

Comparative study of Nalbuphine/Dexmedetomidine Versus Nalbuphine/Midazolam for extra corporeal shock wave lithotripsy in adults

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Abstract

Background: ESWL is a painful procedure and vast majority of patients do not tolerate the procedure without analgesia and sedation. Practicing combination of two agents can provide better patient control and allows the use of smaller doses of each single agent avoiding its undesirable effects. This study evaluate and compare the effects of dexmedetomidine versus midazolam along with nalbuphine in adult patients during ESWL procedure.

Methods: A prospective, randomized, double-blind and comparative study was conducted on 80 patients. These patients were randomized into two groups with forty patients in each group. Group D received an initial

loading dose of 1 µg/kg of dexmedetomidine infused IV over 10 minutes followed by an infusion rate of 0.4 µg /kg/hr. Group M received the initial loading dose of 20 µg /kg of midazolam was infused IV over 10 min followed by an infusion rate of 40 µg /kg/hr. In both the groups Nalbuphine 0.5 mg/kg was given intravenously (IV) to all patients over 10 min before the ESWL procedure.

Results: Recovery score (Modified Aldrete score) at 60 minutes was statistically significant in group-D as compared to M. Need of rescue drug (nalbuphine) was significantly lower in group D. Post-operative side effects like nausea, vomiting and respiratory

depression were higher in group M as compared to group D but it was statistically insignificant.

Conclusion: We found that both dexmedetomidine-nalbuphine has better hemodynamic and respiratory stability, faster recovery and less need of rescue drug as compared to midazolam. So we concluded that combination of dexmedetomidine and nalbuphine may be a better alternative than combination of midazolam and nalbuphine in the adult patients undergoing ESWL.

Keywords: Dexmedetomidine, Nalbuphine, Midazolam, ESWL

Introduction

Extra Corporeal Shock Wave Lithotripsy (ESWL) is widely used for the treatment of urinary tract calculi. It is a painful procedure and vast majority of patients do not tolerate the procedure without analgesia and sedation. Adequate analgesia is mandatory to achieve good treatment results, as well as patient compliance and comfort.(1) Several anaesthesia care techniques have been used to provide such sedation and analgesia. However, most of the analgesic drugs administered for ESWL carry the risk of respiratory depression, delayed discharge, and/or unplanned hospital admission .(2)TIVA(Total intravenous anaesthesia) is considered to be better than inhalation technique for short day care procedure.(3)

Drug used for sedation during this procedure includes propofol, opioids and benzodiazepines.(4,5,6,7) However, propofol may cause oversedation and disorientation , when administered to elderly patients, and opioids are associated with increased risk of respiratory depression and oxygen desaturation.(4)

Nalbuphine is potent mixed opioid analgesic without undesirable side effects.Nalbuphine is structurally related to oxymorphone. It is a highly lipid soluble agonist-antagonist opioid. It has a short duration of

action and rapid clearance compared with other opioids and is less likely to cause side effects such as pruritus, respiratory depression, urinary retention and excessive sedation (8).

Midazolam is benzodiazepine group of drug. Midazolam with its quick onset, but a relatively long half-life can cause prolonged sedation after repeated administration. Combining midazolam with opioids increases the risk for hypoxemia and apnea. (9)

In contrast, dexmedetomidine is a highly selective α_2 -adrenoceptor agonist with both sedative and analgesic properties and is devoid of respiratory depressant effect. It reduces opioid requirements and stress response to surgery ensuring a stable hemodynamic state . These properties along with its relatively short elimination half-life of 2 h (compared with 3–4 h for midazolam) make dexmedetomidine an attractive agent for sedation.(4) So, it has been used to premedicate and sedate patients undergoing day care procedures like ESWL, D &E (Dilation and evacuation) and colonoscopy without adverse effects.

Practicing combination of two agents can provide better patient control and allows the use of smaller doses of each single agent avoiding its undesirable effects (8)So, we decided to evaluate and compare the effects of dexmedetomidine versus midazolam along with nalbuphine in adult patients during ESWL procedure.

Type of study: Prospective randomize double blind comparative study.

Study Location: IKDRC-ITS, Civil Hospital, Ahmedabad (Year 2016-2019)

Sample size : Sample size calculation was based on a Modified Ramsay Sedation Score by considering mean difference of 0.32 and standard deviation 0.48.To detect a difference in sedation score , minimum 35 samples

per group are required at 80% power and 5% level of significance.

After obtaining written informed consent, 80 patients of either sex between group of 18 to 60 years, of ASA grade I or II, were selected and allotted in group-D and group-M by closed envelope.

Exclusion Criteria

- Patient refusal
- Current respiratory & psychiatric disorders
- Severe bradycardia
- Heart blocks
- Allergic to medication used in study
- Chronic use of alpha2 agonist
- BMI > 30
- Paediatric patients

Pre-anesthetic examination

It was carried out in detail which included General examination, Systemic examination, airway assessment and investigations. Written and informed consent was taken from all the participants. Pre-operative counselling will be done to gain the confidence of the patient and to minimize the emotional component of pain.

Premedication

(1) inj. Glycopyrrolate 0.004mg/kg and inj. Ondansetron 0.08 mg/kg.

(2) Inj. Nalbuphine 0.5 mg/kg was given intravenously (IV) to all patients over 10 min before the ESWL procedure.

Sedation

In **Dexmedetomidine** group, patient received an initial loading dose of 1 µg/kg of dexmedetomidine infused IV over 10 minutes followed by an infusion rate of 0.4 µg /kg/hr till the end of procedure .

In **Midazolam** group, the initial loading dose of 20 µg /kg of midazolam was infused IV over 10 min followed by an infusion rate of 40 µg /kg/hr till the end of procedure .

Oxygen supplementation was given via O2 cannula in all patients but when saturation decrease < 92% , 100 % O2 was given via mask till saturation maintain above 92 %.

Adverse effects such as bradycardia ($\geq 20\%$ decrease to baseline), hypotension (MAP < 50 mmHg), desaturation (SpO₂ < 92%), and nausea/vomiting were also recorded during the procedure. Atropine 0.01 mg/kg IV for bradycardia, 0.9% NaCl infusion for hypotension and 100% oxygen with mask for desaturation were given as part of the treatment. Inj. Naloxone was kept ready for antagonizing over dose of nalbuphine.

Intraoperative

Ramsay sedation score and hemodynamic parameter ; Heart rate ,Blood pressure & SpO₂ were recorded.

Inj. Nalbuphine (5mg) was given as rescue analgesic when **Modified Ramsay sedation score 3 with complain of pain**. Need of supplemental nalbuphine in both groups was noted.

Post-operative

Modified Aldrete score was observed

The sedation score (RSS) and the hemodynamic (NIBP, HR) and SpO₂ were recorded every 5 min during the ESWL procedure. After the termination of ESWL, patients were shifted in recovery room . Modified Aldrete score was noted by another anesthetist who did not take part in the operating room care. Time of achieving Modified Aldrete score was noted at 60 minutes. Patient was observed till discharge.

Statistical Analysis

Sample size calculation: To compare dexmedetomidine and nalbuphine (group-D) and

midazolam and nalbuphine (group-M) as intravenous anaesthetic agents in adult patients undergoing ESWL. Sample size calculation was based on Modified Ramsay Sedation Score by considering mean difference of 0.32 and Standard Deviation 0.48. To detect a difference in sedation score, minimum 35 samples per group are required at 80% power and 5% level of significance.

Hence we decided to include 40 patients in each group considering some exclusion.

The data from 80 patients was collected and statistical analysis was performed using Independent t test and Mann Whitney test for carrying out significant P-value.

Demographic Data

Table 1

	Group-D (N=40)	Group-M (N=40)	P-value
Age	35.78±10.11	34.10±9.24	0.44 (NS)
Gender : M	26 (65%)	25 (62.5%)	0.82 (NS)
F	14 (35%)	15 (37.5%)	
Weight	55.60±10.96	58.40±9.31	0.22 (NS)
Duration of surgery	35.54 ± 5.82	35.50 ± 2.57	0.88(NS)
Duration of anaesthesia	45.54 ± 5.82	45.50 ± 2.57	0.88(NS)

P<0.05 is considered as significant

Patients in our study were demographically comparable in both the groups. There were no statistically

Intraoperative Heart rate

Table-2

Time (Minutes)	Group-D (N=40)	Group-M (N=40)	P-value
0	79.95±13.61	82.45±16.25	0.10 (NS)
1	76.83±11.25	82.08±16.98	0.13 (NS)
5	74.18±13.06	86.63±15.48	<0.01*
10	71.93±9.78	88.73±14.41	<0.01*
15	75.26±9.72	88.73±13.78	<0.01*
20	74.15±9.80	88.40±13.46	<0.01*

Data analysis has been done in SPSS V20.

Observation And Results

Prospective randomize double blind comparative study was carried out in 80 ASA I-II adult patients undergoing ESWL in a year 2016 - 2019.

Statistical Analysis

All Collected data were entered into the SPSS V20. Continuous data were expressed as Mean ± SD form. Continuous data follows parametric and Non-Parametric data both. Independent t test and Mann Whitney test have been used for carrying out significant P-value.

significant difference in the two groups with regard to age, gender, weight. (P >0.05).

30	75.54±8.57	87.45±13.85	<0.01*
45	74.77±9.38	84.80±16.07	<0.01*
60	74.54±9.55	83.13±14.70	0.04*
120	73.62±8.58	83.73±12.93	<0.01*

p value <0.05 *-significant

statistically significant reduction HR in Group-D as compared to Group-M.

As seen in table-2 intra-operative heart rate was noted in both groups at frequent intervals. There was

Intra Operative Systolic Blood Pressure

Table-3

Time (Minutes)	Group-D (N=40)	Group-M (N=40)	P-value
0	133.93±13.68	130.83±14.99	0.29 (NS)
1	133.50±16.80	131.85±14.94	0.55 (NS)
5	131.15±17.83	131.90±13.66	0.42 (NS)
10	133.55±19.71	125.08±12.20	0.14 (NS)
15	126.87±22.19	125.65±11.47	0.91 (NS)
20	126.67±19.31	125.28±11.22	0.55 (NS)
30	127.87±19.40	128.60±14.22	0.90 (NS)
45	127.10±19.24	130.08±15.58	0.91 (NS)
60	125.00±16.87	127.65±11.81	0.33 (NS)
120	123.41±16.59	124.00±12.79	0.96 (NS)

p value <0.05 significant

Table-3 suggest that there were no statistically significant difference in both the groups in systolic blood pressure (P > 0.05).

Intraoperative Diastolic Blood Pressure

Table-4

Time (Minutes)	Group-D (N=40)	Group-M (N=40)	P-value
0	85.50±12.71	85.60±12.04	0.45 (NS)
1	89.40±10.74	85.73±13.27	0.23 (NS)
5	88.43±13.19	85.08±11.89	0.32 (NS)
10	87.25±16.32	84.75±10.79	0.28 (NS)

15	85.90±16.78	83.13±14.69	0.38 (NS)
20	84.13±14.70	78.53±13.46	0.08 (NS)
30	85.82±16.68	80.90±16.73	0.20 (NS)
45	82.51±15.42	79.70±16.28	0.55 (NS)
60	80.97±14.70	77.95±14.57	0.36 (NS)
120	77.85±11.64	76.70±15.05	0.61 (NS)

p value <0.05 significant

Table-4 and suggest that there were no statistically significant difference in both the groups in diastolic blood pressure (P > 0.05).

Modified Ramsay Sedation Score

(As shown in proforma) **Table-5**

Time (Minutes)	Group-D (N=40)	Group-M (N=40)	P-value
0	1.00±0	1.00±0	1.00 (NS)
1	1.00±0	2.00±0	<0.01*
5	3.00±0	3.00±0	1.00 (NS)
10	5.00±0	4.00±0	<0.01*
15	5.00±0	4.68±0.47	<0.01*
20	5.76±0.64	4.00±0	<0.01*
30	5.59±1.04	3.45±0.50	<0.01*
45	5.00±0	4.00±0	<0.01*
60	3.00±0	4.00±0	<0.01*
120	2.00±0	3.00±0	<0.01*

p value <0.05 significant Graph-4

Table-5 suggest that Modified Ramsay Sedation Score was statistically significant at 1 min in midazolam group whereas it was statistically significant in group D

up to 45 minutes. But at 60 minutes and 120 minutes patient were more sedated in midazolam group .

Percentage of person required extra nalbuphine

Table 6

	Group-D(N=40)	Group-M(N=40)	P-value
Percentage of person required extra nalbuphine	12.5%	55%	<0.01*

p value <0.05 significant

As shown in the table rescue dose of Nalbuphine statistically significant more in group M as compared group D.

Postoperative parameters: Modified Aldrete Score: Table 7 (As shown in proforma)

Time (Minutes)	Group-D (N=40)	Group-M (N=40)	P-value
0	3.00±0	3.00±0	1.00 (NS)
1	3.00±0	3.00±0	1.00 (NS)
5	3.05±0.32	3.00±0	0.31 (NS)
10	4.89±0.31	5.00±0	0.04*
15	5.00±0	5.00±0	1.00 (NS)
20	5.24±0.43	5.00±0	<0.01*
30	6.03±0.16	6.00±0	0.31 (NS)
45	7.00±0	6.90±0.30	0.05 (NS)
60	7.84±0.37	7.10±0.30	<0.01*
120	8.00±0	8.00±0	1.00 (NS)

p value <0.05- *-significant

As seen in the above table-7 Modified aldrete score .

There was statistically significant recovery from sedation in group-D after 20 min.

Postoperative side effects: Table-8

	Group-D (N=40)	Group-M (N=40)	P- Value
Nausea	03 (7.5%)	07 (17.5%)	0.18(NS)
Vomiting	02 (5%)	04 (10%)	0.68(NS)
Hypertension	-	-	
Arrythmia	-	-	
Shivering	-	-	
Respiratory depression	-	05 (12.5%)	0.55(NS)
Dellusion	-	-	

p value <0.05- *-significant

The side effects were evaluated and the incidence of side effects were comparable in Groups D and M.

Discussion

Treatment of urolithiasis has been revolutionized with the introduction of extracorporeal shock wave

lithotripsy (ESWL) due to its simplicity, non-invasive nature, efficacy , and minimal morbidity.(27,28) The pathogenesis of pain in ESWL is still poorly understood but is consider to be multifactorial. The cutaneous superficial skin nociceptors and visceral nociceptors

such as periosteal/pleural/ peritoneal, and musculoskeletal pain receptors are two important component responsible for causing pain during ESWL. (29) Patient-related factors and several physical variables including the type of lithotripter, size and site of stone burden, location of the shockwave front, cavitation effects, shockwave peak pressure, size of focal zone, and area of shockwave entry at the skin are additionally responsible for pain.(34) Recent development have made ESWL more effective, with minimal morbidity , making it possible to perform ESWL in an outpatient setting without need for general or spinal anaesthesia. (30,31) Though avoidance of general anaesthesia is beneficial to patients , there is a significant concern regarding jeopardizing treatment outcome due to use of less potent analgesic methods. (32)

The use of general anaesthetic agents results in more controlled respiratory excursion , which translates into more effective stone targeting and fragmentation. Therefore , general anaesthesia may be preferred in following condition- children , extremely anxious individuals, when a lengthy treatment is anticipated e.g. bilateral ESWL concomitant renal and ureteral stones. Calculi composed of cystine , calcium oxalate monohydrate or brushite are known to be resistant to fragmentation . Therefore , if their presence is anticipated , delivery of higher levels of shockwave energy with attendant increased anaesthesia requirements should be expected.

A relaxed, cooperative patient during treatment is paramount in maintaining stone targeting for optimal fragmentation. Therefore , it is essential to choose an appropriate analgesia with minimal adverse effects. Despite reports of various studies comparing different analgesic techniques during ESWL (33,34,35)

guideline for pain management during the procedure are not established.

Different analgesic agents including opioids (morphine , pethidine and fentanyl) , nonsteroidal anti-inflammatory drugs (NSAIDS- diclofenac , propofol, ketorolac and piroxicam) , local anaesthetic agents and a number of combination have been used during ESWL by various techniques (general anaesthesia , regional anaesthesia , total intravenous injection(TIVA) , patient- controlled analgesia(PCA) and monitored anaesthesia care (MAC) , cutaneous cream).(36,37)

Jalowiecki et al. (11) used **dexmedetomidine** alone at an initial loading dose of 1 µg /kg infused IV over 15 min, followed by an infusion rate of 0.2 µg /kg/h to provide analgesia/sedation for colonoscopy is limited by its many adverse effects, such as hemodynamic instability, a prolonged recovery time, vertigo, nausea, vomiting and a complicated administration regimen. Supplemental fentanyl was required in 47% of patients to achieve a satisfactory level of analgesia.

The therapeutic as well as adverse effects of **midazolam** are due to its effects on the GABA receptors and it produce sedation, hypnotic, anxiolytic, anterograde amnesia, muscle relaxation and anticonvulsant. It has no analgesic effect.

Fentanyl, a strong synthetic narcotic has rapid onset and short duration of action. It is a commonly used during ESWL but has significant adverse effects like centrally mediated respiratory depression along with decrease in oxygen saturation, nausea, vomiting, drowsiness, and hypersensitivity reactions.(38,39,40)

Nalbuphine is a partial k(kappa) agonist / µ antagonist opioid of phenanthrene series. It was synthesized in an attempt to produce analgesia without the undesirable side effects of a µ agonist, especially less respiratory depression .

Combination of two anaesthetic agents from the beginning of the procedure allows the use of lower dose of each agent and there by decreasing its own undesired effects and gains the augmented desirable effects of each.

Therefore we decided to do double blind randomise study to compare hemodynamic, sedation, analgesic effects of dexmedetomidine and midazolam in combination with nalbuphine during ESWL

Hemodynamics

Heart rate: In our study, Intra-operative heart rate was recorded in both groups at frequent intervals and there was statistically significant reduction HR in Group-D as compared to Group-M. We had observed decrease in HR but it was never less than 50 beats per minutes. This can be explained by decreased sympathetic activity caused by dexmedetomidine by virtue of its alpha 2 agonist effect(8). Our result matches with study done by **Raafat A. Salem et al.** in ESWL and **Srinivasa Rao Nallam et al** in middle ear surgery (1,8).**Mohd. Asim Rasheed et al** compared dexmedetomidine & Midazolam with ketamine for monitored care anaesthesia along with local infiltration or nerve block, also observed bradycardia with use of dexmedetomidine.(22)

Prezemyslaw Jalowiecki et al compared dexmedetomidine for colonoscopy and found that heart rate decreased to <50 beats/minute in four case which were treated with atropine which is contradictory to our study. The reason may be in our study nalbuphine was used with dexmedetomidine as an adjuvant as well as rescue analgesic which is partial kappa (k) agonist / μ antagonist which can counter bradycardia. In their study fentanyl was used as rescue analgesic.(11)

G.Guler et al used dexmedetomidine for extubation pressure response. In his study bradycardia occurred in one patient out of 30. This is not similar to our study because in their study they infused 0.5 μg / kg dexmedetomidine in sixty seconds, single iv dose 5 minutes before extubation . Whereas we have given bolus dose of dexmedetomidine via infusion.(41)

Systolic & Diastolic blood pressure: In our study, there was no statistically significant difference in both the groups with regard to systolic and diastolic blood pressure. But, decreased SBP and DBP compared to baseline was observed in both the groups. This is similar to study done by **Dere K , et al** and **Wafaa G. Ahmed et al.** They compared dexmedetomidine and midazolam with fentanyl as rescue and observed that there was no stastically significant different in mean arterial pressure.(16,17)

Kazim karaaslan et al(12)compared dexmedetomidine and midazolam as primary drug for MAC with tramadol bolus followed by infusion via PCA. They observed SAP, DAP and MAP were higher in group-M than group-D. This is not similar to our study, because,we have used nalbuphine which has better hemodynamic stability and better pain control in comparison with tramadol in both the groups. (3)

Prezemyslaw Jalowiecki et al found hypotension and bradycardia in 3 of 19 patients receiving dexmedetomidine for colonoscopy which is not similar to our study . This may be because fentanyl was used in their study which is strong synthetic opioid so predisposed to hypotension.(11)

Respiratory effects: There was no significant difference in spo2 during the procedure (average duration : 45.54 ± 5.82 minutes) in both the group as O2 was supplement via nasal cannula . But in midazolam group there was fall in spo2 in five patients(12.5 %) in

recovery room in spite of 2 L of oxygen given via nasal cannula. Supplemental O₂ was given with O₂ mask. Despite the deep sedation, Dexmedetomidine does not cause severe concomitant respiratory effects because of it is alpha-2 adrenergic agonist. More respiratory depression in post operative period group M is explained by the fact that in group-M, requirement of rescue analgesia in form of nalbuphine was significantly more because midazolam is devoid of analgesic effect. Rescue opioid is often given to prevent the unintentional reflex to painful stimuli. 55 % patients in group-M received nalbuphine as compared to 12.5 % patient in group-D because of its analgesic property, and prolonged effect of midazolam caused respiratory depression in recover room. Which is similar to **Wafaa G. Ahmed et al.**(16)

Kazim k et al.(12) compared dexmedetomidine & midazolam for MAC combined with tramadol via PCA endoscopy sinus surgery and found no fall in spo₂ even in midazolam group. This is not similar to our study this may be because in their study tramadol was used as rescue analgesic whereas we used nalbuphine. Analgesic dose of tramadol produce less respiratory depression than other opioids, owing in part to its non-opioid receptor mediate action.(3)

Sedation : In our study, sedation was noted using modified Ramsay sedation score (M RSS). Sedation Score was statically significantly more in group D as compared to group M **up to 45 minutes**. This could be explained at least in part, by the additional analgesic property of dexmedetomidine that could have contributed to improved patient perception of this form of sedation and in part by potential difference in the quality of sedation of the two drugs. **Srinivasa Rao Nallam et al** compared dexmedetomidine and Propofol with nalbuphine and found similar result.(8) **Dere K,**

et al. also observed that RSS score of dexmedetomidine group at the 10th and 15th minutes were significantly higher than midazolam group. (17)

In our study sedation was statistically significant and more in group M as compared to group **Dat 60 and 120 min**. Reason may be in group-M requirement of rescue analgesia in the form of nalbuphine was significantly high which was given in 55 % patients around 10 minutes before the end of procedure. Because in previous studies fentanyl was used as rescue which is short acting opioids than nalbuphine. This may be due to elimination half life of dexmedetomidine is 2-3 hr while Midazolam half life is 3-4 hrs.

Intra-operative rescue analgesia: In our study group-M, **55 %** patient required rescue analgesia whereas in group – D **12.5 %** patient required rescue analgesia in the form of nalbuphine. Reason being inherited sedative and analgesic properties of dexmedetomidine and midazolam is devoid of analgesic effect. **Devangi A Parikh et al** found that percentage of patients requiring rescue fentanyl was higher in Group MF than Group D (**40% vs. 11.1%**, P = 0.01).(9) This findings are similar to our study. **Mohd. Asim Rasheed, et al** also found that mean extra ketamine dose requirement was greater but non-significant in group KM than in group KD.(22)

In contrast to our study **P. Zeyneloglu et al** compared dexmedetomidine and midazolam/fentanyl combination in outpatient shock wave lithotripsy. They observed that rescue sedative(midazolam)and analgesic(fentanyl) need was significantly higher in dexmedetomidine group. The reason behind this in dexmedetomidine group fentanyl was given as rescue whereas in midazolam group fentanyl was given before starting the procedure.(14)

Post – operative recovery: Modified Aldrete Score was used for determining post operative recovery. In our study, Modified Aldrete Score was higher in dexmedetomidine group than midazolam group. It suggested faster recovery in dexmedetomidine group compared to midazolam group.

In Dexmedetomidine group modified Aldrete score was 8 at 60 min in most of the patient. But, Average discharge time was similar in both group (3 hr 20 ± 5 minutes). This is because we have taken actual patient's discharge time from the recovery area rather than considering patient's readiness for discharge using post-anaesthesia discharge criteria. (eg. modified Aldrete score) It has been demonstrated that a difference between patient's readiness for discharge and actual discharge time does exist. (2)

This is similar to study done by **Dere et al** found no difference regarding end of surgery and actual discharge. (17)

In contrast, **Waffa G et al** observed recovery time was significantly prolonged in the dexmedetomidine/fentanyl group compared with midazolam/fentanyl group. They have used dexmedetomidine bolus plus maintenance infusion throughout ESWL whereas midazolam was given as bolus followed by saline infusion. (16)

Side effects

17.5 % patients had nausea & 10 % had vomiting in midazolam group as compare to 7.5 % & 5 % in dexmedetomidine group. This is similar to study done by **Murat Gunduz et al** nausea/vomiting (3.2 % vs. 4.7%; p = 0.02). (19)

This is because total dose of nalbuphine used significant more in midazolam which is self explanatory.

We have already discussed respiratory side effects previously.

Limitations

- Visual analogue score (VAS) like pain score was not used.
- Use of Modified Ramsay sedation score in this study as an endpoint for administering study drugs as opposed to bispectral index. This was done because bispectral index is not a standard monitor during MAC and is not readily available in all institutions. One could also argue that the dose of study drug were not comparable: however, as both drugs were titrated to a predefined endpoint (M-RSS 3), it is unlikely that was an issue as far as study outcomes were concerned. (2)
- There are no published studies that compare the dose-response relationships of dexmedetomidine and midazolam.
- The lack of well defined criteria for determining urologist's degree of satisfaction.

Summary And Conclusion

We have done "Comparative study of nalbuphine /dexmedetomidine versus nalbuphine/midazolam for extra corporeal shock wave lithotripsy (ESWL) in adults". It was conducted in 80 patients of 18-60 years with ASA physical status I-II. They were randomly divided into two groups of 40 patients each.

During perioperative period hemodynamic, respiratory parameters, Ramsay sedation score, modified Aldrete score, need of rescue analgesia and side effects were observed. We concluded that

- No statistically significant differences in demographic data, duration of procedure and anaesthesia found between two groups.

- There was statistically significant reduction of HR in Group-D as compared to Group-M (p value < 0.01). Which did not require any treatment.
- No statistically significant changes in systolic and diastolic blood pressure between two groups.
- No statistically significant changes in oxygen saturation between two groups in intra-operative period. But five patient required oxygen supplementation via mask in spite of nasal canula in recovery period.
- Intraoperative sedation score (Modified Ramsay Score) was higher in group D as compared to group M up to 45 min. But it is higher in group M at 60 and 120 min. (p value < 0.01)
- Recovery score (Modified Aldrete score) at 60 minutes was statically significant in group-D as compared M (7.84 ± 0.37 vs 7.10 ± 0.30).
- Need of rescue drug (nalbuphine) was significantly lower in group D (12.5% vs 55% patients, p value < 0.01)
- Post-operative side effects like nausea, vomiting and respiratory depression were higher in group M as compared to group D but it was statistically insignificant (p value > 0.05).

Conclusion

We found that both dexmedetomidine-nalbuphine and midazolam-nalbuphine combinations had satisfactory sedative and analgesic effects. But, dexmedetomidine has better hemodynamic and respiratory stability, faster recovery and less need of rescue drug as compared to midazolam. So we concluded that combination of dexmedetomidine and nalbuphine may be a better alternative than combination of midazolam and nalbuphine in the adult patients undergoing ESWL.

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