Morphine-Dexmedetomidine Mixture Versus Morphine Alone for Postoperative Analgesia

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ABSTRACT

Objective: To compare the quality of postoperative analgesia between intraoperative administration of Morphine-Dexmedetomidine versus Morphine alone

Methods: A total of 82 adults of both gender, aged between 42 and 71 years. All according to (American Society of Anesthesiologists) class I-II were assigned for various elective abdominal operations under general balanced anesthesia at King Hussein Medical Center during the period from January to October 2010. Patients were divided into two groups. Group D (n=41) received intravenous Morphine sulphate 0.1 mg/kg and Dexmedetomidine (primary loading dose of 1 mcg/kg over 10 min. followed by 0.4 mcg/kg/h) and group M (n=41) received intravenous Morphine sulphate 0.1 mg/kg, both given half an hour before the completion of surgery. Postoperative analgesia quality was evaluated using Visual Analog Scale and Morphine consumption in the recovery room for the first 1 hour then in the surgical ward for the next 24 hours.

Results: Median pain severity score was 3 in group D and 6 in group M during the first postoperative 60 minutes and 2 minutes in group D, 3 minutes in group M after 24 hours. About 83% of patients in group M needed additional Morphine compared to 26.8% of patients in group D ($P<0.05$) in the recovery room to attain equivalent analgesia.

Conclusion: Intraoperative administration of intravenous Morphine-Dexmedetomidine mixture produces higher postoperative analgesia than Morphine alone.

Key words: Analgesia, Dexmedetomidine, Morphine, Postoperative.

JRMS March 2012; 19(1): 15-19

Introduction

Pain is not just a sensory modality but is an experience. It is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Selection of analgesic technique is generally based on 3 factors: the patient, the procedure and the setting (inpatient versus outpatient). Improving postoperative analgesia is crucial to recovery from surgery and anesthesia.[1] Alfa 2 adrenreceptor agonists have been used widely in veterinary anesthetic practice for many years. Their properties of sedation, anxiolysis and analgesia have been recognized as potentially beneficial in humans, but they have not found a place in routine clinical practice previously. Alfa 2 adrenergic receptors are involved in the regulation of the release of the neurotransmitter norepinephrine. These receptors were initially classified anatomically as presynaptic, but alfa2 adrenoreceptors are also found postsynaptically and

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Manuscript received January 22, 2011. Accepted March 24, 2011

extrasynaptically. Alfa 2 adrenoreceptors are located peripherally and centrally, with the centrally mediated effects of particular relevance in anesthesia. They has analgesic properties. Descending fibers from the locus caeruleus decrease nociceptive transmission at the spinal level. In addition, Alfa 2 adrenoreceptors located in primary sensory neurons and the dorsal horn of the spinal cord. Many ligands at alfa 2 adrenoreceptors are substituted imidazoles.[2] Medetomidine is the prototype of the newer selective alfa 2 agonists. Its active ingredient, the D-stereoisomer Dexmedetomidine with the alfa2:alfa1 selectivity Ratio of 1600:1. It has a MAC (Minimal Alveolar concentration)-sparing effect.[3] Dexmedetomidine has insignificant alfa 1 agonism and is a potent alfa 2 adrenreceptor agonist [2] with analgesia sparing characteristic [3] used for postoperative analgesia after major painful operations.[4] When Dexmedetomidine is given with Morphine it has been shown to improve analgesia in comparison to Morphine alone.[3] It has sedative, analgesic and sympatholytic effects that blunt many of the cardiovascular responses seen perioperatively. When used intraoperatively it reduces intravenous and volatile anesthetic needs. When used postoperatively, it reduces concurrent analgesic and sedative needs in the recovery room.[5]

This study was conducted compare the quality of postoperative analgesia between intraoperative administration of Morphine-dexmedetomidine versus Morphine alone.

Methods

A total of 82 patients of both genders, ASA I-II, aged 42-71 years, assigned for various elective inpatient abdominal general operations under general balanced anesthesia at King Hussein medical centre during the period from January to October 2010, after obtaining the Jordanian Royal Medical Services Ethical Committee Approval. Patients with any type of heart block or receiving other alfa 2 agonists during the previous preoperative 30 days were excluded. Induction of general anesthesia was achieved using intravenous fentanyl 2 mcg/kg, propofol 2 mg/kg and atracurium 0.5 mg/kg. Anesthesia was maintained using atracurium 0.1 mg/kg, remifentanil 0.1-0.5 mic/kg/min and isoflurane 1-1.5%. Patients were monitored at least by ECG, non-invasive blood pressure, oxygen saturation and end tidal CO2, Half an hour before the expected completion of surgery, patients were randomized by drawing envelopes indicating the groups by a letter D or M written on a paper inside, to receive intravenous Morphine sulphate 0.1mg/kg and Dexmedetomidine (Precedex, Dexmedetomidine Hcl inj equivalent to 100 mcg/ml, Hospira, Inc. Lake forest, IL, USA) (primary loading dose of 1 mcg/kg over 10 min. followed by 0.4 mcg/kg/h) group D (n=41) or Morphine sulphate alone 0.1mg/kg group M (n=41).

In the recovery room, for the first postoperative hour, patients were assessed at 10 min. intervals for postoperative analgesia quality using Visual Analog Scale (VAS) score which is used to measure the amount of pain a patient feels. The VASof pain is usually a 100 mm-long horizontal line, which may contain word descriptors at each indicated by the patient.

In the surgical ward patients were evaluated at 4 hours intervals for the next postoperative 24 hours. Patients and nursing team preparing drugs and collecting data were blinded to the investigation.

Postoperative intravenous Morphine 2mg at 10 min interval was administered if VAS score for pain was equal or more than 4 at any 10 min .interval evaluation in the recovery room or at any 4h interval assessment in the surgical ward. Patient satisfaction was collected (yes/no) at the end of the first postoperative 24 hours. Total Morphine needs and pain severity were recorded within the first postoperative 24 hours.

Statistics

Data were presented as means and analyzed using student's t test. Variables and satisfaction were analyzed using Chi square. P value was considered significant if it was <0.05.Pain scores were analyzed with Mann-Whitney test.

Results

Groups were similar regarding patient characteristics, type and duration of surgery and intraoperative use of anesthetics (Table I). The study included a total of 88 patients of whom 6 patients were excluded, four patients had bradycardia preoperatively and 2 patients were transferred intubated to the ICU postoperatively. Weight of all subjects ranged from 60 to 95 kg.

Median VAS score for group D and group M were 3 and 6 respectively during the first postoperative 60min. while it was 2 and 4 respectively at the end of the first postoperative 24 hours (Table II). Thirty-four patients (82.9%) in group M needed

Table I: Demographic and intraoperative anesthetics characteristics (frequency, mean, median and P value of the study group

	Group D	Group M	P value
Number	41	41	> 0.05
Age (yr)			
42-52	21	18	> 0.05
53-63	11	15	> 0.05
64-71	9	8	> 0.05
Gender			
M	20	19	> 0.05
F	21	22	> 0.05
ASA			
I	15	18	
II	26	23	
Type of surgery			
Incisional hernia	9	8	
Whipple	5	2	
Gastrojejunostomy	1	1	
Liver hemangioma	3		
Open chole	1	2	
Laparotomy (diagnostic)	5	4	
Gastric outlet obstruction	1		
Liver hydatid cyst	5	5	
Closure colostomy	2		
Gastrectomy	2	1	
Reversal Hartmann	2		
Splenectomy	1	2	
Hepaticojejunostomy	1		
Liver resection	2	5	
Gastric band		1	
Ant.resection	1	3	
Sigmoidectomy		2	
Lap.gastric sleeve		1	
Common bile duct surg		2	
Hemicolectomy		1	
Suprarenal mass		1	
Surgery duration (minutes)	119	131	
Intraoperative analgesics			
Fentanyl (mcg)	120-150	120-150	
Dexmedetomidine (mcg)	60-75 and 24-30/h	-------	
Morphine (mg)	6-7.5	6-7.5	

Table II: Visual analog scale score in the recovery room and the surgical ward

	GD	GM
Recovery room (minutes)		
10	4	6
20	4	6
30	3	5
40	3	4
50	3	3
60	2	4
Surgical ward (hrs)		
4	4	4
8	3	4
12	4	4
16	3	3
20	2	3
24	2	3

Table III: Mean value of additional Morphine use in the recovery room and the surgical ward. (Mean)

	GD	GM
Recovery room	4 mg	10 mg
Surgical ward	15 mg	20 mg

Table IV: Analgesic failure and patient satisfaction (number)

	GD	GM
Analgesic failure	0	3
Satisfaction	36	32

significantly more Morphine compared to 11 patients (26.8%) in group D ($P<0.05$) in the recovery room to attain equivalent analgesia. Patients in group D required 4mg while patients in group M required 10 mg of intravenous Morphine sulphate in the recovery room during the first postoperative one hour, this requirement was 15 mg and 20mg respectively in the surgical ward during the first postoperative 24 hours. Group M received double the amount of Morphine than group D in the early postoperative period while the amount of Morphine received was not different significantly between the two groups at 24 hours postoperatively (Table III).

Three patients in Morphine alone group reported failure of analgesia and received other analgesic modality (Table IV). Regarding patient satisfaction, 87.8% of group D and 78.04%of group M reported satisfaction ($P>0.05$). About 63% of patients in group D reported better pain relief in comparison with previous experience while it was 39.02% of patients in group M (Table IV).

Discussion

Agonism at Alfa 2 adrenoreceptors in the spinal cord produces analgesia, so exmedetomidine has analgesic sparing action via central effects in the dorsal horn of the spinal cord.[6] After the primary action of Dexmedetomidine on peripheral alfa 2 receptors, a more gradual central action becomes clear. Dexmedetomidine is a parenteral selective alfa 2 agonist but at higher doses it looses its selectivity and also stimulates Alfa 1 adrenergic receptors. The drug is used for short term (<24 hours) with a terminal half life of 2 hours. Morphine consumption in the first 24 hours after surgery depends on an opioids needs and varies between patients. Intraoperative administration of Dexmedetomidine decreases the postoperative Morphine needs.[7] Our study showed that Morphine-Dexmedetomidine combination can improve analgesia significantly; however, administration of Dexmedetomidine can cause unnecessary sedation. This was not found in our study because the dose of the administered Dexmedetomidine was within the lower range of the recommended 0.2-0.7 mcg/kg/h infusion.[8] The results of our study are similar to another study on patients who were given Morphine and dexmeditomidine by Patient Controlled Analgesia (PCA) after abdominal hysterectomy.[3] We have used direct intravenous method as to find an alternative method in the situation and places in witch the patient is closely observed and can be given the dose immediately in addition we started infusion before the patient recovered from anesthesia. Dexmedetomidine has opioids sparing effect as shown in other studies[9] also it has been effective in pediatrics patient post tonsillectomy.[10] In the presence of analgesic and sedative actions, it is difficult to differentiate which one is responsible for the decreased Morphine needs, although in our study analgesia effect was more likely to produce Morphine sparing by Dexmedetomidine because sedation was not significant. Enhanced analgesia by Dexmedetomidine is caused by the synergistic analgesic interaction with opioids.[11] decrease of stress and reduction on the affective-motivational component of pain. The administration of intravenous intraoperative Dexmedetomidine-Morphine mixture half an hour before the completion of surgery reduced significantly the early need for postoperative Morphine administration and enhanced the quality of analgesia. Long term use of Dexmedetomidine leads to supersensitisation and upregulation of receptors, with abrupt discontinuation, an acute withdrawal syndrome can occur. Because of the increased affinity of Dexmedetomidine for the alfa 2 receptors, this syndrome may manifest only 48 hours of Dexmedetomidine use when drug is discontinued. [5]

Conclusion

Intraoperative intravenous Morphine-Dexmedetomidine mixture administration produces higher postoperative analgesia than Morphine alone

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