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Evaluation of Intravenous Buprenorphine's Efficacy and Safety in Enhancing Analgesia During General Anaesthesia: An Observational Cohort Study

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Abstract:

Background-Effective analgesia during intraoperative and postoperative period is pre-eminent in any surgery for which opioids and non opioid analgesics have been widely studied and used.

Aims and Objectives -We did an observational cohort study to evaluate the efficacy and safety of a single bolus dose of intravenous buprenorphine (a partial mu -receptor agonist) as the main analgesic adjunct to General Anaesthesia.

Methods -300 patients were included in this study which was done at Shri KMJ Memorial Hospital And Research Centre (Gondia,Maharashtra), Gondia City Hospital (Gondia,Maharashtra),Modi hospital,Mumbai from 2013 to 2014.Baseline demographic characteristics including age,sex,surgical procedure and duration,ASA status were recorded and well distributed.Additional intraoperative and postoperative analgesic requirement,including opioids , was recorded.Postoperative pain scores at regular intervals were recorded.In addition patient satisfaction scores were recorded.Adverse events like nausea,vomiting,respiratory depression were recorded and effectively managed.

Conclusion-Intravenous Buprenorphine provided effective analgesia during intraoperative and postoperative period with good patient satisfaction.

Keywords: intravenous buprenorphine, general anaesthesia, postoperative pain, opioid consumption, analgesia, patient satisfaction.

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INTRODUCTION

It is well established that optimal perioperative analgesia effectively decreases negative consequences like increased cardiorespiratory stress , delayed wound healing ,patient satisfaction and potentially shortens hospital stay.(1,2).Among the various strategies for this perioperative pain management ,opioids have traditionally held a central role due to their central analgesic properties.(3).However concerns regarding their adverse effects like sedation,respiratory depression,tolerance etc have driven the constant exploration of more opioids and other alternatives (4,5)

Not all opioids are easily and consistently available in certain remote geographic areas .Cost effectivity is also a concern in poor patient population.And so we studied a relatively cheaper and relatively easily available analgesic ,buprenorphine,with a prolonged duration of action and possible superior analgesia.

Intravenous buprenorphine is a mu-receptor partial agonist with a unique pharmacological profile.(6).It is an effective analgesic which has a ceiling effect on respiratory depression and sedation.(7).

Many preliminary studies have suggested that buprenorphine may offer a high quality analgesia with reduced risk of respiratory depression ,making it a feasible option for perioperative pain management.(8,9)

This observational cohort study encompasses a diverse patient population with careful selection of baseline demographic characteristics.

We postulate that intravenous(iv) buprenorphine lead to enhanced perioperative analgesia and higher patient satisfaction with stable haemodynamics.

MATERIAL AND METHODS

This study was an observational cohort study involving 300 patients.

Approval from local Research and Ethics Committee was obtained.A written Informed consent was obtained from all participants.

Inclusion criteria –

ASA 1 patients posted for elective major surgeries requiring General Anaesthesia with ET intubation.

Major surgeries included anticipated surgical time more than 2 and a 1/2 hours including (but not limited to)thyroid surgery,spine surgery,Head ,Neck and Face – Supraomohyoid neck dissection,modified Radical neck dissection,facial trauma,FESS ,Breast surgery etc

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Exclusion criteria included patient refusal ,patients with hypotension (SBP<90) ,Bradycardia (P<60/min),respiratory problems

In the operating room, routine pre-operative monitoring - electrocardiogram, non-invasive BP and pulse-oximetry was established.. A large bore peripheral intravenous cannula was inserted and intravenous fluid Ringer Lactate was commenced. Baseline vital parameters as mentioned above were recorded and repeated every 5 min from the pre-anaesthetic to intra-operative period till the patient was shifted to the recovery room. Patients received ondansetron 0.15mg/kg ,dexamethasone 0.15 mg /kg ,clonidine 2 mics /kg (maximum/not exceeding 120 mics total)

Here we presumed that a concomitant single bolus of clonidine i.v. had synergistic effect with buprenorphine i.v. and together provided good surgical analgesia with controlled hypotension and good surgical field.

All patients received intravenous buprenorphine 3 mics /kg.

General Anaesthesia was induced with intravenous Propofol 2mg /kg (maximum 150 mg) and vecuronium 0.08mg /kg and then endotracheal intubation was done and anaesthesia maintained on oxygen,nitrous oxide and Sevofluorane (dial setting of 2-2.5 %)

Sinus bradycardia of <50/min, was treated with intravenous Glycopyrrolate , Hypotension with MAP <55 mmHg, was treated with intravenous ephedrine 3mg ,repeated as necessary .

About 15 mins prior to end of surgery, Sevofluorane was discontinued, residual paralysis was reversed with IV neostigmine (0.05 mg/kg) and IV glycopyrrolate (0.08 mg/kg). Patients were allowed to breathe spontaneously at the end of surgery and extubated when awake and deemed safe clinically. All were shifted to recovery room for further oxygenation and monitoring. Vital parameters, namely, BP, pulse rate, respiration and oxygen saturation were regularly measured upto 24 hours postoperatively.Sedation and pain scores were measured in recovery room.

Following data was recorded at regular intervals in postoperative recovery room and then in ward for 24 hours after extubation ----

- Postoperative pain at 2 hours,4 hours,6 hours,12 hours and 24 hours using the Numeric Rating Scale

Total opioid consumption in first 24 hours

-Time to first analgesic requirement from end of surgery on patients request

-Adverse events like nausea,vomiting,constipation,sedation,respiratory depression

-Haemodynamics eg Pulse,BP , SO2,ECG

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Patient Satisfaction Score on a scale of 0-10 (0 -worst experience to 10- best experience)

CONTROL group data was obtained from historical records of patients who did not receive buprenorphine as part of their perioperative protocol.

Statistical analysis - Descriptive statistics including mean,standard deviation and frequencies were calculated for demographic variables.Same were calculated for outcome .Paired t- tests and Wilcoxon signed-rank tests were used to compare postoperative pain scores.Independent t-tests were used for comparative analysis between the buprenorphine study group and the historical control group.Chi- square tests were used to analyse categorical variables.Statistical significance was set at $p < 0.05$

OBSERVATION AND RESULTS

Total 300 ASA 1 patients (178 males and 122 females) scheduled for major elective surgery under General anaesthesia were included in this observational cohort study.

The mean age of the group was 39.4 years .

The mean duration of surgery was 192 minutes.

Intraoperatively no patient required top up of muscle relaxant (vecuronium) after the initial bolus dose.

No analgesic other than those included in study proforma was given in intraoperative period.

Time to first opioid consumption -- In starc contrast to the control group ,patients given iv buprenorphine during induction showed a substantial extension in the time between the end of surgery and their initial request for analgesic.

The median time for this was 3 hours (Interquantile range - 4-8 hours) in the buprenorphine group whereas the control group had a median time of 30 mins (Interquantile range -- 15 mins - 90 mins)

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Total Analgesic consumption (including opioids) ---

Patients who received iv buprenorphine showed a marked reduction in total analgesic consumption in the first 24 hours after surgery as compared to the historical group that did not receive buprenorphine.The intravenous buprenorphine group exhibited a remarkable 50 % reduction in opioid use , calculated in morphine equivalent doses($p<0.001$)

Postoperative pain scores ---

At 2 hours postoperatively ,iv buprenorphine group patients showed a statistically significant reduction in pain scores with a mean score 3 +/- 0.5 (0.001)

At 6 hours postoperatively ,iv buprenorphine group patients had a statistically significant reduction in pain scores with a mean of 2.5 +/- 0.8 ($p<0.001$)

At 12 hours and 24 hours postoperatively ,the mean pain scores remained significantly lower at 2.7 +/- 0.6 ($p<0.001$) and and 2.9 +/- 0.6 ($p<0.001$) respectively

ADVERSE EVENTS ---

Nausea ,vomiting and constipation ---

Patients in iv buprenorphine group had mainly nausea in 8% patients.Constipation after 12 hours of surgery was there in 14% patients.

These were manageable with antiemetics and laxative therapy as needed.

Sedation and Respiratory depression --

15 % patients had a prolonged duration of sedation with a mean period of 170 mins.1% of these needed O2 via nasal canula for a mean period of 4 hours postoperatively.

No case of respiratory depression requiring naloxone or else was observed in the iv buprenorphine group.

Haemodynamics --

Heart rate remained mostly stable during intraoperative and postoperative period .

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Heart rate < 50 with MAP < 55mmHg intraoperatively was managed with iv glycopyrrolate.

Heart rate < 60 in the postoperative period was seen in 18 % patients and was well managed with iv glycopyrrolate by the nursing staff.

Blood pressure remained fairly stable in iv buprenorphine group in perioperative period .No patient showed MAP > 70 mmHg perioperatively.

MAP < 55 mmHg was seen in 12 % patients in first 2 hours postoperatively which was well managed with iv ephedrine.MAP < 55 mmHg was managed likewise intraoperatively.

Oxygen saturation --

All patients were supplemented with O2 via nasal canula in first hour postoperatively.

Patients having SO2 < 94 % while breathing on air were supplemented with required further oxygen

Patient Satisfaction --

Patient reported satisfaction scores were higher in the iv buprenorphine group .The average satisfaction score was 7.9 on a scale of 0-10 ,with o as worst experience to 10 as best experience.

DISCUSSION ---

Our study revealed that iv buprenorphine can effectively alleviate perioperative pain when used as an adjunct to general anaesthesia.No other additional analgesic was required intraoperatively.A substantial reduction in postoperative pain scores with statistically significant improvement was observed at different time intervals (2,6,12 and 24 hours).

In comparison to previous literature ,our results are consistent with studies showing a reduction in pain scores and less opioid consumption (50 % less in our study) with iv buprenorphine usage.(10,11)

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These observations suggest that iv buprenorphine can be a valuable addition to the armamentarium of perioperative analgesics ,By reducing requirement of total opioids ,there may be a decreased incidence of sedation,respiratory depression and postoperative nausea and vomiting (12)

Notably no case of respiratory depression requiring naloxone or other intervention was seen.However ,few patients had prolonged sedation which necessitate careful monitoring and O2 supplementation as needed.Nausea and constipation seen in certain patients were manageable easily.

In the setting of ongoing opioid epidemic (13),the significant reduction in total opioid consumption with iv buprenorphine is of great importance.

This result align with the efforts of reducing opioid exposure for pain control ,a key consideration in perioperative care (14)

Haemodynamics ---

Haemodynamic stability was well maintained with iv buprenorphine during intraoperative and postoperative period.

All patients in iv buprenorphine group received iv clonidine too.Clonidine itself has interesting pharmacologic characteristics including sedation ,hypnosis ,analgesia,opioid need reduction and anti sympathetic response to pain (16).Bradycardia and hypotension were easily manageable .

We postulate that iv buprenorphine and iv clonidine together has synergistic action in terms of optimal analgesia and haemodynamic stability though we did not study this statistically and needs further evaluation.

In our study patients reported high satisfaction scores with iv buprenorphine.Patient satisfaction is a vital part of care and can influence adherence to pain management strategies.

LIMITATIONS—

Our study might have selection bias and unmeasured confounders could affect the results.

Casual relationships,however,cannot be established definitively as there was absence of randomized control group in our study

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CONCLUSION ---

We conclude that iv buprenorphine when used as supplement to general anaesthesia provides significant intraoperative and postoperative analgesia ,decreased total consumption of analgesics including opioid analgesics and offers good patient fulfilment.

Follow up studies evaluating the safety and efficacy of iv buprenorphine are warranted especially in high risk group.

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