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DEXMEDETOMIDINE AND NALBUPHINE VS. PROPOFOL AND FENTANYL IN MINIMALLY INVASIVE GYNAECOLOGICAL PROCEDURES: A COMPARATIVE STUDY

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ABSTRACT

Background and aims: For a long time anaesthesiologists are in search of best suited anaesthesia technique for day care surgery to reduce hospital stay, financial burden, safety of patients and complete short procedure list within the scheduled time frame. For the above mentioned purpose we compared two sets of drugs: dexmedetomidine / nalbuphine versus propofol/fentanyl. **Material and methods**: 18-50 years, ASA I and II, 60 patients having BMI 18-25kg/m^2 undergoing minimally invasive gynecological procedures were divided into two equal groups: ND and FP. In this double blind study Group ND received loading dose dexmedetomidine 1 mcg/kg as infusion and maintenance dose of 0.3 mcg/kg along with nalbuphine 100mcg/kg. Group FP received Propofol 2mg/kg in titrating dose with maintenance of 75 mcg/kg/min along with Fentanyl 2mcg/kg to achieve targeted RSS ≥ 4. Patient's pulse rate (PR), mean arterial pressure (MAP), post operative analgesia demand, time to reach Modified Aldrete score of 10 were recorded. **Results:** At the start of procedure there was a considerable decline in pulse rate in group ND as compared to group FP ($p<0.001$) which persisted throughout the procedure. There was fall in MAP in both the groups but it was more in group FP ($p<0.001$) and was persistent. 20% of the patients in group FP demanded rescue analgesia as compared to none in group ND in postoperative period. The mean duration to reach the Aldrete score of 10 in group ND was 65.5±3 minutes and 75.4±1 minutes in group FP which was statistically significant ($p<0.0001$). **Conclusion:** The combination of dexmedetomidine / nalbuphine found to be better because of hemodynamic stability along with longer postoperative analgesia with Lesser duration of stay in PACU.

KEYWORDS: Dexmedetomidine, nalbuphine, propofol, fentanyl, minimally invasive procedures, aldrete score.

INTRODUCTION

At present times with increasing population, day care surgery or ambulatory surgery is in demand. Exponential advancement in the field of anaesthesiology provides better anaesthesia care using modern anaesthesia equipments, safe anaesthetic drugs and techniques. Simultaneous emergence of minimally invasive surgical techniques has resulted in reduction in duration of hospital stay and therefore financial burden and need for human resources. Considering above facts we designed our study to compare intraoperative hemodynamic changes, respiratory events, postoperative analgesia and readiness for early discharge in two sets of drugs: dexmedetomidine/nalbuphine vs propofol/fentanyl in cases of minimally invasive gynaecological procedures which included dilatation and curettage, cervical polypectomy, hysteroscopy and vaginal hematomas.

Fentanyl and propofol is the most frequently used combination for minimally invasive gynaecological procedures in most of the centers which provides good analgesia and sedation but respiratory depression and delayed emergence may sometimes be encountered with it.[1] Cumulative effect of the time taken in emergence may in turn affect the planned surgical list. Moreover since fentanyl is a short acting opioid, postoperative analgesic effect does not last long.

Nalbuphine is lipid soluble agonist-antagonist opioid with lesser side effects like respiratory depression, pruritus and urinary retention. Dexmedetomidine is an alpha-2 agonist which provides anxiolysis, cardiovascular stabilizing effect[2] along with arousable sedation so delayed emergence should not be a problem with it. Dexmedetomidine has been known to have an analgesic action and also potentiates the action of opioids, so the combination of dexmedetomidine with nalbuphine could prove to be a better alternative to the propofol /fentanyl combination regarding intraoperative and post operative analgesia with lesser risk of respiratory depression.

In this study we tried to compare the effect of both the combinations on perioperative hemodynamics, postoperative analgesia and fitness of patients for early discharge.

MATERIAL AND METHODS

After institutional ethical committee approval and written informed consent this prospective, randomized, double blind comparative study was done on ASA I and II female patients, aged between 18-50 years. Patients with cadiac, renal, liver, endocrine disorders, uncontrolled diabetes, hypertension and BMI<18 or BMI>25 were excluded from the study. All the patients were explained about the anesthesia technique and instructed to keep fasting for 8 hours.

In the pre operative room, i.v. access was established and ringer's lactate infusion started. Premedication with inj. ranitidine 50 mg, inj. ondansetron 4 mg, inj. glycopyrrolate 0.2 mg was done. Then patients were shifted to the operation theatre and all the standard monitors like pulse oximeter, non invasive blood pressure, ECG leads were attached.

Patients were divided into two groups of 30 each and group was allocated randomly using computerised randomization table. Double blinding was ensured by an anaesthesiologist, not participating in the study, prepare the drug. The syringe and the infusion set were covered by aluminium foil and an opaque sheet was used to separate the cannulated arm from the monitor. The anesthesiologist who administered drugs and recorded data was also blind to the groups allotted.

Group ND received infusion of dexmedetomidine 1 mcg/kg dissolved in 50 ml of normal saline given over a period of 10 minutes. After completion of infusion inj. midazolam 1 mg i.v. was given. After waiting for 5 minutes inj. nalbuphine 100mcg/kg was given dissolved in 10 ml of normal saline.

Group FP received inj. fentanyl 2mcg/kg dissolved in 10 ml of normal saline followed by inj. midazolam 1mg i.v. Propofol bolus dose of 2mg/kg was given in titrating dose to achieve a targeted Ramsay sedation score (RSS ≥ 4).

Oxygen and air (1:1) ratio was given to both the groups @ 4 litre/min by Hudson mask. Surgeon was notified to start the case.

Thereafter in group ND dexmedetomidine infusion was restarted @ 0.3mcg/kg/hour and in group FP propofol infusion was started @ 75 mcg/kg/min and titrated according to need. The targeted sedation level was RSS ≥4 in both the groups. (1 = anxious, agitated, restless; 2 = cooperative, oriented, tranquil; 3 = responds to commands only; 4 = brisk response to light glabellar tap or loud noise; 5 = sluggish response to light glabellar tap or loud noise; 6 = no response). Bolus dose of propofol 1mg/kg was to be given as rescue sedation in both the groups, if needed.

Pulse rate (PR), respiratory rate (RR), mean arterial pressure(MAP) and Spo_2 were recorded every 5 minutes till end of procedure and every 15 min in the postoperative room. The drug infusion in both the groups was stopped 5 minutes before the completion of procedure.

Bradycardia (heart rate <50 or <20% from baseline) was treated with atropine 0.6 mg i.v. Hypotension (mean arterial pressure <60 mm Hg or <20% below baseline) was treated primarily by crystalloids. If not controlled by crystalloids, then inj. mephentermine was given in increments of 6 mg. Desaturation was treated primarily by increasing the flow of oxygen or keeping patient on bain's circuit according to the need.

After completion of procedure, patients were shifted to postanaesthesia care unit where PR, MAP, Spo_2 were recorded. Inj. diclofenac 75 mg i.m. was given as rescue analgesia on demand. Postoperative recovery was assesed by modified Aldrete scoring system every 5 minutes. Patients were discharged when they achieved modified Aldrete score more than 10. Duration of stay in PACU was defined as the time since patient arrived in PACU upto discharge.

Modified Aldrete Score

Consciousness
Fully awake [2 points]
Arousable [1 point]
Not responding [0 point]

Mobility
Able to move four extremeties on command [2 points]
Able to move two extremeties on command [1 point]
Able to move zero extremeties on command [0 point]

Breathing
Able to breath deeply [2 points]
Dyspnea [1 point]
Apnea [0 point]

Circulation
Systemic BP ≠ 20% of the pre anesthetic level [2 points]
Systemic BP between 20% and 49% of the pre anesthetic level [1 point]
Systemic BP ≠ 50% of the pre anesthetic level [0 point]

Color
Normal [2 points]
Pale, jaundiced and blotchy [1 point]
Cyanotic [0 point]

O_2 saturation
Maintaining O_2 saturation >90% on room air [2 points]
Needs inhalation to maintaining O_2 saturation >90% [1 point]

O_2 saturation <90% despite O_2 supplementation [0 point]

Statistics

SPSS version 19 for windows was used to check and analyse data. Power analysis was based on the results of a previous study. Data are expressed as mean and standard deviation for quantitative variables and number and percentages for categorical variables. Z test and chi square test were used for comparison in between groups. $p<0.05$ was considered significant. $P<0.01$ was considered highly significant. $P<0.001$ was considered extremely significant.

RESULTS

Table 1: Comparison of patients according to age, BMI and mean duration of procedure.

	Group ND	Group FP	P value
Mean Age	33.4±1	34.5±3	0.06
BMI	21.7±5	20.1±1	0.09
Mean duration	25.5±4	26.8±3	0.16

Table 2: Pulse rate (PR).

Time	Group ND	Group FP	P value
Baseline	76.0±3	75.7±4	0.74
0 min (start of procedure)	64.5±3	71.2±1	<0.0001
5 min	65.2±2	72.2±4	<0.0001
10 min	63.8±3	71.7±6	<0.0001
15 min	64.6±4	73.1±4	<0.0001
20 min	65.4±2	72.1±2	<0.0001
25 min	66.1±1	73.4±6	<0.0001
30 min	67.2±3	74.1±2	<0.0001
5 min after completion of procedure	75.6±4	80.1±4	<0.0001

Table 3: Mean arterial pressure (MAP).

Time	Group ND	Group FP	P value
Baseline	82.5±5	83.6±2	0.26
0 min(start of the procedure)	78±2	74.3±2	<0.0001
5 min	76.5±1	72.3±4	<0.0001
10 min	75.1±4	72.2±5	0.03
15 min	74.2±4	73.1±3	0.0004
20 min	75.2±2	72.1±4	0.0004
25 min	76.1±3	76.2±2	0.87
30 min	78.4±1	76.3±4	0.007
5 min after completion of procedure	82.5±1	84.3±5	0.06

Table 4: Demand for rescue analgesia (% of patients).

Group	% of patients
ND	None
FP	20%

Table 5: Time to achieve Modified Aldrete score of 10.

Group	Mean Duration (in minutes)
ND	65.5±3
FP	75.4±1
P value	0.0001

OBSERVATION

Demographic data such as age, weight and duration of surgery were comparable in both the groups and the difference was not statistically significant.

There was no statistical difference in the baseline pulse rate between the two groups. At the start of procedure there was a considerable decline in pulse rate in group ND as compared to group FP ($p<0.001$) which persisted throughout the surgery.

As regards the MAP, the baseline MAP was comparable in both the groups. At 0 minutes there was fall in MAP in both the groups but it was more in group FP ($p<0.001$). This fall in MAP persisted throughout the surgery and the difference between the two groups remained statistically significant.

20% of the patients in group FP demanded rescue analgesia as compared to none in group ND in postoperative period.

The mean duration to reach the Aldrete score of 10 in group ND was 65.5±3 minutes and 75.4±1 minutes in group FP. The difference between the mean duration of stay was statistically significant (p<0.0001).

None of the patients in either group showed respiratory depression with maintenance of oxygen saturation above 95% throughout the perioperative phase. Neither of the patients showed any evidence of opioid related side effects in the form of pruritus or nausea and vomiting.

DISCUSSION

The anaesthetic agents needed for day care anaesthesia are supposed to have rapid onset with rapid recovery along with maintenance of a deep plane of anaesthesia. Propofol in combination with an opiod, for years, has been the drug of choice for this purpose because of rapid onset and recovery with least postoperative nausea and vomiting. But propofol too has it's own pros and cons of causing respiratory depression, hypotension and pain on injection. So we chose to use dexmedetomidine as an alternative to propofol to avoid it's complications, along with a longer acting opioid, nalbuphine, in place of fentanyl.

In our study, the use of opioids was made common in both the groups in form of fentanyl and nalbuphine as they produce some degree of sedation but more pronounced analgesia by binding with mu, kappa, delta and sigma receptors.[6] Because of high fat solubility, onset of action of fentanyl is short, it's less protein binding capacity results in short duration of action but it has it's own side effects of respiratory depression and chest wall rigidity.

Nalbuphine, a semisynthetic opioid is an agonist antagonist structurally resembling oxymorphone which binds to mu, kappa and delta but not to sigma receptors.[7] It has analgesic property with onset and duration of action between 5-10 minutes and 3-6 hours respectively. It is more stable hemodynamically and is less likely to cause excessive sedation, respiratory depression, pruritus and urinary retention so is considered safe analgesic in ambulatory surgical procedures. Dexmedetomidine is an alpha-2 adrenoceptor agonist, sympatholytic, sedative and analgesic agent producing a state of sedation in which patient is easily arousable with mild tactile and vocal stimulus.

There was a fall in pulse rate in both the groups FP and ND but in group ND it was more throughout the procedure (p<0.0001) which was extremely significant. The maximum fall in pulse rate in group ND was 63.8±3 at 10 minutes after start of procedure. In group FP the maximum decline in pulse rate was 71.2±1 just after administration of propofol. There was a significant difference statistically as is evident by p value(p<0.0001) but none of the patients in either group required treatment. In both the groups the pulse rate returned to almost baseline 5 minutes after stopping the infusion. In a similar study done by Srinivasa Rao Nallam et al they found that the fall in mean pulse rate in dexmedetomidine group was more as compared to propofol group. This was supposed to be due to decreased sympathetic activity caused by virtue of it's alpha-2 agonist action.[7]

Regarding mean arterial pressure it was found that there was definite and significant fall in MAP in both the groups at start of procedure and at 5 minutes. In group FP the fall was more pronounced as compared to group ND (p <0.05) and there was a sustained fall upto 20 minutes. In both the groups MAP again returned towards the baseline 5 minutes after stopping the infusion. In a similar study conducted by G.S. Tomar et al comparing dexmedetomidine with propofol and fentanyl, fall in MAP was found in both the groups but more so in propofol and fentanyl group.[8]

In our study 20% of the patients in FP group complained of pain, whereas none of the patient in ND group demanded analgesia. This finding is consistent with previous study done by F.A. Khan et al where they observed that lesser number of patients required analgesia in recovery room in nalbuphine group as compared to fentanyl.[9]

The patients in group ND reached Aldrete score of 10 at 65.5±3 minutes and group FP at 75.4±1 minutes with a p value of < 0.0001 which is extremely significant. Ufuk kurukluyildiz et al compared dexmedetomidine with propofol in endoscopy and found a higher Aldrete score in dexmedetomidine group.[10]

In a previous study done by Srinivasan Nallam et al it was observed that nalbuphine /dexmedetomidine combination provides better sedation and analgesia than nalbuphine/ propofol in monitored anaesthesia care.[7] In our centre we have been using as a routine, a combination of propofol and fentanyl for such type of surgeries. In search for a better combination of drugs for such surgeries we combined dexmedetomidine with nalbuphine as nalbuphine gives longer duration of analgesia with lesser side effects and dexmedetomidine due to it's arousable sedation property might help in getting the desired aldrete score earlier in day care surgeries. We got similar results in our study although it needs further evaluation.

CONCLUSION

In our study we observed that discharge criteria reached earlier to Aldrete score of 10 in dexmedetomidine / nalbuphine group as compared to propofol /fentanyl group (pvalue<0.0001). Both the groups showed significant difference in hemodynamic changes but it did

not require any intervention. Since we could achieve favourable conditions of discharge earlier along with longer duration of postoperative analgesia in dexmedetomidine/nalbuphine group so it was considered to be a better option for minimally invasive gynaecological procedures on day care basis.

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