ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 01, pp.45822-45827, January, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

TO COMPARE THE EFFICACY OF DEXMEDETOMIDINE VERSUS FENTANYL AS SEDATIVE & ANALGESIC IN SHORT GENERAL ANAESTHESIA IN DAY CARE OBSTETRICS & GYNAECOLOGICAL SURGERIES

***Dr. Piyush Kumar Sengar, Dr. Smita Priyadarshini, Dr. Manish Raj and Dr. Pratibha Rai**

Department of Anesthesiology and Critical Care, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi – 110029

ARTICLE INFO

Article History:
Received 05th October, 2016
Received in revised form
28th November, 2016
Accepted 10th December, 2016
Published online 31st January, 2017

Key words:

Dexmedetomidine,
α_{2A}-adrenoreceptor agonist,
Day care surgery,
Ramsay sedation score,
Standard Aldrete score.

ABSTRACT

Introduction: Dexmedetomidine being a highly selective & potent α_{2a} agonist has a wide therapeutic actions. Dexmedetomidine was used as a sole analgesic & sedative agent in day care surgeries.
Methods: The study was conducted on 40 patients divided in 2 groups, A & B of ASA-I & ASA-II. In group A patients received inj. Dexmedetomidine 1 µg/kg i.v slowly & in group B received inj. Fentanyl 1 µg/kg i.v slowly prior to induction. Following preoxygenation induction done with inj. Propofol i.v 2mg/kg & maintained with 33% O2, 66% N2O & 0.6-0.8% of Isoflurane with patient breathing spontaneously. Patients were evaluated in post operative recovery room with help of visual analogue scale for pain, Ramsay score for sedation & Standard Aldrete score for recovery.
Results: There were no statistically significant differences in both group's demographic profile. Comparison of pulse rate in Dexmedetomidine group shows significant fall immediately after premedication but remained equivalent to baseline throughout surgery & significant fluctuation of pulse rate seen in Fentanyl group and this significant difference remain throughout the surgery. Similar results were seen in systolic blood pressure. Statistically highly significantly fall in saturation was observed in fentanyl group. The post operative analgesia duration was more with Dexmedetomidine than Fentanyl. The sedation was highly significant in fentanyl group & the quality of recovery with Aldrete was highly significant in Dexmedetomidine group at 15, 30, 60 minutes.
Conclusion: Dexmedetomidine used as a sole sedation / analgesia is not only very effective but produces excellent hemodynamic stability, minimal side effect, prolongs post operative analgesia, early recovery and has no residual CNS depressant effect.

Citation: Dr. Piyush Kumar Sengar, Dr. Smita Priyadarshini, Dr. Manish Raj and Dr. Pratibha Rai, 2017. "To compare the efficacy of dexmedetomidine versus fentanyl as sedative & analgesic in short general anaesthesia in day care obstetrics & gynaecological surgeries", *International Journal of Current Research*, 9, (01), ***45822-45827.***

INTRODUCTION

Since the first report of clonidine, an α_{2A}-adrenoceptor agonist, the indications for this class of drugs have continued to expand. In December 1999, Dexmedetomidine was approved as the most recent agent in this group and was introduced into clinical practice as a short-term sedative (<24 hours). α_{2A} adrenoceptor agonists have several beneficial actions during the perioperative period. They decrease sympathetic tone, with attenuation of the neuroendocrine and hemodynamic responses to anesthesia and surgery; reduce anesthetic and opioid requirements; and cause sedation and analgesia. They allow psychomotor function to be preserved while letting the patient rest comfortably. With this combination of effects, α_{2A} adrenoceptor agonists may offer benefits in the prophylaxis and adjuvant treatment of perioperative myocardial ischemia. Furthermore, their role in pain management and regional anesthesia is expanding. Side effects consist of mild to moderate cardiovascular depression, with slight decrease in blood pressure and heart rate. The development of new, more selective α_{2A} adrenoceptor agonists with improved side effect profiles may provide a new concept for the administration of perioperative anesthesia and analgesia. This review aims to give background information to improve understanding of the properties and applications of the novel α_{2A}-adrenoceptor agonist, Dexmedetomidine. Presynaptic activation of the α_{2A}-adrenoreceptor in the locus ceruleus inhibits the release of norepinephrine (NE) and results in the sedative and hypnotic effects. In addition, the locus ceruleus is the site of origin for the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission. Stimulation of the α_2 adrenoceptors in this area terminates the propagation of pain signals leading to analgesia. In the spinal cord, stimulation of α_2-receptors at the substantia gelatinosa (SG cells) of the dorsal horn leads to inhibition of the firing of nociceptive neurons and inhibition of the release of substance P. Also, the α_2-adrenoceptors located at the nerve endings have a possible role in the analgesic

***corresponding author: Dr. Piyush Kumar Sengar,**
Department of Anesthesiology and Critical Care, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi – 110029

mechanisms of α_2-agonists by preventing NE release. The spinal mechanism is the principal mechanism for the analgesic action of Dexmedetomidine even though there is a clear evidence for both a supraspinal and peripheral sites of action.
Fentanyl is a potent narcotic analgesic with a rapid onset and short duration of action. Historically it has been used to treat chronic breakthrough pain and is commonly used pre-procedures. Many other fentanyl analogs were developed and introduced into the medical practice. Fentanyl's major side effects include respiratory depression, diarrhea, nausea, constipation, dry mouth, somnolence, confusion, asthenia, abdominal pain, headache, fatigue, anorexia and weight loss, dizziness, nervousness, hallucinations, anxiety, and urinary retention. Fentanyl listing as scheduled drug & its illicit use making its availability difficult.

MATERIALS AND METHODS

After obtaining approval from the Institutional Ethical Committee, and written informed consent, forty patients of ASA grade I and II, between ages 18 – 65, scheduled for obstetrics & gynaecological day care surgery were included in the study. The study was conducted in Anaesthesia Department Vardhman Mahavir Medical College and Safdarjung Hospital in June 2015. Patients were excluded on the basis of the following criteria: labile hypertension, history of arrhythmias, or an absolute contraindication to general anaesthesia. The patients were randomized into two equal groups of twenty each by a computer generated model. Patients allocated to Group A (Dexmedetomidine Group) were given 1µg/kg of Dexmedetomidine Prior to induction. Patients allocated to Group B were given 1µg/kg body weight of Fentanyl prior to induction. An independent consultant anesthesiologist who was completely blinded to the drug being used did the intraoperative and postoperative assessment of all the parameters. All the patients selected for study had a detailed general examination including airway assessment; spine and systemic examination will be done. Any other sedatives and hypnotics were avoided in premedication as well as intra operatively. Pre-operative parameters like pulse rate, respiratory rate, oxygen saturation (SpO2), blood pressure were noted. Following preoxygenation induction of GA was done with inj. Propofol 2.0 mg/kg body wt. After the loss of eyelash reflex / in apnea patients were ventilated by Magill circuit till the patient regains the spontaneous ventilation. Anaesthesia was be maintained with 33% oxygen, 66% nitrous oxide and Isoflurane (0.5% to 0.8%), with the patient breathing spontaneously. Any untoward incidence or any abnormal event were noted throughout the surgery. Strict monitoring of side effects such as nausea, vomiting, pain, shivering, pruritus, sedation, hypotension, bradycardia and respiratory discomfort was done. Hypotension was defined as a systolic blood pressure lower than 90 mm Hg or a decrease in systolic blood pressure of greater than 20% of baseline. Bradycardia was defined as a heart rate lower than 50 beats per minute and was treated with 0.6 mg of i.v. Atropine.

Subsequently, patients were transferred to the Post Anaesthesia Care Unit (PACU) where in the recovery room patient were followed up for vitals, for pain using visual analog scale- 10 cm line, for sedation using Ramsay sedation scale & standard Aldrete score for recovery every 30 minutes. In the ward, post-operative analgesic drugs were given when patients complained of pain (VAS ≥5). This was taken as the time of wearing off of analgesia, and the time of injection of rescue analgesic drug (i.e., Inj. Diclofenac 75 mg im/iv infusion) was noted.

Statistical Analysis

Data was conveyed as either mean and standard deviation or numbers and percentages. $P < 0.05$ was considered to be statistically significant. Continuous covariates (age, height, weight) were compared using unpaired student's t-test, with the p-value being reported at the 95% confidence interval. Categorical covariates (sex, ASA grade, bradycardia, and hypotension) were explained using percentages as comparisons amongst the 2 groups.

RESULTS

There were no statistically significant difference in both groups demographic profile. Comparison of pulse rate shows that in group A there is significant fall in pulse rate immediately after pre medication as p value <0.05 & without any intervention within 30 sec to 1minutes returned to baseline & remained equivalent to baseline throughout surgery as shown in line diagram. Significant fluctuation of pulse rate seen in group B & this significance remained throughout the surgery. Similar results were seen with systolic blood pressure where in group A there is mild rise after premedication & after induction a dip in blood pressure can be seen, whereas constant fluctuation remained throughout the surgery in group B. There were no significant change in diastolic blood pressure & respiratory rate seen in any of the groups. Statistically highly significantly fall in saturation was observed with group B (87.91 ± 26.93%). The post operative analgesia duration was more in group A (approximately 4-6hrs), whereas in group B patient required rescue analgesia within 1 to 1.5 hrs of surgery. At 1.5 hrs p value<0.001.it was statistically as well as clinically significant. The time of eye opening was highly significant in group A p<0.0001 & delayed eye opening seen with group B. The sedation was highly significant in group B according to Ramsay sedation score as p <0.001 after 15 minutes of surgery.

Table 1. Comparison of age in study groups

Parameters	Group A	Group B	t-Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
Age (Yrs)	28.80 ± 7.45	29.91 ± 9.16	0.30	>0.05

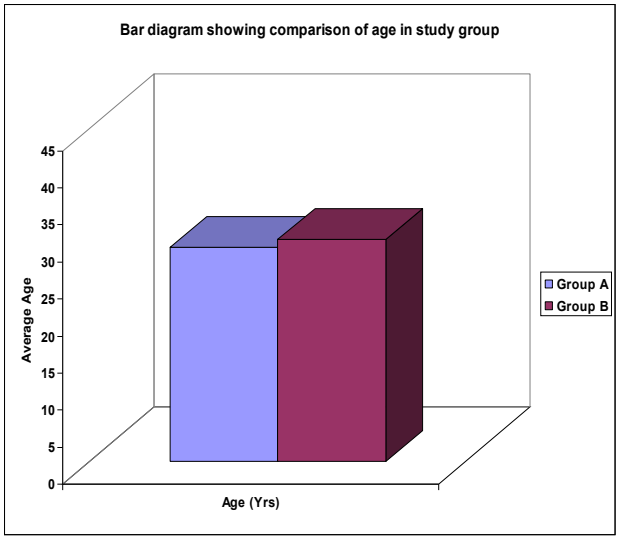


Table 2. Sex wise distribution of cases in study groups

Parameters	Group A (%)	Group B (%)	Total (%)
Male	0 (0)	1 (5)	1 (5)
Female	10 (50)	9 (45)	19 (95)
Total	10 (50)	10 (50)	20 (100)

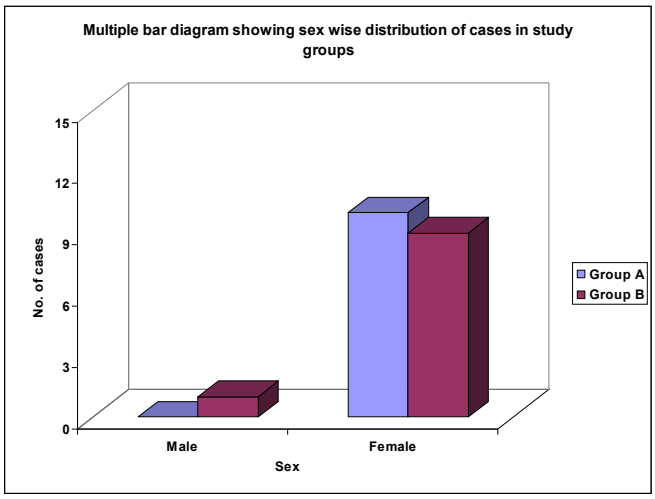


Table 3. ASA grade wise distribution of cases in study groups

ASA grade	Group A (%)	Group B (%)	Total (%)
I	8 (40)	7 (35)	15 (75)
II	2 (10)	3 (15)	5 (25)
Total	10 (50)	10 (50)	20 (100)

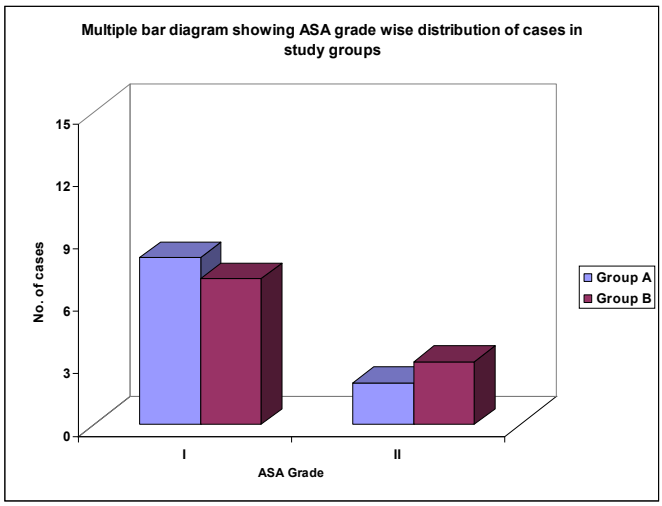


Table 4. Comparison of pulse rate in study groups

Pulse Rate (min)	Group A	Group B	t-Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
On table	76.30 ± 9.71	72.18 ± 8.70	1.00	>0.05
AFT PMD	64.00 ± 6.75	74.82 ± 11.12	2.63	<0.05
AFT IND	78.70 ± 11.92	66.00 ± 12.10	2.36	<0.05
At 5 min	79.00 ± 8.73	68.27 ± 11.38	2.37	<0.05
At 10 min	79.20 ± 7.55	75.00 ± 9.46	1.10	>0.05
At 15 min	79.60 ± 6.29	71.91 ± 7.82	2.42	<0.05
At end	75.40 ± 8.98	68.91 ± 7.19	1.78	>0.05
Post - op	73.00 ± 7.62	70.64 ± 6.23	0.76	>0.05

The quality of recovery in group A was highly significant as score of 9 on standard Aldrete score were seen in most of the patients after 30 minutes P<0.001, whereas in group B same results were seen only after 1.5-2 hrs in post op recovery according to standard Aldrete score.

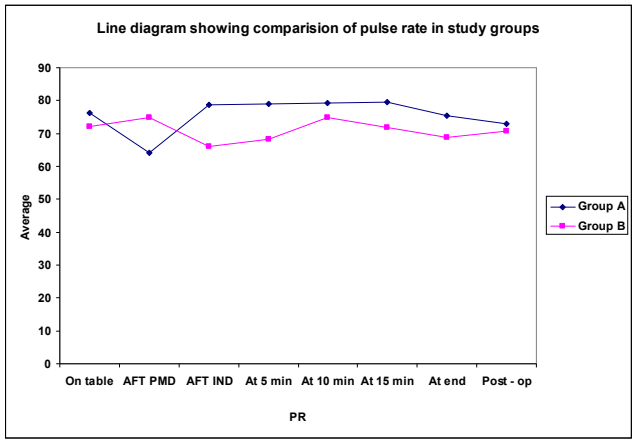


Table 5. Comparison of systolic blood pressure in study groups

SBP (min)	Group A	Group B	t-Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
On table	115.90 ± 10.39	123.18 ± 17.04	1.15	>0.05
AFT PMD	122.70 ± 9.88	116.55 ± 17.74	0.96	>0.05
AFT IND	109.30 ± 7.67	103.91 ± 11.92	1.20	>0.05
At 5 min	122.60 ± 10.96	104.73 ± 13.24	3.29	<0.001
At 10 min	119.30 ± 9.67	111.00 ± 13.33	1.59	>0.05
At 15 min	123.30 ± 6.91	111.00 ± 13.42	2.58	<0.05
At end	120.80 ± 6.21	113.73 ± 7.60	2.28	<0.05
Post - op	117.30 ± 8.38	112.73 ± 7.76	1.17	>0.05

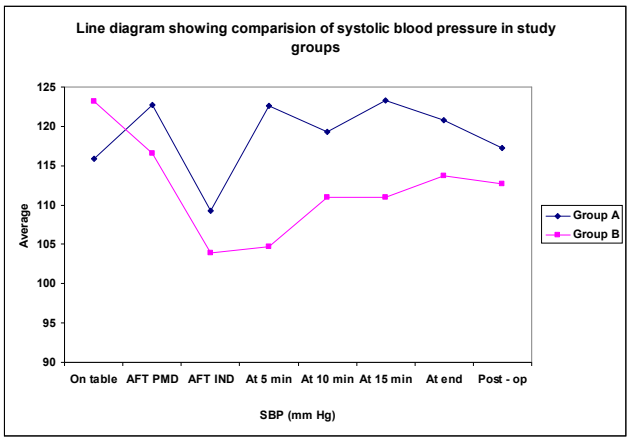
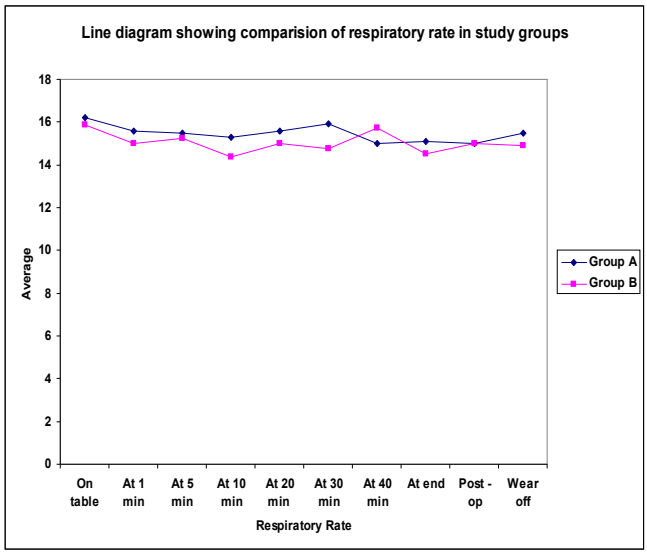


Table 6. Comparison of diastolic blood pressure in study groups

DBP (min)	Group A	Group B	t-Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
On table	70.10 ± 11.47	79.64 ± 14.47	1.63	>0.05
AFT PMD	73.10 ± 10.28	68.36 ± 15.28	0.81	>0.05
AFT IND	70.60 ± 8.90	64.18 ± 12.11	1.35	>0.05
At 5 min	73.00 ± 9.23	64.82 ± 9.79	1.92	>0.05
At 10 min	72.80 ± 10.41	65.27 ± 7.07	1.89	>0.05
At 15 min	75.30 ± 9.42	69.91 ± 7.25	1.43	>0.05
At end	74.50 ± 5.87	67.09 ± 7.67	2.42	<0.05
Post - op	74.30 ± 6.34	67.36 ± 6.38	2.44	<0.05

Table 7. Comparison of SPO2 in study groups

SPO2 (min)	Group A	Group B	t-Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
On table	99.20 ± 0.79	96.31 ± 7.81	1.14	>0.05
AFT PMD	99.30 ± 0.82	87.91 ± 26.93	1.34	>0.05
AFT IND	99.90 ± 0.32	97.64 ± 0.67	9.61	<0.0001
At 5 min	99.40 ± 0.70	97.27 ± 1.10	5.15	<0.0001
At 10 min	99.40 ± 0.70	97.27 ± 1.01	5.48	<0.0001
At 15 min	99.30 ± 0.67	97.36 ± 1.03	4.98	<0.0001
At end	98.70 ± 0.67	98.00 ± 1.00	1.83	>0.05
Post - op	98.20 ± 0.63	97.45 ± 0.69	2.52	<0.05



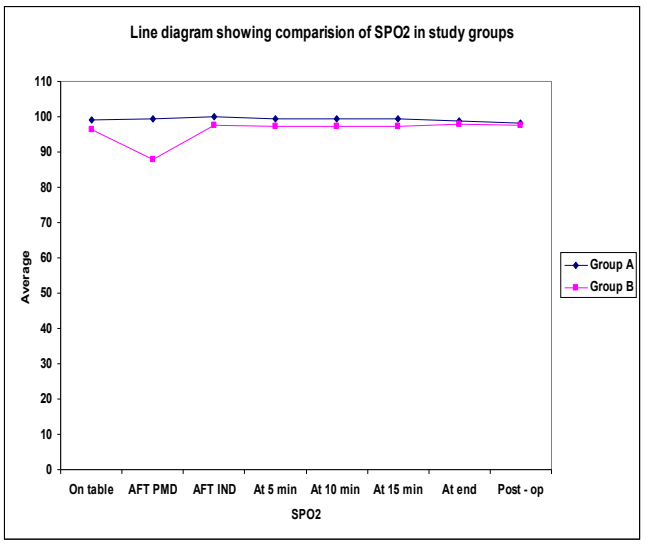


Table 8. Comparison of VAS score in study groups

VAS	Group A Mean ± SD (n=10)	Group B Mean ± SD (n=10)	Z Value	P Value
At End of surgery	2.10 ± 0.74	1.64 ± 0.67	1.47	>0.05
At 30 min	2.20 ± 0.79	2.00 ± 0.63	0.63	>0.05
At 1 hr	2.70 ± 0.48	2.45 ± 0.52	1.09	>0.05
At 1.5 hr	3.30 ± 0.48	4.27 ± 0.90	3.00	<0.001
At 2 hr	3.70 ± 1.06	6.00 ± 0.89	5.25	<0.0001

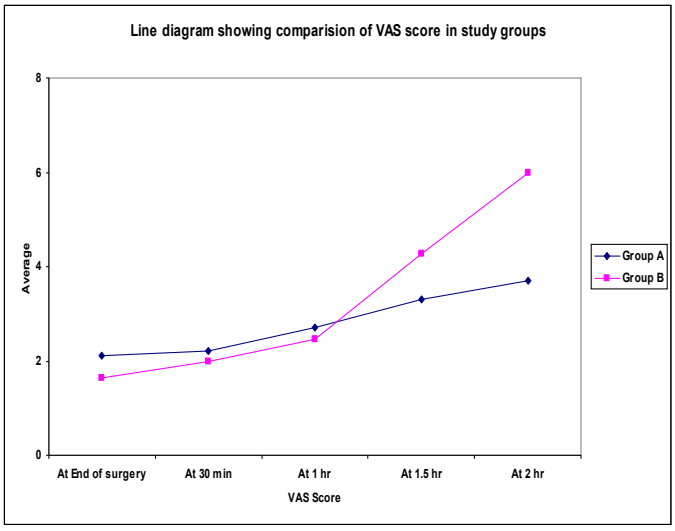


Table 9. Comparison of Ramsay sedation in post operative in study groups

Ramsay sedation in post op	Group A Mean ± SD (n=10)	Group B Mean ± SD (n=10)	t Value	P Value
End of surgery	2.90 ± 0.88	3.45 ± 0.69	1.58	>0.05
At 15 min	2.30 ± 0.48	3.27 ± 0.79	3.33	<0.001
At 30 min	2.00 ± 0.00	3.09 ± 0.70	4.92	<0.0001
At 1 hr	2.00 ± 0.00	2.64 ± 0.50	3.99	<0.001
At 2 hr	1.80 ± 0.42	2.27 ± 0.79	1.68	>0.05

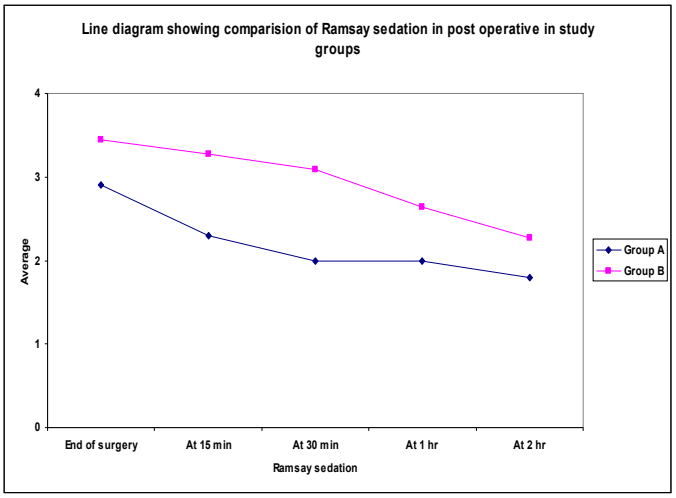


Table 10. Comparison of standard aldrete score in post operative in study groups

Aldrete score	Group A Mean ± SD (n=10)	Group B Mean ± SD (n=10)	t Value	P Value
End of surgery	7.90 ± 0.74	7.45 ± 0.93	1.18	>0.05
At 15 min	8.90 ± 0.74	7.91 ± 0.70	3.08	<0.001
At 30 min	9.30 ± 0.67	7.91 ± 0.70	4.52	<0.0001
At 1 hr	9.80 ± 0.42	8.55 ± 0.52	5.91	<0.0001
At 1.5 hr	9.80 ± 0.42	9.27 ± 0.90	1.67	>0.05
At 2 hr	10.00 ± 0.00	9.55 ± 0.52	2.75	<0.05

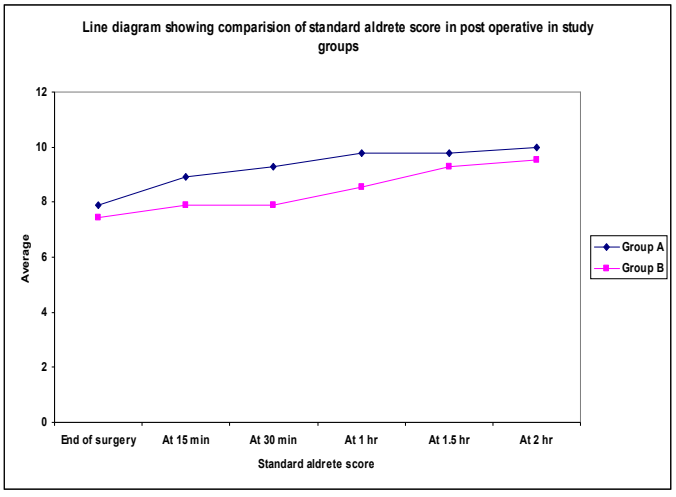
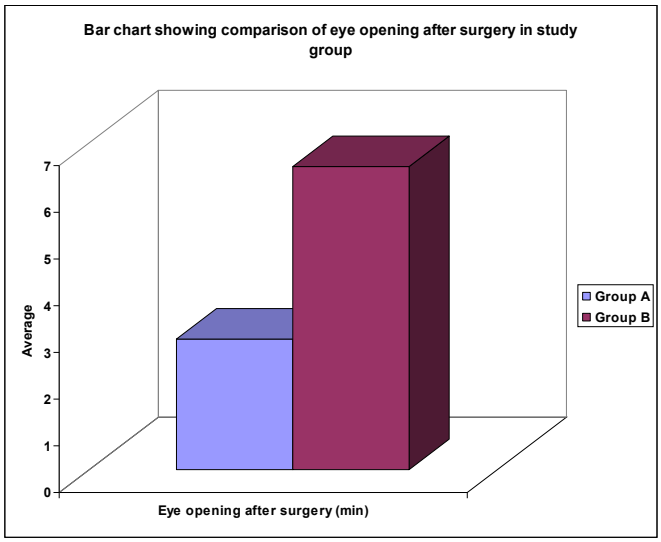


Table 11. Comparison of eye opening time after the surgery in study groups

Parameter	Group A Mean ± SD (n=10)	Group B Mean ± SD (n=10)	t-Value	P Value
Eye opening after surgery (min)	2.81 ± 0.80	6.50 ± 0.96	9.35	<0.0001



DISCUSSION

The α_{2A} adrenergic agonists are a unique class of drugs because of their pharmacological action, specially Dexmedetomidine has a very specific profile which can be exploited for specific indications. Till now its use & comparison with most commonly used intra operative analgesic Fentanyl has not been carried out widely. There are comparisons with routinely used sedative agents like Midazolam. In our stydy we found greater hemodynamic stability in group Dexmedetomidine group, similar findings were also observed by Dere *et al* in their comparative study of Dexmedetomidine & Midazolam for sedation & analgesia during colonoscopy found that Dexmedetomidine provides more efficient hemodynamic stability, higher Ramsay sedation scale scores, higher satisfaction scores and lower NRS (numeric rating scale)scores in colonoscopies. We also found that patient in group A had longer post operative analgesia period, which were also studied by Mccutcheon *et al* in 2006 When they compared Dexmedetomidine with standard technique such as combined use of Midazolam & Fentanyl for carotid endarterectomy & found that there was better hemodynamic control, better score of Ramsay sedation & lesser no of patient required additional pain relief in post operative anesthesia care unit in Dexmedetomidine group. Only two papers have been published on comparision of Dexmedetomidine & Fentanyl. One by Turgut *et al* in September 2008, in which they have used these agents for sole sedation & analgesia for patients undergoing lumbar laminectomy. They found that Propofol-Dexmedetomidine is suitable for patients undergoing elective spinal laminectomy and provides stable perioperative hemodynamic responses. Propofol-fentanyl medication requires a higher dosage of postoperative analgesics and causes frequent postoperative nausea and vomiting compared with Propofol-Dexmedetomidine.In our study Post operative analgesia was better in group A & no untoward effect such as nausea, vomiting were found in either of the groups. Second in December 2010 by Ali *et al* where they have compared these drugs as adjuvant to Propofol in children undergoing extracorporeal shockwave lithotripsy. They observed that Propofol/Dexmedetomidine combination was accompanied with less Propofol consumption, prolonged analgesia and lower incidence of intraprocedural and postprocedural complications.

Dexmedetomidine has been successfully used as sole sedative for awake intubation in the management of critical airway by Abdelmalak *et al*. We have maintained anesthesia on Isoflurane as cardiopulmonary effects of the Dexmedetomidine CRI(constant rate infusion) in Isoflurane anaesthetized ponies were small as observed by Marcilla *et al* in July 2010, they evaluated the cardiopulmonary effects of two different constant rate infusions (CRI) of Dexmedetomidine. In 2010 July Cooper *et al* have shown that Dexmedetomidine appears equivalent in achieving adequate levels of sedation without increasing the rate of respiratory depression or decreasing oxygen saturation compared with standard therapy, and it may be better in achieving desired hemodynamic results for Providing Adequate Sedation and Hemodynamic Control for Awake, Diagnostic Transesophageal Echocardiography. The Dexmedetomidine offers remarkable pharmacological properties including sedation, anxiolysis & analgesia with the unique characteristic to cause no respiratory depression. In addition it posses sympatholytic & antinociceptive effects that allow hemodynamic stability during surgical stimulation. Different from most of clinically used anaesthetics, Dexmedetomidine brings about not only sedative - hypnotic effects via action on single type of receptors, but also an analgesic effect and an autonomic blockade that is beneficial in cardiac risk situation. Dexmedetomidine has shown to consistently reduce opioids, Propofol & benzodiazepine requirements. It has demonstrated to be an efficacious & safe adjuvant in premedication, general surgery, neurosurgery, cardiac surgery, bariatric surgery, and for procedural sedation & awake fibre optic intubation. This remarkable therapeutic profile has prompt us to use the dexmedetomidine as a sole sedative & analgesic agent in day care obstetrics & gynaecological surgeries, where we have achieved outstanding results considering the stability of hemodynamic profile, no or lesser requirement of post op analgesia & early recovery in post operative unit with better satisfaction of patient & surgeon. It appears that Dexmedetomidine is superior to standard sedative agents as shown in our experiment that is why we recommend this drug not only for day care surgeries but also in procedure where greater hemodynamic stability, better sedation, decreased opioid & other anaesthetics requirement & smooth recovery needed.

REFERENCES

Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. 1992. Dexmedetomidine infusion for maintenance of anesthesia in patients undergoing abdominal hysterectomy. *AnesthAnalg*., 75:940-6.

Asano Y, Koehler RC, Kawaguchi T, McPherson RW. 1997. Pial arteriolar constriction to alpha 2-adrenergic agonist dexmedetomidine in the rat. *Am J Physiol*., 272:H2547-56.

Brown, BR, *et al*. 1993. Baillieres Clinical Anaesthesiology, Vol.7, No.3. London:Bailliere Tindall, 597—614.

Ginosar Y, Riley ET, Angst MS. The difference in action of fentanyl infusion and bolus administration. *Anesth Analg*., 97:1428–38.

Kadoi Y, Saito S, Kawauchi C, Hinohara H, Kunimoto F. 2008.Comparative effects of propofol vs. dexmedetomidine on cerebrovascular carbon dioxide reactivity in patients with septic shock. *Br J Anaesth*., 100:224-9.

Nakazawa K, Hikawa Y, Maeda M, *et al*. 1999. The pretreatment with fentanyl in day care surgeries & comaprision with clonidine using Laryngeal mask airway

& continuous propofol infusion without muscle relaxant. *Eur J Anaesthesiol.,* 16: 550–5.

Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. 2003. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiology*, 98:428-36.

Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, Whitten P, Margolis BD, Byrne DW, Ely EW, Rocha MG, 2009. SEDCOM (Safety and Efficacy of Dexmedetomidine Compared With Midazolam) Study Group. Dexmedetomidine vs. midazolam for sedation of critically ill patients: A randomized trial. *JAMA,* 301:489-99.

Waters CM, Avram MJ, Krejcie TC, Henthorn TK. 1999. Uptake of fentanyl in pulmonary endothelium. *J Pharm Exp Ther*., 288: 157–63.

Yaksh TL, Jage J, Takano Y. Pharmacokinetics and pharmacodynamics of medullary agents. The spinal actions of α-2 adrenergic agonists as analgesics. In:Atikenhead, AR, Benad, G.

****