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To Evaluate Clinical Efficacy of Intravenous Midazolam Alone and Along with Propofol for Sedation in Patient Management During Interventional Endoscopic Procedures

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ABSTRACT

Objective: Ample patient's sedation is a requisite for most interventional endoscopic procedures. A study was conducted to evaluate clinical efficacy of sedation using short acting anesthetic propofol with midazolam than midazolam alone in patient management during diagnostic and therapeutic endoscopic procedures.

Study Design: Prospective observational study

Place and Duration of Study: This study was conducted at radiology suite and endoscopy unit, by Department of Medicine, Gastroenterology & Hepatology Division, Holy Family Hospital, Rawalpindi, from 23-12-2009 to 21-6-2010

Materials and Method: A total of ninety two patients undergoing endoscopic procedures randomly received either midazolam (n = 47, group A) or propofol plus midazolam(n= 45, group B) sedation.Patient vital sign's were notedas well as recovery scores, patient's tolerance of the procedure (visual analog scale).Modified Richmond Agitation-Sedation Score (RASS Scale) was used to assess degree of sedation.The immediate and intermediate recovery was assessed using Steward's recovery score and Post Anesthesia Discharge score (PADS) respectively.

Results: Chi- square test value was 79.23 with P value of 0.001 and is significant,while Correlation co-efficient(r) value was 0.800 and the correlation was significant at 0.02 level.

Conclusion: Propofol along with midazolam is safe for interventional endoscopic procedures under adequate patient monitoring and is more effective than sedation with midazolam alone as post procedural recovery is concerned while sedation efficacy being similar.

Key Words: Midazolam, Propofol, Endoscopic Procedures

INTRODUCTION

Gastrointestinal endoscopic procedures can be unpleasant minimally painful and prolonged e.g., Endoscopic Retrograde Cholangiopancreaticography ordrainage procedures.It requires relative patient's immobility to prevent degradation of fluoroscopic image. Therefore, sedation should on principle be offered to patient.[1] This challenges the anesthesiologist of providing adequate sedation, analgesia, while ensuring rapid recovery. A variety of agents have been used for sedation.[2,3]

Midazolam short-acting benzodiazepine is commonly used for endoscopy[4], with potency 1.5–3.5 greater than diazepam.[5] It reaches maximum effect after 3–4 minutes, the duration of effect being 15 - 80 minutes[6] depending on cofactors such as obesity, age, and systemic disease. It's short initial distribution half-life of 3-10 minutes is responsible for awakening.[7] The drug produces reliable amnesia, and antianxiety effects. Midazolam is preferable to diazepam due to rapid recovery and nonpainful induction.[8] In few cases where benzodiazepines fail to provide adequate patient comfort opioids are added.[9]

Propofol (2,6-diisopropylphenol) is a sedative,the mechanism of action involve facilitation of inhibitory neurotransmitter γ-aminobutyric acid.Propofol is lipophilic, onset of action is rapid and awakening from single dose is due to short initial distribution half life.[7]Favorable results have been reported for propofol sedation during endoscopy but is expensive and may lead to respiratory arrest when used in higher doses.[10]

Recent data suggest synergism of pharmacological effects between midazolam and propofol as combination will reduce dosage needed,[11]expensemay be less and also reduces side-effects while retaining the individual advantages.[12]In view of above stated facts, a study was conducted with aim of observing clinical effects of sedative agents i.e. midazolam alone and alongwith propofol administered by anaesthesiologist for interventional endoscopy on hemodynamic, respiration, operator easiness and comfort, amnesia, recovery time and scores, patient acceptability and procedure tolerance (visual analogue scale),along with complications.

MATERIALS AND METHODS

After approval of hospital ethical committee and acquiring informed consent, this prospective observational study, was conducted at radiology suite and endoscopy unit, by Department of Medicine, Gastroenterology & Hepatology Division, Holy Family Hospital, Rawalpindi, from 23-12-2009 to 21-6-2010. All patients had pre-procedure evaluation done. A total of ninety two patients were studied with age group from 18 to 85 years and belonging to American Society of Anesthesiologist(ASA) physical status class 1-3 and medically optimized class-4. Excluded were patients aged less than 18 years, difficult airway,bronchial asthma, heart disease, uncompensated hepatic/ renal disease, pregnant and lactating mother and emergency situation cases (e.g. upper gastrointestinal bleeding).All patients received Inj.Drotaverine 20mg and Inj.Nalbuphine 1-2mg intramuscularly.Patients randomly received either midazolam alone (n=47, group A, loading dose of 2.5-3.5 mg intravenously and repeat doses of 0.5-1mg) or propofol plus midazolam (n=45, group B, loading dose of propofol 40-60 mg intravenously and bolus dose of 20 mg and a initial midazolam dose of 2.5-3.5 mg) intravenously. The patients were placed comfortably on radiology table in lateral position. Electrocardiograhy, pulse oxymeter, and blood pressure were noted serially. Oxygen at 2-4L/min via nose cannula was given. The time between injection of sedative and moment of final withdrawal of endoscope wastotal procedure duration. The modified RASS Scale[13]was used to assess level of sedation during procedure. At end of procedure, Steward's recovery score[14] was noted to assessimmediate recovery. The PADS system[15,16] was employed to assess intermediate recovery before shifting patients to either respective wards/home. Before discharge patient were asked to stateexperiance of procedure on visual analogue scale of 0 - 10, i.e, poor to good experiance.

Data was analyzed by SPSS version 18. Chi-square test was used to compare Stewart recovery score and grades of PADS score attained for association, while Spearman's Rank correlation was also used to check interdependence between them. The P-value of <0.05 will bestatistically significant.

RESULTS

In group A, mean bolus dose of 1± 0.5 mg midazolam was used plus additional mean dose of 6.12 mg during procedure with a standard deviation of 3.65, in group B initial loading propofol dose of 20 mg used in a single patient, plus mean additional dose of 113mg with a standard deviation of 66.16 along with initial dose 2.5mg±0.5 of midazolam and intra-procedure midazolam dose of 2.76mg with a standard deviation of 0.85 was used. The lowering of systolic blood pressure < 90 mmHg observed in two out of 47 patients i.e. 4.25% of cases in group A and while in group B noted in one out of forty five patients i.e. 2.2% of cases respectively. The temporary oxygen desaturation (< 85 %) in group A and B occurred in four patients i.e, 8.5% and in two patients i.e, 4.4% of cases respectively. The mean saturation in group A and B being 97.23% and 97.45% respectively.

The mean recovery time in group A being 10±5 min and mean procedure times being 79.11 min whereas in group B same figures were 3±2min and 88.6 min respectively .The minimal recommended Stewart recovery score andPADS was attained by all cases in study. The sedation efficacy was rated similar in both groups by endscopist.Visual Analogue score being stated as good to excellent in both groups. The modified RASS Scale score in group A and B being 1 and 2 in 95% of cases and in 5% cases was scale 3 sedation score. The demographic data of both groups is shown in table-1.

Table No.1: Demographic Data

	Group A	Group B
Age[years (mean/standard deviation)]	50.80/13.07	49.08/ 14.19
Sex (male/ females)(n/%)	18/29 - 38.8/61.7	19/26 - 42.2/57.8
ASA-class I (n/%)	16/34	17/37.8
ASA-class II (n/%)	12/25.5	14/31.1
ASA-class III (n/%)	19/40.4	13/28.9
ASA-class IV (n/%)	0/	1/ 2.2

In the study drugs used for premedication in group A were Inj.Drotraverine which was used in 42 cases i.e, 95.4% of cases and in seventeen cases i.e, 38.6% was used during procedure ,while in 4.5% i.e, two cases it was not used. Inj.Drotraverine median dose was 40mg, with a standard deviation of 22.33 before and during procedure, whereas Inj.Nalbuphine was used in fortyone i.e, 91.1% of cases in dose of 2mg and Inj. gravinate was used as pre-medication in fortythree i.e, 97.7 % of cases in a dose of 25mg. Meanwhile in group B, Inj.Drotraverine was used in 44 cases i.e, 97.7% of cases and in fortyone cases i.e, 38.6% was used during procedure ,while in 2.1% i.e, one case it was not used. Inj.Drotraverine median dose was 30mg, with a standard deviation of 26.20 before and during procedure, whereas Inj.Nalbuphine was used in fortyone i.e, 89.1% of cases in a dose of 2.5 mg as pre-medication and in similar dose used in a single case during procedure whereas in four i.e,8.7% of cases it was not used,while Inj. gravinate was used as pre-medication in fortythree i.e. 91.5 % of cases in a dose 25 mg whereas in four i.e, 8.5% of cases it was not used. In study, Chi-square test value was 79.23 with P-value of 0.001 and significant . Spearman's Rank

correlationtest value (r) came out to be 0.800 and was significant at 0.02 level.

DISCUSSION

Safe proceedings of interventional endoscopy demand meticolous follow-up of standardprotocols. The examination is usually of shorter duration has low complication and mortality rate.[17,18] In the United States and the United Kingdom, 88% endoscopic examinations are done under sedation[2,3] a recent survey shows sedation frequency of 87% for endoscopyin Germany.[19]Every patient has right to endoscopic examination as stress-free as possible. It therefore appears ethically unjustifiable to withhold sedation.[1] In our study a single case was postponed due to non co-operative patient and request was to repeat under supervision of anesthesiologist as it was the only case in which sedation was given by medical personal.The higher rate of patient acceptance of endoscopic examinations owing to sedation is demonstrated in other studies,[20] but this increases cost and is responsible for about 50% of complications.[21] However, a few national study of european countries have investigated the rate of using conscious sedation for routine diagnostic upper gastrointetinal endoscopy in their country.[22]The decision of using premedication is influenced by national and cultural differences among countries, as well as patients wishes and endoscopists attitude.[23]

The drug dose was tailored to type of intervention and patient's ASA grade in our study. Since most complications in sedated gastroscopy are of cardiopulmonary nature, monitoring is important to prevent them,[24]mild hemodynamic alterations during our study were immediately managed.Endoscopist satisfaction was noted withpresence of anesthesiologist in our study.

In complex interventions moderate sedation is needed to ensure that examination is done safely.[25]In study by Jung and colleagues[26] significantly higher endoscopist satisfaction was noted with propofol.The intermittent bolus administration of propofol is currently the best documented form of administration in endoscopy.[27,28,29]It was used in our study. There is evidence supporting use of propofol with benzodiazepines(eg, midazolam) and/or opiates (eg, fentanyl),a study done in this regard by Van Natta[30] and colleagues employing combination therapy,depicted smaller dose requirementof propofol to obtain moderate rather than deep sedation.

Midazolam is given as a bolus of 30–80µg/kg body weight for gastroscopy,[31] subsequently, lower-dose boli are given for desired sedation depth,[32] the use of lower doses of midazolam is recommended for patients older than 60 years.[33]In our study similar protocol was followed.

In risk factor analysis by Wehrmann and Riphaus[34] a total of 135 adverse events (1.4%) were documented. Assisted ventilation was necessary in forty patients (0.4%); nine patients required endotracheal intubation (0.09%); twenty eight needed further monitoring on the intensive care unit (0.3%); and four patients died, three potentially due to sedation-related side effects (mortality, 0.03%). In our study surgical exploration was advised in one case immediately on assessment, mild bleeding was noted in four cases which settled with adrenaline local application,in eight cases fresh frozen plasma had to be given and in one case inj.vitamin K was administered.

Post-interventional monitoring is necessary to detect any sequelae of sedation. The duration of this phase depends on the expected risk.[35] Close monitoring of the patient by qualified personnel should be continued, patients can be released when their vital signs are stable and are fully oriented.[36] In our study patients were kept in recovery area with full resuscitation facility before shifting to medical intensive care or respective wards depending upon recovery score attained. However,in our study a single case of anaphylactic reaction/shivering leading to respiratory distress had to be managed by mask ventilation and later intubated briefly (lasting 8 minutes) in the patient receiving propofol/ midazolam sedation in recovery area.

The minimum discharge criteria as stated in the guidelines[37] was implemented in our study. Prophylactic oxygen administration via a nasal tube can significantly reduce the frequency of hypoxemic events during endoscopy.[38]

In the study done by Ladas and colleagues[4] atleast two sedatives were reported to be in use in every country. In about 1/3rd of the countries or representative endoscopy units, more than one category of personnel was responsible for administering sedation. Endoscopists are required to obtain training in the safe administration of propofol before using it in clinical practice,for this purpose "The American Society for Gastrointestinal Endoscopy" has published recommendations regarding the learning objectives required for formal training in propofol administration.[39]In study done by Byrne and colleagues,[40] they recommeded that endoscopists seeking to use propofol in their practice should undergo:1) certification in 'advanced cardiac life support'; and 2) a preceptorship or formal course of instruction with an individual (such as an anesthesiologist) who is familiar with propofol use.

CONCLUSION

Propofol along with midazolam is safe for interventional endoscopic procedures under adequate patient monitoring and is more effective than sedation with midazolam alone as post procedural recovery is concerned while sedation efficacy being similar. Sedation also required availability of adequate

monitoring and resuscitation facilities in the endoscopy unit.

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