

COMBINED DEXAMETHASONE AND MIDAZOLAM PRE-MEDICATION FOR POST-OPERATIVE PAIN CONTROL AMONG PATIENTS UNDERGOING SPINE SURGERY IN GENERAL ANESTHESIATabish Hussain^{*1,2}, Asifa Anwar Mir², Vijay Parikh¹, Jawad Zahir³¹Ex-Consultant Anesthesia, Department of Anesthesia & ICU, Noor Specialist Hospital, Manama, Kingdom of Bahrain.²Onco-Anesthetist, Department of Anesthesia, Sultan Qaboos Comprehensive Cancer Care & Research Center, Muscat, Sultanate of Oman.³Department of Anesthesia, Intensive Care and Pain Medicine, Holy Family Hospital, Rawalpindi Medical College, Rawalpindi, Pakistan.***Corresponding Author: Dr. Tabish Hussain**

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ABSTRACT

Introduction: There are various medicines and techniques available for prevention and treatment of post operative pain. Combination of various medicines and adjuvant therapy as multimodal analgesia has recently evolved as the main stay of pain treatment. The aim of this study was to determine the score and intensity of pain in the postoperative period while using Dexamethasone and Midazolam combination as pre-medication among patients undergoing general anesthesia for Spine Surgery by comparing with controls. **Methods:** The study was conducted at Department of Anesthesiology, Noor Specialist Hospital, Manama, Kingdom of Bahrain from 1st March 2021 to 30th Aug 2021 over a period of 6 months. The study design was a randomized control trial. A total of 50 patients undergoing open spine surgery were enrolled in the study. Patients were randomly divided in group A and B by consecutive non probability lottery method. Group A received 0.1 mg/Kg Midazolam oral 2 hour before surgery combined with 0.1mg/Kg Dexamethasone Intravenous (IV) and Group B were taken as controls. Post operative pain was measured by visual analog scale (VAS) in terms of pain scores at 2 hours postoperatively after the arrival of patient in the post-anaesthesia care unit (PACU). SPSS version 17.0 was used to analyze the data. **Results:** A total of 50 patients were included in the study. There were 25 patients in each group. With respect to individual visual analogue pain scores, there were 14 patients in group A who did not experienced any post operative pain in comparison to 4 patients in group B. Similarly there were 3 patients in group A, who reported a pain score of 1 where as 8 patients in group B had a VAP score of 1. There were 2 patients in group A and 7 patients in group B with VAP score of 2. For VAP score of 3, there were 2 patients in group A and 2 patients from group B. For a VAP score of 4, there were 2 patient in group A and 2 patients in group B. Two patients in both group A and group B experienced a VAP score of 5. All this data was significant with chi square p value of 0.05. **Conclusion:** In conclusion, oral Midazolam premedication in combination with injection Dexamethasone administered 2 hours before the spine surgery was effective in reducing postoperative pain. Further studies for evaluation of side effects, different dosing schedules and at different time intervals post operatively for both rest and dynamic pain are needed.

KEYWORDS: Spine Surgery, Midazolam, Dexamethasone, Pre-Medication, Postoperative Pain, General Anesthesia.

INTRODUCTION

Pain is the most common and generalized postoperative complaints after major surgical procedures.^[1,2,3] It can contribute significantly towards the enhanced recovery after surgery and prognosis of surgery success. The postoperative pain control has a direct relationship with postoperative morbidity, reflecting importance of its on time and adequate management.^[2,3,4]

Persistent pain can lead to various metabolic disturbances along with neuro-endocrine stress activation. Postoperative pain is involved in creating complications by increasing circulating level of catecholamines and systemic vascular resistance, thus putting the patients on increased risks of having multiple complications like stroke and myocardial infarction.^[5,6] In addition, it increases the number of days in hospital stay, which in turn cause burden over economic as well

as healthcare infrastructure. Various research centers are working efficiently to control this segment of surgery for the successful outcome with least complications.^[7,8] However, the control of pain has been given less priority in the as reflected by number of health care programs conducted for pain education and its funding resources.^[9] Multiple hazards have been linked in not controlling the pain timely. Early post operative pain can decrease early ambulation, decrease the return of bowel function and be a major problem in acceptance of early discharge by patients.^[10,11]

The physiological consequences of post-operative pain can delay or impair postoperative recovery and increase the economic cost of surgery as a result of the longer period of hospitalization. Inadequate post-operative pain control may also lead to the development of chronic pain after surgery. Thus attenuation of early post operative pain remains an important concern for medical personal especially the anaesthetist.^[12]

Pain after major surgeries, especially spine surgery is a common complaint.^[13,14] Various analgesics have already been tried for the control of postoperative pain among these patients ranging from simple non-steroidal anti-inflammatory drugs (NSAIDs) to strong opioids, but none of them is specific and the adequate control of such pain is only possible with multi-modal approach. Some recent studies have shown that use of combined Midazolam and Dexamethasone as premedication can effectively control the postoperative pain and consumption of rescue analgesic medications after surgical procedure.^[12,13,14,15]

A variety of post operative anesthetic strategies ranging from simple analgesic agents administered orally to nerve blocks to combat the pain has been sought.^[16,17,18] A simpler strategy of preemptive analgesic agent may be more acceptable for both anesthetist and patients as a reliable pain relief technique.^[7,8,14,15] Preemptive analgesia is defined as an antinociceptive treatment that prevents establishment of altered central processing of afferent input from injuries.^[12,13,14]

This can effectively prevent earlier onset of the pain than that of the preventive administration of the drugs after surgical procedures, but it was controversial whether preemptive or preventive analgesia should be used to describe the difference between the two analgesic techniques.^[6,7,8]

Midazolam is a benzodiazepine used for anxiety reduction before surgery. It is commonly used as a premedication. Dexamethasone is a steroid used for multiple purposes. Usually used as part of anti-emetic measure. Combination can prove beneficial effects in terms of anxiolysis, anti emesis and reduction of inflammatory response.^[11,12,16,17] Post-Op analgesia have been reported by some studies. But none of the study has ever evaluated the role of combination pre-medication

therapy in control of post-operative pain after spine surgery in Bahrain. The purpose of this study was to evaluate the effectiveness of Combined Midazolam-Dexamethasone premedication for the control of post-operative pain among patients undergoing Spinal surgeries under General Anesthesia.

METHODS

The study was conducted at Department of Anesthesiology, Noor Specialist Hospital, Manama, Bahrain over a period of 6 months from 1st Mar 2021 to 30th Aug 2021. The study design was a randomized control trial. 50 patients undergoing open spine surgery were enrolled in the study. Patients were randomly divided in group A and B by consecutive non probability lottery method. SPSS version 17.0 was used to analyze the data.

Inclusion criteria:

1. ASA – I (normal healthy patient), II (mild systemic disease with no functional limitation).
2. Age: Adults, 20-50 years.
3. Elective surgery (Spine Surgery-Open Tech)-based on evidence from MRI-CT Radiological Studies.

Exclusion criteria:

1. Patient with concomitant co-morbid conditions like diabetes mellitus, hypertension, malignancy, pulmonary, hepatic or renal diseases.
2. Contraindications for using Midazolam and Dexamethasone (Allergic reactions/hypersensitivity).
3. Patients already taking Benzodiazepines or Steroids.
4. Contraindication to General Anaesthesia.
5. Obesity BMI > 35.
6. Failed Back Surgery Syndrome
7. Chronic Post-Surgical Pain Syndrome
8. Diagnosed Fibromyalgia, Muscle Dystrophies, Polymyalgia Rheumatica.
9. Chronic Neuropathic Pain
10. Repeat Surgeries/Re-Do surgeries.

DATA COLLECTING PROCEDURE

A total of 50 patients were studied in the prospective manner. 25 patients were recruited in each group according to the selection criteria. All patients were assessed a day before surgery (at least 8 hours before surgery as preoperative anaesthesia fitness procedure) and written informed consent was taken. Patients were prepared by overnight fasting. Patients were randomly divided in group A and B by consecutive non probability lottery method. Group A received 0.1mg/Kg Midazolam Tablet Oral plus 0.1mg/Kg Injection Dexamethasone Intravenous (IV) 2 hours before surgery while Group B were taken as controls without receiving any drugs except tablet Midazolam 0.1mg/Kg oral as part of anxiolysis.

Intravascular access with two 18G cannula was established in the pre-operative room before arriving in

the operation theater. After arrival in Operation Theater, monitoring included Electrocardiography, pulse oximeter, noninvasive blood pressure will be attached and base line heart rate and blood pressure will be noted. Each group was preloaded with 10ml/kg crystalloids. Patients were pre-oxygenated for 3 minutes via face mask.

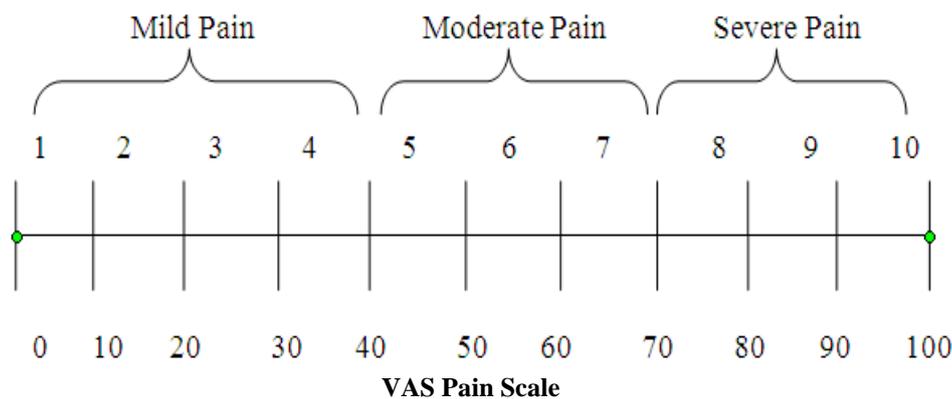
General anesthesia was administered with 1.5ug/Kg Fentanyl, 0.2mg Glycopyrrolate, followed by 2 mg/kg Propofol, and 0.1 mg/kg Cis-Atracurium for induction and intubation respectively. After intubation, anaesthesia was maintained with 60% Air, 40% Oxygen and 1.0 - 1.2% Isoflorane. Injection Atracurium 1/5th of the induction dose was repeated every 30-40 minutes to maintain muscle relaxation. Vitals monitoring and appropriate interventions were done accordingly at regular intervals of 5 minutes.

Patients were reversed with injection Neostigmine 2.5 mg and 400 ug Glycopyrrolate after completion of

surgery. All the anesthetic administration was performed by the Specialist level anesthetist who was blinded about the drug so as to eliminate bias factor.

At the end of surgery, patients were extubated and shifted to the post-anesthesia care unit (PACU) for 24 hours monitoring, where the control of post-operative pain was strictly monitored. The pain score was measured at 2 hours postoperatively by the another anesthetist.

The post-operative pain was assessed by using Visual Analog scale (VAS) graded no pain (0cm/0mm) to worst unbearable pain (10cm/100mm). Patients complaining moderate to severe pain (pain score 5 or above) in either group at 2 hours or even before postoperatively were given rescue analgesic (Tramadol 100 mg or Ketorolac 30 mg slow intravenous injection), and the pain score measured at that point (Time interval) was considered end point for that patient regardless of the fact that 2 hours have been passed.



RESULTS

A total of 50 patients were included in the study. There were 25 patients in each group. The baseline parameters of all study participants are given in Table 1. Mean age of study patients was 42.65 ± 3.15 years. The mean weight (kg), height (m) and BMI (kg/m^2) of all study

patients were 68.20 ± 6.25 , 1.49 ± 0.36 and 26.23 ± 3.65 respectively. The mean duration of surgery was 110.50 ± 8.90 min. Overall 24 (48%) patients complained of mild pain (Pain Score 1,2 or 3) at 2hrs post operatively where as only 08 (16%) patients had moderate pain. There were no patients with severe post operative pain at 2hrs.

Table 1: Baseline Parameters Of All Study Participants.

Parameter		Mean \pm SD
Age		42.65 ± 3.15
Weight		68.20 ± 6.25
Height		1.49 ± 0.36
BMI		26.23 ± 3.65
Duration of Surgery		110.50 ± 8.90
No. of patients (Frequency)		
Gender	Male	28 (56%)
	Female	22 (44%)
Pain Score	0	18 (36%)
	1	11 (22%)
	2	09 (18%)
	3	04 (8%)
	4	04 (8%)
	5	04 (8%)
Pain Category	Mild (VAP Score 1,2,3)	24 (48%)

	Moderate (VAP Score 4,5)	08(16%)
	Severe (VAP Score >5)	0 (0%)

Overall 18 (36%) patients experienced no pain 2hrs after surgery. The VAP score of 1, 2 and 3 were reported by 11 (22%), 9 (18.0%), 4 (8%) patients respectively. Only 08 (16%) patients reported a VAP score of 4 and 5 (4 in each group). No patient reported VAP score beyond 5. The corresponding pain categories were mild in 24 (48%) and moderate in 8(16%) patients. No patients reported severe post operative pain.

The baseline comparison of the two groups is given in Table 2. The two groups i.e. Group A and Group B were comparable with respect to baseline values in terms of gender, mean age (yrs), mean weight (kg), mean height (m) and mean BMI (kg/m²). Similarly the mean duration of procedure was also not significantly different between the two groups. However, the mean pain score was significantly different between the two groups at 2hrs post operatively (p=0.0001).

Table 2: Baseline Comparison Of The Two Groups.

Gender	Group A	Group B	P value
Males	13 (52%)	15 (60%)	0.15
Females	12 (48%)	10 (40%)	
Age (yrs)	40.85 ± 3.67	41.10 ± 2.95	0.52
Weight (kg)	66.74 ± 3.20	64.87 ± 5.22	0.25
Height (m)	1.56 ± 0.08	1.54 ± 0.15	0.80
BMI (kg/m ²)	26.45 ± 2.50	26.22 ± 3.60	0.52
Duration of Surgery (min)	110.53 ± 8.69	109.65 ± 3.29	0.82
Pain Score at 2hrs	1.45 ± 0.75	3.15 ± 0.25	0.0001

Table 3: Vap Score In Group A (n=25).

VAP SCORE	Frequency (Percentages)
0	14 (56%)
1	3 (12%)
2	2 (8%)
3	2 (8%)
4	2 (8%)
5	2 (8%)

Table 4: Vap Category In Group A.

VAP Category	No of patients (%)
No pain	14(56%)
Mild	7 (28%)
Moderate	4 (16%)
Severe	0

Table 5: Vap Score In Group B. (n=25)

VAP SCORE	Frequency (Percentages)
0	04 (16%)
1	08(32%)
2	07(28%)
3	02(8%)
4	02 (8%)
5	02 (8%)

Table 6: Vap Categories In Group B.

VAP Category	
No pain	04 (16%)
Mild	17 (68%)
Moderate	04 (16%)
Severe	0

Table 7: Comparison Of Different Visual Analogue Score.

Visual Analogue Scale Pain Category	Group A	Group B
0	14(56%)	04 (16%)
1	03 (12%)	08(32%)
2	02 (8%)	07(28%)
3	02 (8%)	02 (8%)
4	02 (8%)	02(8%)
5	02 (8%)	02(8%)
Chi square: p= 0.0001		

Table 8: Comparison Of Different Pain Categories.

Visual Analogue Scale Pain Category	Group A	Group B
NO PAIN	14 (56%)	04 (16%)
MILD	07 (28%)	17 (68%)
MODERATE	04 (16%)	04 (16%)
SEVERE	0	0
Chi square p value 0.004		

DISCUSSION

Pain is thought to be inadequately treated in one-half of all surgical procedures. Early postoperative pain is the most common complaint after elective spine surgery.^[18]

The combination approach simulates the multimodal technique for the control of pain in the post operative surgical period. The Dexamethasone has been involved not only in reducing the mediators of inflammation, but also the mediators involved in the pain pathways at spinal and supraspinal levels.^[19]

The cost effectiveness of simple regimens in the control of pain can help alleviate the problem of expense in managing immediate post operative pain. Spinal surgery has been associated with significant inflammation and pain with reflex spasm in the after periods leading to limited mobility.^[20] The limited mobilization can cause severe hazards including deep venous thrombosis and long term disability. Immediate management of pain at this stage can effectively solve these problems.^[21]

CONCLUSIONS

In conclusion, combination of Dexamethasone and Midazolam as premedication administered 2 hours before surgery was effective in reducing postoperative pain in patients undergoing spine surgery. Further studies for evaluation of side effects, different dosing schedules and at different time intervals may help out to explore more significance for the post op pain management.

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