no significant difference in time required for onset of analgesia at T-10 dermatomal level and to achieve motor block (Bromage grade 3) in both groups. Similarly maximum number of patients from both groups achieved highest sensory level at T8 (Table no 7). Onset of sensory block in our study was 3.60±0.498 min in placebo group and 3.57±0.568 min in clonidine group and onset of motor block in placebo group was 6.13±0.9 min as compared to 5.73±0.868 min in clonidine group which was statistically insignificant($p>0.05$) (Table no 5).

Our study coincided with study done by **R**. **Sudar codi et al[18] and Anita Kumari et al[22]** as they also showed statistically insignificant difference in terms of initial block characteristics. But **Shruthi Jararam et al [20]** found time taken to achieve highest sensory level was earlier in clonidine group than control group.

Table no 6 – shows the duration of sensory and motor block in our study. Duration of sensory blockade{2 segment regression} in placebo group was 67±5.08 min whereas in clonidine group it was 122.77±5.34 min similarly duration of motor block in placebo group was 112.27±12.929 min and in clonidine group it was 209.20±16.666 min.

Thus the differences in duration of sensory and motor block between two groups was very highly significant ($p<0.001$). Our study was in accordance with **Shruthi jayaram et al [20]**study in which mean duration for 2 segment regression in clonidine group was 121±19.71 min and in control group it was 76.26±13.66 min ($p=0.000$) which was highly significant . Similarly **R.Sutar codi et al** [18] who used 100µg clonidine as a premedication with bupivacaine in subarachnoid block found longer duration of motor block in clonidine group. **Dziudbziela et al[15] and Anita kumari et al[22]** also proved that oral clonidine prolong the sensory and motor block produced by Bupivacaine. Clonidine has also prolonged the motor block produce by lignocaine as shown by **Spencer et al[55] .**

Clonidine is highly lipid soluble, easily crosses blood brain barrier and interact with α receptor at spinal and in central nervous system [60]. It causes constriction of spinal vasculature and therefore prolongs effect of local anesthetics. Clonidine inhibits neurotransmission in A-delta and c fibres and potentiates inhibitory effect of local anesthetics on C fibre activity[20].This is the mechanism by which clonidine enhance the block produce by local anaesthetic.

Duration of analgesia in our study was 133.27±27.001 min in control group and in clonidine group it was 221.23±44.049 min. Thus premedication with oral clonidine provide significantly longer duration of analgesia {$p<0.001$}.our study coincided with study done by **Sudar codi et al[18]** which showed highly significant difference in duration of post operative analgesia between control group(115.90±90 min**)** and clonidine group (183.30±20.21 min) ($p=0.000$). Similarly **Dobrydnjov et al[14]** also showed prolong time requirement for first dose of analgesic in clonidine group ($p<0.05$). **Anita kumar et al[22]** also found longer postoperative analgesia with both clonidine groups (150µg and 300 µg) than control group but groups receiving clonidine had similar duration of post operative analgesia thus by increasing the dose of clonidine duration of analgesia will not get prolong.

According to **Anita Kumari et al** [22] " the analgesic effect of clonidine is by activation of presynaptic α-2 adrenoceptor in locus coeruleus and by inhibiting the release of norepinephrine . Thus it prevents the propagation of signals responsible for pain" [61]. Whereas according to **R.Sudar Codi et al [18]study " α_2** adrenergic receptor are strategically located on the dorsal horn neurons of the spinal cord where they can either inhibit the release of nociceptive neurotransmitters such as substance P or calcitonin gene related peptide".Another mechanism of analgesica according to **R.Sudar Codi et al[18]** is by senergistic interaction between α_2 adrenergic agonist and opiods in the spinal cord.

In our study difference in pulse rate between two groups throughout intraoperative period was statistically insignificant (p>0.05) (table no. 9). Similarly systolic and diastolic blood pressure with or without clonidine premedication did not show significant changes. p>0.05) (table no.10,11) but only 2 pts had bradycardia in clonidine group as compared to 1 patient in placebo group. **Anita Kumari et al** [22]also did not find significant haemodynamic changes in patient treated with 150µg clonidine. Since clonidine is an antihypertensive drug so we expected significant fall in pulse and blood pressure with it. And the underlying mechanism for hemodynamic depression is activation of centrally situated α_2 adrenoceptors which causes reduction in peripheral sympathetic tone and bradycardia through vagus whereas peripheral presyneptic α receptor activation leads to reduction in sympathetic tone of heart[62]. Other studies with 150µg clonidine did not find significant changes in haemodynamic parameter[20,21].

But the study of **Ota et al[12]** found significant bradycardia with 4-5 µg oral clonidine[57]. **Muzi M , Godd M & Kampine[63]** found that" anaestheticalty effective dose of clonidine do not prevent increase in serum catecholamine in response to modulation of efferent sympathetic stimulus and baroreceptor activity is also enhance after clonidine premedication".

The sedation score in clonidine group was significantly higher compare (table no.13) to control group in our study but there was no respiratory depression(table no.13) .it is in accordance with study done by **wright** [58]and **Anita Kumari et al[22]** .

Shurthi jayram[20] also found good sedation in patients who received 150µcg oral clonidine and they said that sedative is due to decrased activity of locus coeruleus at the central nervous system by clonidine. According to **Sequeira Trevor et al[64]** oral clonidine has excellent sedative property and it also reduces post operative shivering and vomiting when used in paediatric patients.

Similar to other studies by **Anita et al[22], Sudar Codi et al[18], Anu Prasad et** al[21], no significant complication were noted in clonidine group in our study (Table no.14) Nausea and vomiting occurred in only 3 patients from clonidine group who had concomitant hypotension. As such, Clonidine itself does not induce nausea or vomiting rather it has antiemetic property[65].

This shows that oral clonidine as a premedication can prolong the spinal anaesthesia produce by bupivacaine with longer postoperative analgesia.

Conclusion:-

Hereby, we observed, that clonidine as an oral premedicant produces incidence of moderate sedation. Clonidine, as an oral premedicant doesnot affect the initial block characteristics, rather it prolongs the mean duration of sensory block, motor block and duration of analgesia. When dose of 150 µcg is used clonidine doesnot show any greater change in haemodynamics following subarachnoid block.