The analgesic and sedative properties of dexmedetomidine infusion after uvulopalatopharyngoplasty

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ABSTRACT

Background: Dexmedetomidine is an alpha$_2$ - adrenergic agonist with **se**dative and analgesic properties. This study aimed to investigate if the use of continuous dexmedetomidine infusion with i.v. morphine patient-controlled analgesia (PCA) could improve postoperative analgesia while reducing opioid consumption and opioid-related side effects.

Materials & methods: In this prospective randomized, double-blinded, controlled study, 24 patients with obstructive sleep apnea syndrome undergoing uvulopalatopharyngoplasty were assigned to two groups. Group D received a loading dose of dexmedetomidine 1µg kg⁻¹ i.v., 30 min before the anticipated end of surgery, followed by a continuous infusion at a rate of 0.6 µg kg⁻¹ hr⁻¹ for 24 hr. Group P received a volume-matched bolus and infusion of placebo. In both groups, postoperative pain was initially controlled by i.v. morphine titration and then PCA with morphine. Cumulative PCA morphine consumption, pain intensities, sedation scores, cardiovascular and respiratory variables and narcotic-related adverse effects were recorded for 48 h after operation.

Results: Extubation time was significantly prolonged in dexmedetomidine group (16±7 vs. 11±6 min p=0.074) in the placebo group. Visual analogue scale scores were significantly greater during the first 2h after tracheal extubation in the placebo group than in the dexmedetomidine group. The time to first analgesic request was significantly longer in the dexmedetomidine group than in the placebo group (21±11 vs. 9±4min; p=0.002). Compared with group P, patients in group D required 52.7% less morphine by PCA during the first 24h postoperative period, whereas levels of sedation were similar between the 2 groups at each observational time point. Fewer patients in group D experienced nausea and vomiting than those in group P (P< 0.05). There was no bradycardia, hypotension, or respiratory depression. Continuous dexmedetomidine infusion may be a useful anesthetic adjuvant for patients who are susceptible to narcotic-induced respiratory depression.

Conclusion: Continuous infusion of dexmedetomidine for pain relief after uvulopalatopharyngoplasty significantly reduces the amount of PCA morphine used by the patients postoperatively without affecting their ventilatory parameters and was associated with fewer morphine-related side effects. This novel drug could become a useful anesthetic adjuvant for patients with obstructive sleep apnea who are susceptible to narcotic-induced respiratory depression.

Key words:*Dexmedetomidine; Uvulopalatophayngoplasty; Morphine; Patient controlled analgesia.*

Introduction

Obstructive sleep apnea (OSA) is a syndrome characterized by periodic, partial or complete upper airway obstruction resulting in the disruption of sleep and hypoxemia with potentially serious physiologic consequences. It has been estimated to affect 4% of men and 2% of women in middle age and has been identified as a major health problem (Kim & Lee 2006).

Uvulopalatopharyngoplasty (uppp) is still the most commonly performed surgical procedure for the treatment of OSA (Zodpe *et al.,* 2006). it is safe and effective (Lundkvist *et al.,* 2009) Pain, which is

caused by irritation of the nerve endings, inflammation, and pharyngeal muscle spasm, is a major complication of uppp and continues until mucosal recovery is complete(Zodpe *et al.,* 2006) (Patrocinio *et al.*, 2007).The treatment of post operative pain after uppp; which is usually severe during the first 24 hours after surgery presents a challenge(Nikanne *et al.,*2003) . Opioids can cause sedation and respiratory depression. Nonsteroidal anti-inflammatory drugs can increase postoperative bleeding (Virtaniemi *et al.,* 2009). Thus, a drug that has few or no adverse effect, does not increase postoperative bleeding, and provides complete postoperative analgesia, or at least reduces the amount of analgesic used, is still needed to reduce the complications related to analgesia.

Dexmedetomidine is an α2 adrenoreceptor agonist that has a unique mechanism of action. The agent induces sedation and anxiolysis via receptors in the locus ceruleus, analgesia via receptors in the spinal cord and attenuation of the stress response without significant respiratory depression (Riker *et al.*, 2009). Given its beneficial sedative and analgesic properties and limited adverse effect profile, dexmedetomidine may be useful in the postoperative period for patients with OSA who are susceptible to narcotic-induced respiratory depression and having surgical procedures that are associated with significant pain (Arain *et al.,*2004) &(Hofer *et al.,* 2005).

The aim of this study was to investigate whether continuous dexmedetomidine infusion provides effective analgesia and reduces the need for postoperative self-administration of i.v. morphine and to assess if decreased morphine consumption is associated with a reduction in sedation, nausea and vomiting. Elimination of these adverse effects is important to facilitate recovery from surgery.

Method

This study took place in king Abdulaziz Navel Base Hospital, Jubail, KSA, from July 2007 to January 2009. The study was approved by the Hospital Ethics Committee and written informed consent was obtained from each patient. We studied 24 ASA I-II patients, aged 38-55 years with OSA and scheduled for uppp. Inclusion criteria include history of airway obstruction during sleep, frequent loud snoring and arousal from sleep. Physical examination was done to all patients for tonsillar size, palate tongue position and degree of hypertrophy of the lateral sides of the oropharynx. All patients underwent fibrooptic endoscopy with Muller's manouver, nasoendoscopy and Polysomnography and positive diagnosis of OSA was obtained before surgery. The apnea hypopnea index ranges from 20-40. The surgical procedure included tonsillectomy and resection of excess fat and mucosa in the soft palate including uvula with preservation of palpable musculature. Several sutures approximated the anterior and posterior pillars.

Patients were excluded if there was a history of ischemic heart disease, conduction disturbance, long term use of certain medications (β-blockers, analgesics, sedatives or tricyclic antidepressant), if they had impaired renal, hepatic or pulmonary function, a history of allergy to opioids or any other drug used in the study, contraindications to the self-administration of opioid (i.e. inability to understand the patient-controlled analgesia (PCA) system).

The evening before surgery, patients were instructed in the use of a 10-cm visual analogue scale (VAS) on which 0-cm represented no pain and 10-cm the worst imaginable pain. The use of a (PCA) system

(Fresenius vial, Brezins, France) was also explained at this time. No premedication was given and the anesthetic technique was standardized. Heart rate (HR), non invasive mean arterial pressure (MAP) and oxygen saturation (SpO2) were noted before induction and repeated at regular intervals thereafter. A forearm vein was cannulated for administration of anesthetics and Ringer's lactate solution was infused at a rate of 10 ml kg^{-1} h^{-1}. Patients were preoxygenated for 3 min by mask with 100% oxygen. Anesthesia was induced with propofol 2 mg kg^{-1}, fentanyl 1µg kg^{-1} and atracurium 0.5mg kg^{-1} to facilitate orotracheal intubation. After tracheal intubation, the lungs were ventilated to maintain normocapnia (end-tidal carbon dioxide pressure (ETCo2) between 4.5 and 5.6 kPa) with 1-2% sevoflurane in 60% nitrous oxide and 40% oxygen for maintenance of anesthesia. Supplemental boluses of atracrium 0.1mg kg^{-1} were administrated as required to maintain muscle relaxation during surgery.

Randomization was carried out by computer-generated codes maintained in sequentially numbered, opaque envelopes, which were opened before induction of anesthesia. Patients were allocated randomly to one of two groups, 30 min before the anticipated end of surgery. Group D (Dexmedetomidine group) received a loading dose of dexmedetomidine 1µg kg^{-1} in 100 ml of normal saline (Precedex, Abbott Laboratories Inc., Abbott Park, IL,USA) over 20 min followed by an infusion of 0.6µg kg^{-1} h^{-1}. This rate was maintained uninterrupted for 24 h (until the end of the first post operative day). Group P (placebo group) received the same volume of normal saline as a loading dose followed by a continuous saline infusion.

Blinding was carried out by a nurse, not involved in the data collection, who made up syringes and infusions of dexmedetomidine and normal saline under sterile conditions such that they appeared identical.

At the end of surgery, residual neuromuscular block was antagonized with atropine 20 µg kg^{-1} and neostigmine 50 µg kg^{-1}. The trachea was extubated after recovery of adequate spontaneous ventilation (adequate respiratory rate and good oxygenation) with good muscle strength as evidenced by sustained head-lift test. Extubation time was noted. All patients were transferred to the post anesthesia care unit(PACU) where they were monitored and received oxygen via a face mask at 6L/min for 1 h and then at 4 L/min until discharge from the PACU, 4 h after extubation.

Initially, pain was controlled only by titration of i.v. morphine administered by nurses who were blinded to the treatment group. Pain intensity was assessed by the patients during swallowing using a VAS. The first analgesic medication was given when the VAS reached 4cm after extubation. Intravenous morphine 2 mg at 10 min interval was titrated until the VAS decreased to < 4 cm. Morphine consumption at this time was recorded. When the VAS was < 4 cm after titration, patients had access to a PCA device. This device was set to deliver morphine 1mg as an i.v. bolus with a lockout interval of 5min, without background infusion. This PCA regimen was continued as long as needed in the PACU and the surgical ward. Patients were encouraged to push the analgesic-demand button when they experienced pain, and to repeat until they felt pain relief. Lornoxicam 8mg i.v. was used as (rescue analgesic) if pain scores remained higher than 4. The cumulative doses of morphine

given by PCA were recorded at 12, 24, 36, 48 h postoperatively.

Pain scores were recorded using a VAS scale every 30 min during the first 2 h, every 60 min during the next 10 h and every 4 h during the next 36 h. The time between extubation and the first administration of analgesic medication was recorded.

Arterial blood samples for blood gases analysis were drawn at extubation and every 8h thereafter and when clinically indicated. Respiratory depression was defined as a persistent respiratory rate < 10 bpm, oxygen partial pressure (PaO2) < 9.0 kPa or a carbon dioxide partial pressure (PaCo2) > 7.5 kPa.

The degree of sedation was monitored using a four-point scale (0=awake and alert, 1=drowsy, 2=mostly sleeping, 3=difficult or impossible to awaken).

Sedation scores were recorded at regular intervals after surgery.

The presence of nausea and vomiting was noted using a four-point scale (0=no nausea or vomiting, 1=mild nausea, 2=sever nausea, 3=retching or vomiting).

Patients with a nausea score of 2 or 3 were given an i.v. bolus of metoclopramide 10 mg and ondansteron 4 mg if this was unsuccessful.

Other side effects possibly related to morphine or dexmedetomidine administration (bradycardia, bradypnea, urinary retention, and pruritus) were recorded for each patient. After 24h patients were asked to score their level of satisfaction with their postoperative pain up to that time on a four-point scale (0=totally dissatisfied, 1=moderately dissatisfied, 2=reasonably satisfied, 3=totally satisfied with pain relief).

Statistical analysis was performed using Mann-Whitney U-tests for pain scores, t-tests for parametric data, or chi-square test for categorical data.

Statistical calculations were carried out using computer programs Microsoft Excel version 7(Microsoft corporation, New York, USA) and statistical package for the social science (SPSS INC. Chicago, IL, USA). P<0.05 was considered significant.

Results

Two patients were withdrawn from the study because of endotracheal intubation difficulty. Another patient was excluded from the analysis as he was unable to use the PCA because of sever vomiting and requested alternative analgesia 7h after operation. One more patient was excluded due to sever postoperative bleeding. The remaining 24 patients were studied.

Patient characteristics were similar in the two groups (table1).

Many more males than females were recruited as OSA is more common in males. Postoperative hemodynamic monitoring revealed no significant differences between the two groups. No patient required intervention as a result of cardiovascular problems.

The duration of anesthesia and surgery were similar in the two groups. Extubation time was significantly prolonged in dexmedetomidine group (16 ± 7 min vs. 11 ± 6 min) in the placebo group (p=0.074) (table2).

Figure 1 demonstrates the VAS in the two groups during the first 48 h after surgery. VAS scores were significantly greater during the first 2 h after tracheal extubation in the placebo group (fig1a) and were similar in the two groups thereafter(fig 1b). The mean VAS scores were never > 5 cm in the dexmedetomidine group during the first 2 h after surgery.

The time between extubation and the first

analgesic request in the PACU was significantly longer in the dexmedetomidine group (21± 11 min vs. 9 ± 4 min, p = 0.002) (table2). The cumulative dose of morphine given by nurses in the PACU for titration was significantly greater in the placebo group (21.7 ± 11.1 mg) than in the dexmedetomidine group (9.4 ± 5.2 mg) (p =0.002) (table2). PCA morphine consumption was significantly greater at 12h and 24h after surgery in the placebo group than in the dexmedetomidine group(12h, 34±16.7 and 18.1±10mg, 24h, 65± 29 and 34.3± 16.4 mg respectively, p < 0.05) (Figure2). The cumulative morphine dose used during titration and PCA throughout the study was significantly greater in the placebo group than in the dexmedetomidine group (135.7 ± 37.4 vs. 86.4 ± 26.1 mg) respectively (p = 0.001). In addition, six patients in the placebo group needed rescue analgesia in contrast to only one patient in the dexmedetomidine group (p < 0.05).

The sedation score did not differ significantly between the two groups during the 48h after surgery (table3). There was no difference in the mean respiratory rate and SpO2 at any time between the two groups. One patient in the placebo group experienced a respiratory rate <10 bpm without desaturation below 95% and recovered rapidly without any specific treatment. As patients in the two groups received postoperative oxygen, PaO2 was constantly > 10 kPa at 0, 2, 4 and 6 h after surgery.

Postoperative nausea and vomiting were the most prevalent adverse events. The incidence of nausea and vomiting requiring treatment was significantly reduced in the dexmedetomidine group during the first 24h after surgery (table3), although the severity scores were unchanged. A significantly more patients in the placebo group experienced itching than patients in the dexmedetomidine group (9 vs.3) respectively; p < 0.05). Patient's satisfaction scores were significantly higher in group D (median 4 (range 2-4), compared with 3 (range 1-4) in group p), (p < 0.05).

Table1. Patients characteristics

	Group D (n=12)	Group P (n=12)	P value
Age (Yr)	46.3(9.7)	45.1(9.5)	0.762
Gender (male/female)	11/1	10/2	1.0
ASA (I/II)	5/7	4/8	1.0
Height (Cm)	173.6(6.9)	166.9(5.8)	0.169
Weight (Kg)	98.4(8.7)	96(9.0)	0.514
BMI (Kg.m²)	32.7(3.3)	32(2.9)	0.587
Arterial hypertension (%)	46.8	61.1	0.188
Diabetes mellitus (%)	28.1	24.6	0.808

BMI=body mass index.

Data are presented as mean (SD), absolute number or percentage of patients.

Table2. Duration of anesthesia and surgery, extubation time and postoperative morphine titration

	Group D (n=12)	Group P (n=12)	P value
Duration of anesthesia (min)	96(54)	101(42)	0.802
Duration of surgery (min)	74(43)	78(49)	0.0834
Extubation time (min)	16(7)	11(6)*	0.074
Time to first morphine titration (min)	21(11)	9(4)*	0.002
Morphine given by i.v. titration in PACU (mg)	9.4(5.2)	21.7(11.1)*	0.002

Data are presented as mean (SD). *$p < 0.05$

Table 3. Sedation scores and incidence of nausea and vomiting

Time after surgery (h)	Sedation Scores		Nausea and Vomiting	
	Group D (n=12)	Group P (n=12)	Group D (n=12)	Group P (n=12)
12	2(1-3)	2(0-2)	3	8*
24	1(0-2)	1(0-2)	2	8*
36	1(0-2)	1(0-2)	1	4
48	1(0-2)	1(0-2)	1	4

Data are presented as mean (SD or range) or absolute number. * $p<0.05$
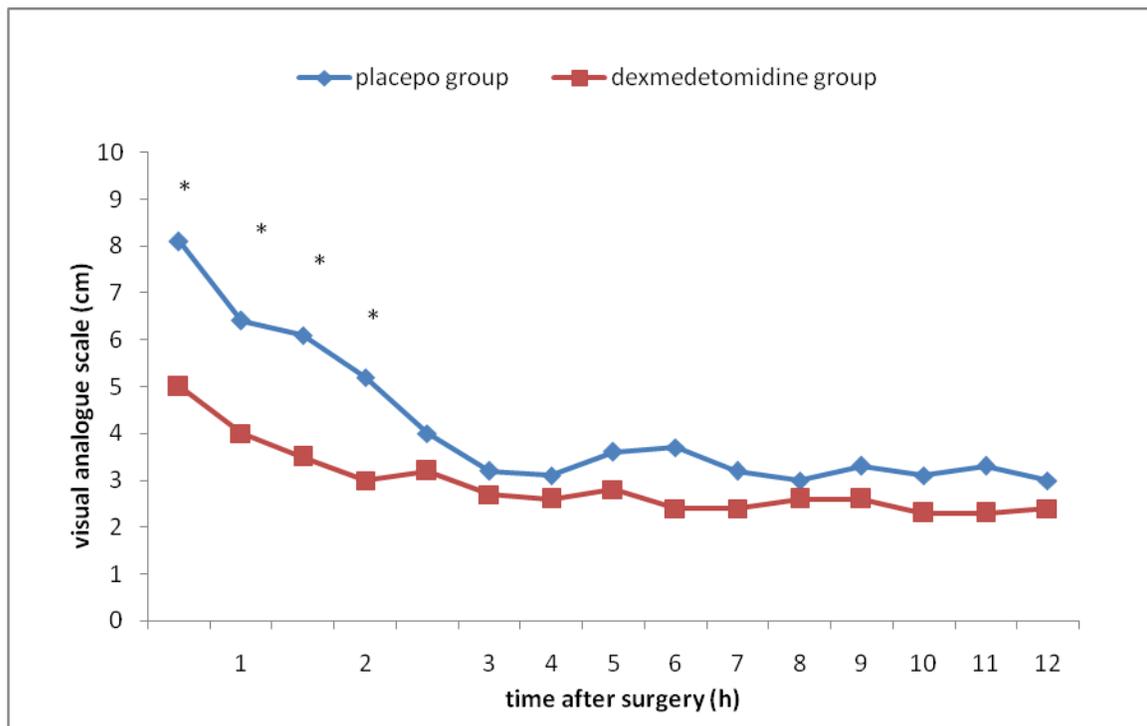
Fig 1a VAS pain scores (0-10 cm) in the two groups during the first 12 h after surgery. Values are mean and SD. Asterisks indicate statistically significant difference between the two groups ($p<0.05$).
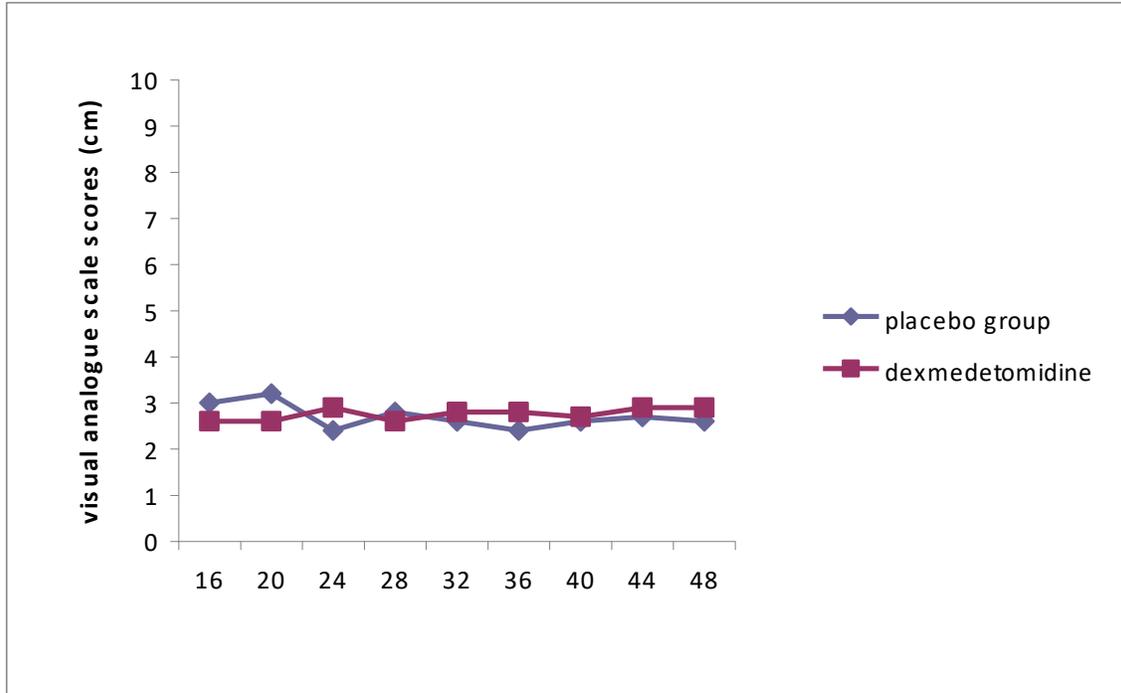
Fig 1b VAS pain scores (0-10 cm) in the two groups 16-48h after surgery. Data are mean and SD.
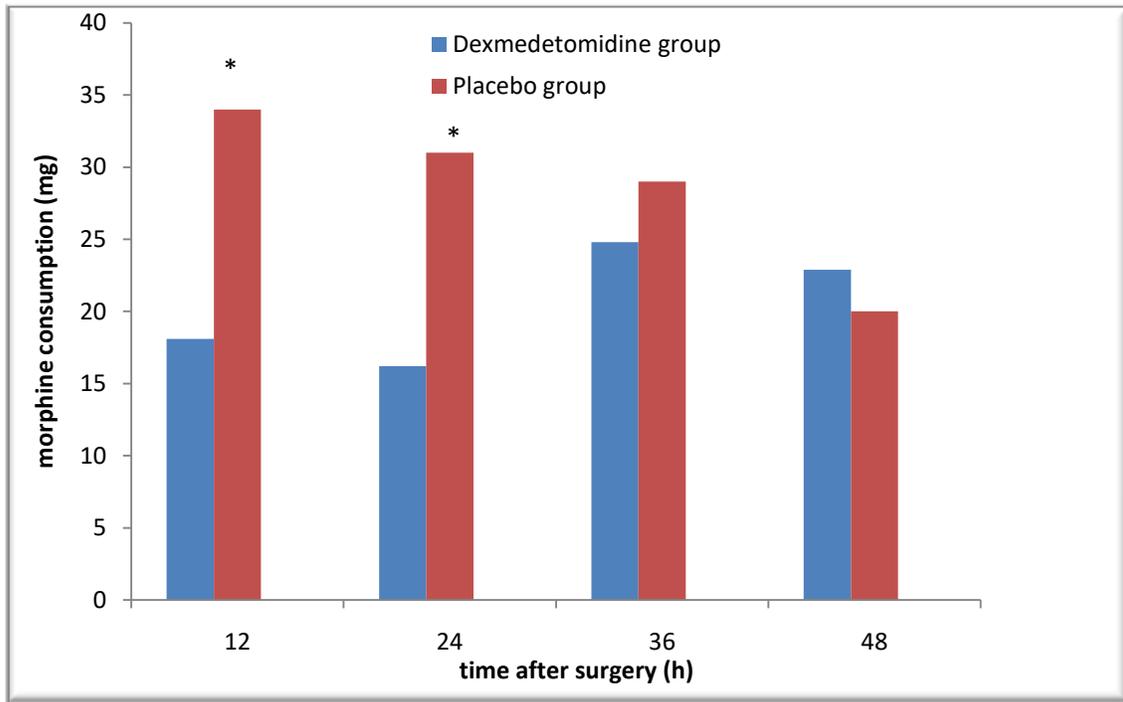

Fig 2 Cumulative postoperative PCA morphine consumption in the two groups during the 48 h after surgery. Data are presented as mean and SD. Asterisks indicate statistically significant differences between the two groups (P < 0.05)

Discussion

This study demonstrates that patients receiving continuous dexmedetomidine infusion for pain relief after UPPP required 52.7% less morphine by PCA in the first 24h post operatively, compared with placebo group receiving only morphine.

Dexmedetomidine stimulates α2-adrenergic receptors and couples in an inhibitory fashion to the L-type calcium channels. These effects differ depending on receptor location; in the locus ceruleus, this stimulation provides sedation, while in the spinal cord it enhances analgesia (Kamibayashi and Maze 2000). The relatively high ratio of α2: α1 activity (1620:1 as compared with 220:1 for clonidine) accounts for the potent sedative effect of dexmedetomidine without unwanted cardiovascular effect from α1receptor activation (Hall *et al.,* 2000). However, its use in large doses is complicated by transient hypertension and bradycardia via activation of α2B adrenoceptor located on smooth muscle cells in the resistance vessels and inhibition of cardiac sympathetic drive (Bloor *et al.,* 1992). Because no particular dose of dexmedetomidine is strongly supported in the literature, in this study we used a dose of dexmedetomidine that was predicated to have no or minimal cardiovascular effects but still might be sufficient to produce sedation and analgesia. The loading dose was administrated approximately 30 min before the end of the procedure (over 20 min to minimize the effects on heart rate and blood pressure) in an attempt to attain a therapeutic level before the completion of surgery. (Arain *et al.,* 2004) administrated dexmedetomidine at an initial loading dose of $1\mu g\ kg^{-1}$ (over 10 min) followed by an infusion at $0.4\mu g\ kg^{-1}\ h^{-1}$ initiated 30 min before the end of elective inpatient surgery.

They observed slower mean heart rates in the dexmedetomidine treated group during the early postoperative period with transient significant increase in MAP that lasted several minutes immediately after the initial loading dose of dexmedetomidine. The transient increase in MAP could be attributed to the direct effects of α2 receptor stimulation of vascular smooth muscle followed by an inhibition of sympathetic outflow that overrode the direct effects of dexmedetomidine on the vasculature. This might be an unavoidable effect of infusion α2agonists, because the time differential between directly binding to vascular receptors and diffusion into the central nervous system to decrease sympathetic outflow during i.v. infusions might be ever present (Hall *et al.,* 2000). However, in our study we did not observe this transient hypertension in the dexmedetomidine treated patients probably due to the relatively long period of infusion of the loading dose.

Obstructive sleep apnea is an increasingly common sleep disorder, which is of particular concern to anesthesiologists because it is associated with increased perioperative morbidity and mortality including respiratory obstruction after extubation or respiratory depression after opioid administration. Pain is one of the most important complications of UPPP (the most common surgical procedure performed by most otolaryngologists for treatment of OSA) despite the use of many medications (Zodpe *et al.,* 2006). Analgesics must be administrated judiciously after UPPP as there is much evidence to suggest that anesthetic and narcotic agents increase the tendency for upper airway collapse; these agents also impair normal arousal mechanisms and may therefore worsen the severity of OSA (Mc Nicholas and Ryan 2006). Several studies have demonstrated the analgesic effects of dexmedetomidine. (Gurbet

et al., 2006) investigated the efficacy of dexmedetomidine vs. morphine for postoperative analgesia after total abdominal hysterectomy. Prior to induction of anesthesia, one group received an initial loading dose of dexmedetomidine 1µg kg⁻¹ over 30 min; followed by an infusion of 0.5 µg kg⁻¹ h⁻¹ that was discontinued when surgery ended. The other group received the same volume of normal saline as a placebo. All patients used a PCA device to receive bolus doses of morphine after surgery. The groups had similar pain scores but the patients who received dexmedetomidine required a lower cumulative amount of morphine during the first 48 h after surgery.

(Arain *et al.,* 2004) examined 34 patients scheduled for elective inpatient surgery and randomized them equally to receive either dexmedetomidine (initial loading dose of 1µg kg⁻¹ over 10 min followed by 0.4mg kg⁻¹ h⁻¹, discontinued at the end of surgery or morphine sulfate(0.08mg kg⁻¹) 30 min before the end of surgery. The groups had similar pain scores but the morphine group required 66% more morphine to achieve this analgesic effect. (Hofer *et al.,* 2005) reported a 433-kg morbidly obese patient with OSA and pulmonary hypertension who underwent Roux-en-Y gastric bypass. They substituted the intraoperative use of narcotics with a continuous infusion of dexmedetomidine (0.7µg kg⁻¹ h⁻¹) that was continued uninterrupted throughout the end of the first postoperative day. They found that the patient had lower narcotic requirement during the first postoperative day (48mg of morphine by PCA) while still receiving dexmedetomidine, compared to the second postoperative day (148 mg of morphine by PCA) with similar pain scores. In a recent study, involving 100 women undergoing total abdominal hysterectomy (Lin *et al.,* 2009) added dexmedetomidine to PCA morphine for one

of their patients' group. The authors observed that the patients in the dexmedetomidine group required 29% less morphine and reported significantly lower pain scores from the second postoperative hour onwards and throughout the study. In agreement with these researches, the patients in our study who received dexmedetomidine required a lower cumulative amount of morphine during the first 24h after surgery, which strongly supports the presence of dexmedetomidine-induced narcotic-sparing effect.

The analgesic effect of dexmedetomidine was also evident in our research by the significantly lower VAS scores observed during the first 2h after surgery in the dexmedetomidine treated patients compared to the placebo group.

Previous animal studies have concluded that systemic administration of α2-adrenergic receptor agonists resulted in dose dependent antinociception and sedation responses (Buerkle and Yaksh 1998) whereas, human data revealed a clear dose-response relationship for sedation, but not for analgesia (Eisenach *et al.,*1996). A possible explanation of the variances between animal and human studies is that many of the animal experiments involved drug doses several orders of magnitude larger than those used in human trials (Hall *et al.,* 2001). In human, a continuous dexmedetomidine infusion was found to maintain a unique level of sedation (patients appear to be asleep, but are readily arousable) without affecting respiration (Venn *et al.,* 2000).

Dexmedetomidine is currently approved by the U.S. Food and Drug Administration for sedation of adults in the intensive care setting for up to 24h during mechanical ventilation (Busick *et al.,* 2008). Patients receiving dexmedetomidine can typically respond to commands and perform psychomotor tests when lightly roused from their sedate state

without a need to decrease or stop the dexmedetomidine infusion (Hall *et al.,* 2000). In our study, we found that the dexmedetomidine treated patients were sedated, they appeared to be asleep but they were easily aroused with verbal or physical stimuli. This is in agreement with the previous report by (Gurbet *et al.,* 2006) who did not observe clinically important sedation in any of their patients who received dexmedetomidine infused at rate of 0.5 µg kg⁻¹ hr⁻¹.

The respiratory effects of dexmedetomidine have been greatly debated (Hall *et al.,* 2000). In this study, we did not observe any clinically significant respiratory effect in any patient who received dexmedetomidine infusion at rate of 0.6µg kg⁻¹ h⁻¹. Besides, as patients in the two groups received postoperative oxygen, PaO2 was constantly kept above 10 kPa all through the postoperative period without significant changes in the PaCo2. (Venn

et al. 2000) demonstrated that, when used in spontaneously breathing patients in the intensive care unit after cardiac surgery and general surgery, dexmedetomidine reduced morphine requirements by over 50% while at the same time had no effect on respiratory rate, SpO2, arterial PH, and PaCO2. Moreover, the PaO2: FiO2 ratios were statistically higher in the dexmedetomidine group compared with their patients receiving morphine and midazolam boluses. On the other hand, (Belleville *et al.,* 1992) reported that dexmedetomidine could be associated with episodes of obstructive apnea, and this was increasingly common at doses of 1 and 2µg kg⁻¹ that were given for two minutes and presumably associated with a rapid increase in sedation. There was a mild decrease in minute ventilation and an increase in PaCo2. Although all these effects are much less pronounced than those of opioids and other

intravenous and volatile anesthetic agents, and appear to be similar in order of magnitude to those seen during profound sleep, we cannot exclude the possibility that more rapid loading doses might cause irregular breathing or obstructive apnea.

Thus an obstruction resulting in apnea is more likely related to the deep sedation and the oral and pharyngeal anatomical events that are common to deep sleep (Hall *et al.,* 2000).

In conclusion, we found that continuous infusion of dexmedetomidine for pain relief after uvulopalatopharyngoplasty significantly reduces the amount of PCA morphine used by the patients postoperatively without affecting their ventilatory parameters and was associated with fewer morphine-related side effects. This novel drug could become a useful anesthetic adjuvant for patients with obstructive sleep apnea who are susceptible to narcotic-induced respiratory depression.

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أستخدام عقار الديكساميديتيمودين لتسكين الآلام بعد جراحة الأستئصال الجزئي للهاه و سقف الحلق والبلعوم واللوزتين

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طب عين شمس

إن عقار الديكساميديتيمودين هومحفز ألفا2 وله تأثير مسكن للالام.

وأجريت هذة الدراسه لبحث استخدامه بالوريد لتسكين الآلام و تقليل الجرعه المعطاه من المورفين,و شملت الدراسه 24 مريض يعانون من مرض توقف التنفس أثناء النوم وتجرى لهم جراحه لاستئصال اجزاء من البلعوم واللهاه و سقف الحلق و كذلك اللوزتين,قسموا إلى مجموعتين المجموعه الاولى تم إعطاء المرضى جرعه من العقار بالوريد قبل نهايه الجراحه بـ30 دقيقه و تبعه إعطاءه بالوريد بالتنقيط لمدة 24 ساعه.

والمجموعه الثانيه كانت مجموعه التحكم, و تم إعطاء مورفين للمجموعتين بعد الجراحه لتسكين الآلام , و تم تسجيل جرعات المورفين المعطاه و شدة الآلام وحاله القلب والدورة الدمويه وحاله التنفس وكذلك المضاعفات الجانبيه على مدار 48 ساعه بعد الجراحه.

وأظهرت النتائج ان المرضى الذين تم إعطاءهم عقار الديكساميديتيمودين احتاجوا إلى جرعات من المورفين أقل من المرضى الذين لم يعطى لهم هذا العقار.

وينصح بأستخدام عقار الديكساميديتيمودين للمرضى المعرضين لمضاعفات بالجهاز التنفسي بعد الجراحات التي تجرى لعلاج توقف التنفس أثناء النوم.