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RESEARCH ARTICLE

DEXMEDETOMIDINE VERSUS FENTANYL WITH INTRATHECAL BUPIVACAINE FOR POSTOPERATIVE ANALGESIA IN UROLOGICAL PROCEDURES: A DOUBLE BLIND COMPARITIVE STUDY.

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Abstract

Seventy six patients of American Society of Anaesthesiologists status I and II scheduled for urological procedures were studied to evaluate the onset and duration of Sensory and motor block, postoperative analgesia and adverse effects of Dexmedetomidine and Fentanyl given intrathecally with hyperbaric 0.5% Bupivacaine.

Material And Methods: Patients were randomly allocated into two groups. Group I received 12.5 mg 0.5% Bupivacaine + 25 µg Fentanyl. And Group II received 12.5 mg 0.5% Bupivacaine + 5 µg Dexmedetomidine (vol-3ml). The onset, time to reach peak sensory and motor level, the regression time for Sensory and motor block, postoperative analgesia and side effects were recorded.

Results: The onset time to reach peak sensory level as well as onset time to reach modified Bromage 3 motor block were insignificant in both the groups. The mean time of sensory regression to S1 in Group I was 276.21 ± 52.23 mins and in Group II was 417.34 ± 38.66 mins ($p<0.05$)). The regression time of motor block to reach modified Bromage 0 in Group I was 168.28 ± 29.84 mins and in Group II was 267.15 ± 34.40 mins ($p<0.05$)). The time for rescue analgesic i.e. post-op analgesia in Group I was 320.57 ± 33.00 mins and in Group II it was found to be 423.68 ± 37.58 mins ($p<0.05$)). The hemodynamics, sedation scores and side effects were not significantly different in both groups except for bradycardia noted with Dexmedetomidine. **Conclusion:** 5 µg Dexmedetomidine provides better hemodynamic stability, minimal side effects, and excellent quality

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of postoperative analgesia as an adjuvant to spinal Bupivacaine in urological procedures.

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Introduction:-

The first planned spinal anaesthesia for surgery in man was administered by August Bier[1] (1861–1949) on 16 August 1898. A number of surgeries have been performed under regional anaesthesia since then including Urological procedures [2]. Adjuvants, such as Opioids,Cclonidine, Midazolam and others have been studied to prolong the effect of spinal anesthesia. The addition of Fentanyl to hyperbaric Bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block.[3] The addition of Opioids to local anaesthetic solution have disadvantages, such as pruritus and respiratory depression. Alpha 2 agonists when administered intrathecally provide stable hemodynamic conditions, improved analgesia with minimal side effects.[4] Kanazi et al found that a dose of 3 mcg of intrathecal Dexmedetomidine (DXM) is equipotent to 30 mcg of Clonidine[4] Earlier human studies show that intrathecal 5 µ g Dexmedetomidine will have better postoperative analgesic effect with hyperbaric bupivacaine in spinal anesthesia with minimal side effects.[5,6,7]

Material And Methods:-

After obtaining the Institutional Ethical Committee approval and written informed consent 76 patients belonging to ASA grade I and II of either sex with age between 18-60 years posted for urological surgeries were enrolled in prospective, randomized double blinded study . ASA grade III & IV patients, Hypertensive patients, patients with cardiac disease, known Allergy to the study drugs or Contraindications to Spinal Anaesthesia were excluded from the study. All patients were examined and investigated a day prior to surgery and were familiarized with visual analogue scale (VAS) and its use for measuring the postoperative pain. They were advised fasting for 6 h and received Alprazolam 0.5 mg as premedication a night before the surgery. Inside the operation theatre NIBP, ECG, pulse oximeter were attached and coloaded with 10ml/kg ringer lactate intravenously. Patient's baseline systolic/diastolic/mean BP, heart rate were noted. Computer generated randomization was used to allocate patients into two groups**.** Subarachnoid block(SAB) was given with 25 G Quicnkes Spinal needle. GROUP I received 2.5 ml of 0.5% Bupivacaine heavy (12.5 mg) + 0.5 ml of Fentanyl (25 µg) & GROUP II recieved 2.5 ml of 0.5% Bupivacaine heavy (12.5 mg) + 0.5 ml of dexmedetomidine diluted with normal saline (5µg) (total vol.- 3ml).The observer was blinded.

Onset of sensory block (by cold swab), onset of motor block (by modified Bromage scale), highest dermatomal level achieved were noted. Heart rate & blood pressure were monitored immediately after injection and then after every 5 minutes for first 0 minutes and then every 10 minutes thereafter throughout the surgery and till the complete recovery from block. Any decrease in heart rate below 60 beats/min was considered as Bradycardia and was treated with 0.3 mg of Atropine. Similarly any fall of systolic blood pressure of more than 20 % of baseline was considered as Hypotension and fall of more than 30 % was treated with 6 mg of Mephentermine and crystalloids. Duration of analgesia was noted using VAS score (0 -no pain to 10- severe pain) Intra-operative side effects like sedation, nausea, vomiting, shivering, bradycardia, hypotension requiring active treatment were noted. Central effects like sedation were monitored using **Modified Ramsey Sedation Scale.**1=Anxious,Agitated, Restless to scale 6= No Response. Postoperatively Motor block recovery (modified Bromage score of zero), sensory block regression were assessed every 15 min after completion of surgery till the time of regression of two segments in maximum block in the post-anesthetic care unit (PACU) along with the vital signs and VAS scores. Any patient showing VAS more than or equal to 3 was administered a supplemental dose of IV. tramadol 50 mg and was taken as the endpoint of the study.

Statistical analysis was done using T-test and ANOVA. P value of less than 0.05 was considered to be significant.

Result:-

There was no statistical difference in patient's demographics or duration of surgery as shown in [Table I]

Table I:- Demographic Parameters And Duration Of Surgery

PARAMETER	GROUP I	GROUP II	P value
Age (years)	38.28±10.92	35.86±12.09	0.363

Sex(M/F)	28/10	26/12	0.618
Height(cm)	162.02± 5.27	162.92± 5.28	0.462
Weight(kg)	64.50 ± 5.63	62.68 ± 6.94	0.215
Duration of surg(min)	59.60 ± 20.83	63.81 ± 21.54	0.389

When compared the time of onset of both, sensory and motor block and time to reach maximum sensory level were statistically insignificant in both the groups ($P > 0.05$). T6 was the highest level of sensory block attained at 10.1 ± 3.5, 9.6 ± 2.9min after injection in 44.73% and 39.47%% patients in group I and II respectively. The time for two segment regression, duration of sensory and motor block were significantly prolonged in group II as compared to group I ($P < 0.05$)

Table II:-Comparison of parameters in two Groups

Parameters	Group I	Group II	P value
	Mean ±SD	Mean ±SD	
Sensory Onset (sec.)	39.94 ±22.01	42.02 ±20.48	0.671
Motor Onset (sec.)	127.52 ± 56.07	151.05 ± 56.79	0.073
Time to reach max level (min.)	24.34 ± 4.28	22.57 ± 3.23	0.046
Time to 2 segment regression(min)	84.63 ± 6.22	116.60±7.59	0.00
Duration of sensory block(min)	276.21± 52.23	417.34± 38.66	0.00
Duration of motor block(min)	168.28± 29.84	267.15± 34.40	0.00

The mean values of systolic BP and diastolic BP were comparable between the groups. [Figure I] and [Figure II].There was no significant fall in the HR in group I(p=0.85) ,however in group II significant fall was observed in HR over 30 min (p<0.05) [figure 3]. None of the patients experienced respiratory distress at any point of time.

None of the patients had sedation score > 2 in both the groups (Group I 68%, Group II 55%). 5 patients (13.15%) in Group I and 9 patients (23.68%) in Group II had Hypotension (p=0.242). Bradycardia was recorded in 7.89% cases in Group I and in 26.31% cases in Group II (p <0.05). Nausea and vomiting were reported in 18.42% cases in Group I and in 13.15% cases of Group II (p =0.535).Shivering was reported in 10.52% cases in Group I and in 23.62% cases of Group II (p =0.131) .

Postoperative analgesia was considered till VAS score >/= 3 and IV tramadol was given as a rescue analgesic. Post-op analgesia in Group I was upto 320.57 ± 33.00 mins with maximum analgesia for 400 minutes and in Group II it was found to be 423.68 ± 37.58 mins with maximum analgesia upto 480 minutes. (p<0.05)

RE I:-Systolic Bp Chnages

FIGURE I:-Systolic Bp Chnages

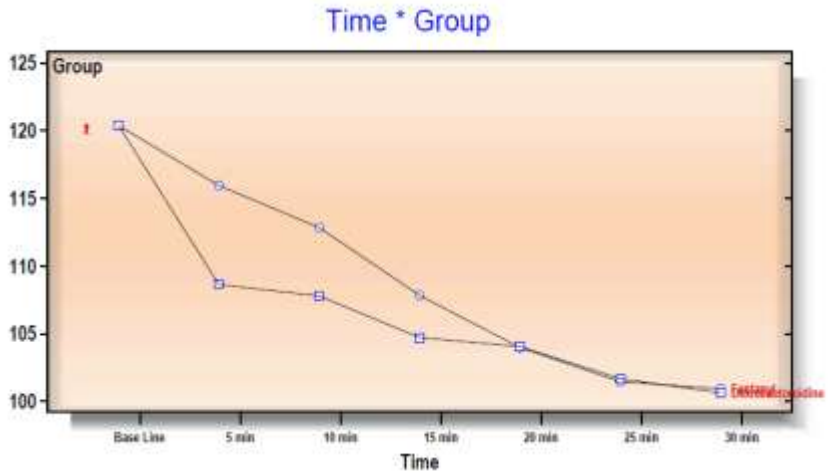


Figure Ii:-Diastolic Pressure Changes

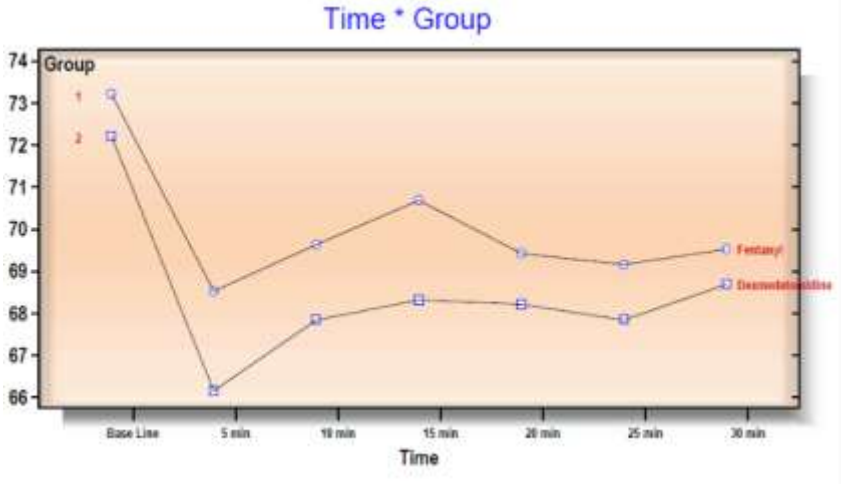
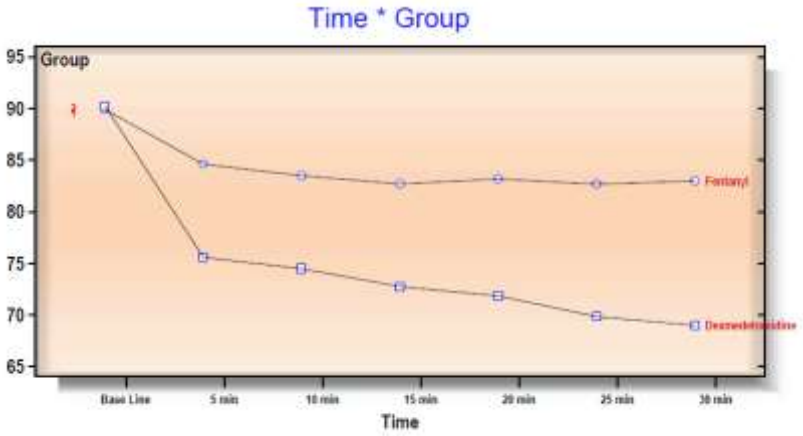


Figure III:-Heart Rate Changes



Discussion:-

Administration of local anaesthetics with Opioids has become a well-accepted practice in the management of spinal anaesthesia for surgical procedures. Fentanyl (10—25 mg) to local anaesthetics during spinal anaesthesia has been shown to enhance and increase the duration of sensory analgesia without intensifying the motor Block or prolonging recovery[8,9,10]. In the literature, Fentanyl- Bupivacaine seems to be the most frequently used combination for this purpose in spinal anaesthesia[8,11-15] . In minor Urological surgery[11] and Caesarean sections[13,14] this combination has been shown to increase the Intraoperative and early postoperative analgesic quality of spinal anaesthesia.

DXM is a highly selective α2-adrenoreceptor agonist approved as intravenous sedative and adjuvant to anaesthesia and has about ten times higher affinity for α2- adrenoreceptor than Clonidine.[18,19] DXM when used intravenously during anaesthesia reduces Opioid and Inhalational anaesthetics requirements [18,19].The use of intrathecal Clonidine for postoperative analgesia alone[20] or co administered with local anaesthetics[21,22,23] or Opioids[24] has been previously described. Animal studies showed that agonists administered epidurally have analgesic effect that correlated with their binding affinity [16] and suggested a 1:10 dose ratio between intrathecal Dexmedetomidine and Clonidine [25] . This was demonstrated clinically by Kanazi et al [4] who reported that intrathecal Dexmedetomidine 3 µg was equipotent to intrathecal Clonidine 30 µg when used for supplementation of hyperbaric Bupivacaine spinal blockade. From Kanazi [4] study and animal studies, we assumed that 3-5 µg DXM would be equipotent to 30-45 µg clonidine when used for supplementation of spinal Bupivacaine.

In our study we did not find any significant difference in onset of sensory, motor blocks and the time for highest level achieved. However, there was a significant prolongation in two segment regression, 84.63 ± 6.22 min with fentanyl as compared to 116.60±7.59 min with Dexmedetomidine. V Mehendru et al [26] in their study found the mean time of two segment sensory block regression as 147 ± 21 min with DXM, 117 ± 22 with Clonidine and 119 ± 23 with Fentanyl. ($P < 0.0001$) In our study, the mean time of sensory block was 276.21± 52.23 min in Fentanyl group and 417.34± 38.66 min in DXM group (P<0.001). The regression time of motor block to reach modified Bromage 0 was 168.28± 29.84min with Fentanyl and 267.15± 34.40min with DXM (P<0.001). Rajni gupta et al [7] in their study observed that the mean time of sensory regression to S1 was 187±12 min in Fentanyl group and 476±23 min in Dexmedetomidine group (P<0.001). The regression time of motor block to reach modified Bromage 0 was 149±18 min with Fentanyl and 421±21 min with Dexmedetomidine (P<0.001). Subhi M. Al-Ghanem et al [5] observed the mean time of sensory regression to S1 was 179±47 min with fentanyl and 274±73 min with Dexmedetomidine (P < 0.001). Also the regression time of motor block to reach modified Bromage 0 was 155±46 min with Fentanyl and 240±60 min with DXM (P< 0.001). The intrathecal 5 µg Dexmedetomidine used in our study had shown comparable onset of motor block with significantly prolonged duration of motor block, which is in consonance with the results observed by investigators in comparison to various adjuvants (Clonidine, Fentanyl, and Sufentanil) used in their studies.[4,5,6,7,27] The duration of motor block as observed in our study was markedly prolonged (273.3 ± 24.6 min) when compared to the duration of motor block of 250 ± 76 min in Kanazi et al.,'s[4] study ($P < 0.001$) and 240 ± 64 min in Al Ghanem *et al*.,'s[5] study ($P < 0.001$), which could be attributed to higher intrathecal volume of drug (3 ml) used in our study as compared to 1.9 and 2.5 ml drug used in the respective studies.

There was a significant delayed requirement of rescue analgesic (VAS score >3). We observed that postoperative analgesia in Fentanyl group was 320.57 ± 33.00 mins with maximum analgesia for 400 minutes and with Dexmedetomidine was found to be 423.68 ± 37.58 mins with maximum analgesia for 480 minutes. (p<0.001) Gupta et al., had similar results on comparison of Dexmedetomidine and Fentanyl as an intrathecal adjuvant ($P < 0.001$). Al-Mustafa et al.,[6] and Hala EA Eid et al.,[28] observed dose dependent reduced analgesic requirement with incremental dosages of intrathecal dexmedetomidine. Bradycardia was seen with the use of DXM and was significant when compared to Fentanyl(p=0.03) Sedation scores were comparable in both the groups, however higher sedation scores with Dexmedetomiodine have been observed with increased doses as were used by Hala EA Eid et al., [28]

The action of intrathecal Dexmedetomidine to inhibit the release of C fibers transmitters, hyperpolarization of post-synaptic dorsal horn neurons and direct impairment of excitatory amino acid release from spinal interneurons may be responsible for its prolonged sensory & motor blockade and longer duration of postoperative analgesia.[4,5,29] Although intrathecal Dexmemdetomidine appears to be a promising option further studies need to be conducted to assess its safety in certain group of patients like ASA III,IV , Geriatrics and patients with cardiac disease.

Conclusion:-

In conclusion, 5 µg Dexmedetomidine seems to be an attractive alternative to 25 µg Fentanyl as an adjuvant to spinal Bupivacaine in urological procedures. It provides good quality of intraoperative analgesia, hemodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia

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