Sys Rev Pharm 2020;11(5):733-737
A multifaceted review journal in the field of pharmacy

The effect of use of Dexmeditomidine hydrochloride as an adjuvant in general anesthesia on rate of awareness

Nasser M. Meazher [1], Jaafar Hameed Mahboba [2], Zuhair Abdul Sada Dhahir [3]

[1] FICMS, Dept. of surgery, medical college/ kufa university, Iraq, nasserm.alabbasyi@uokufa.edu.iq.
[2] F.I.C.M, D.A & I.C, Dept. of surgery, medical college/ kufa university, Iraq
[3] F.I.C.M, D.A, Dept. of surgery, medical college/ kufa university, Iraq

ABSTRACT

Background: Dexmedetomidine can be used as a safe and helpful adjunct in many clinical situations.
Objective: To evaluate the role of Dexmedetomidine as an adjuvant in general anesthesia in relation to rate of awareness.
Patients and methods: This was a prospective quasi experimental study conducted at Al-Sadder medical city during May to November 2016, included 400 patients, assigned randomly into two groups to receive the traditional anesthesia regimen (group I) or traditional anesthesia regimen and Dexmedetomidine (group II). Awareness was assessed via postoperative interview. Appropriate statistical tests were applied accordingly.
Results: The rates of awareness and possible awareness in group II were (0.5%) and (1.0%), respectively, and were significantly lower than that of group I (3.5%) and 4.5%), respectively, (P<0.05).
Conclusion: Dexmedetomidine can improve the outcome of general anesthesia by significant reduction of rate of awareness during operation.

Keywords: Dexmedetomidine, general anesthesia

Correspondence:
Nasser M. Meazher
[1] FICMS, Dept. of surgery, medical college/ kufa university, Iraq, nasserm.alabbasyi@uokufa.edu.iq.

INTRODUCTION

The invention of anaesthesia has modified modern medicine greatly. The first case of anaesthesia was introduced by Morton in 1846 and, in addition, it has been described as the first reported case of awareness during anaesthesia. The patient subjected to anesthesia by Mortons experienced no pain during operation but had some memories about events during surgery [(1)]. It has been stated that fear from pain, paralysis and mental distress during operation is reported in 54% of cases [(2)]. Awareness, although rare, can be added to the list of unsatisfactory events worried about by patients like pain, nausea and vomiting [(3)]. The term "awareness" is defined as the explicit memory of events during general anaesthesia. With time, the incidence of awareness during anesthesia witnessed gradual reduction since the observation of this phenomenon during operation in 1960 [(4,5)]. Various reports around the world gave a range of incidence between 0.3 to 0.8 % in different types of surgery [(4, 6-8)]. Depth of anesthesia is usually assessed by monitoring heart rate, blood pressure and other clinical signs, which have been shown to be unreliable [(9,10)]. These signs, particularly, tachycardia and hypertension failed to predict awareness during anesthesia according to Ghoneim and colleagues who reviewed 271 reported cases of awareness from 1950 through 2005 [(11)]. Detection of awareness is not easy. In the review article by Ghoneim, he states that the "Brice questionnaire" invented by Brice, and colleagues, in 1970 and updated by Lin and colleagues, 1991, has shown to be a reliable an efficient way to detect intraoperative memory. The interview comprised four questions.

1. What was, the final patient remembers before he went to sleep during anesthesia?
2. What did firstly the patient remember when he woke up from anesthesia?
3. Could the patient, memorised anything in between these two periods?
4. Did the patient, patience during surgery?

Timing of the interview is essential. Directly after operation in the "post anaesthesia care unit" (PACU) it is difficult to gain the patients attention while he or she is very focused on more obvious symptoms like pain, postoperative nausea and vomiting (PONV) or simply fatigue. Recent studies found that only 50% of the awareness cases are detected in the PACU. Sometimes recall is delayed by several days, maybe even weeks [(2, 3)].

Frequent observations from patients who have an episode of awareness throughout surgery were in the form of hearing events and conversations, feeling of paralysis, helplessness, weakness, anxiety and impending death. Some patients are uncertain whether what they felt was real or whether it is merely to some wrong thoughts. The after-effects of intraoperative memory can be transient and include sleep disorders, nightmares and daytime fear. In the extreme situation awareness under anaesthesia resulted in posttraumatic stress syndrome (PTSD) with recuurent nightmares, irritability and a feeling of imminent death [(4)]. A prolong follow up by Lennmarken and colleagues demonstrated that four of nine patients who had awareness acquired severe symptoms of PTSD, another three of them had less symptoms, nevertheless still suffered from their bad experience [(12)]. Dexmedetomidine, is a powerful and strongly selective (α-2) adrenoceptor stimulant with sedative, sympatholytic, analgesic and amnestic activities [(13)] which has, been described as a safe adjunct in a number of clinical situations. It reduced central nervous system (CNS) sympathetic outpouring in a dosedependent pattern and has anlgesic effects best described as opioidsparing[(14)].

Patients, materials and methods

This was a prospective quasi experimental study conducted at Al-Sadder medical city/ emergency unite in Al-Najaf province during the period May to November 2016. The present study included 400 patients who were randomly assigned into two groups, to receive either the conventional mode of protocol (pentothal, atracurium and halothane), namely, (group 1) or (pentothal, atracurium and halothane) and (Dexmedetomidine hydrochloride), (group 2). Prior to induction of anesthesia and enrollement of the patients in the study, informed verbal and signed consents were obtained from

all participants, additionally, all official agreements were obtained from the training and research department of AlSader Medical city. The degree of awareness was assessed according to structured Brice post-operative interview and patients were classified into three groups: A) definitely aware, B) Possibly aware and C) Not aware. The next questions were included:

1. What does the patient finally memorize before sleeping due to induction of anesthesia?
2. What is,the patient immediately memorize after recovery from anesthesia?
3. Did the patient memorize what happened in the periods between sleep and recovery from anesthesia? (possible answers: yes, no); If yes, what is it? (light, sound, pain, dyspnoea, etc.).
4. What the patient dream during anesthesia?
5. Ask the patient about the worst memory during anesthesia and surgery?

The later questions important in statistical analysis: age,, gender, American Society of Anesthesiologists (ASA) score, type of anaesthesia and premedication,, muscle relaxants used, time between anaesthesia and administration of the questionnaire, data regarding possible earlier awareness, and substances or drugs used. The patient's notes were divided according to the common classification [15] as definite awareness (1), possible awareness (2), and no awareness (3). Data were entered and analyzed using the statistical package for social sciences (SPSS) version 22 for windows and Microsoft Office Excel 2010, appropriate statistical tests were applied according to the type of variables; Chi square test used to compare frequencies and students to test for independent two sample used to compare means between both groups, Pearson's correlation test used to assess the correlation between age and awareness score, while Spearman's correlation test used to assess the correlation between awareness score and other variables other than age. Level of significance, P.value ≤ 0.05 considered significant difference.

Results

Demographic characteristics of the study sample

The mean, age of patients in group (1) was 29.78 ±12.21 years and in group (2) it was 32.00 ±15.33 years; with no statistically significant difference between both groups (P>0.05), (Figure 1).

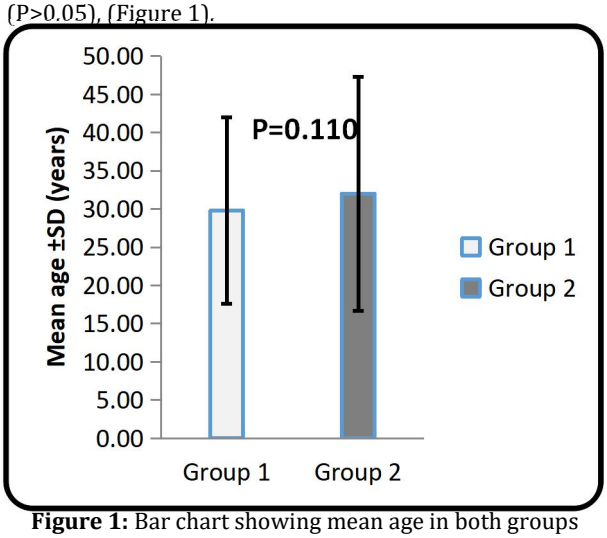

Figure 1: Bar chart showing mean age in both groups

The total sample included 228 (56.5%) female patients and 172 (43.5%) male patients and no statistically significant difference had been found in gender between both groups (P>0.05), (Table 1).

Table 1: Distribution of patients according to gender

Gender	Group 1 N (%)	Group 2 N (%)
Male	116 (58.0)	112 (56.0)
Female	84 (42.0)	88 (44.0)
Total	200 (100.0)	200 (100.0)
χ^2 = 0.163, P. value = 0.686		

Group 1: patients who received pentothal, atracurium and halothane; Group 2: Patients who received pentothal, atracurium and halothane and Dexmedetomidine hydrochloride)

Rate of awareness

The rate of awareness in group (1) (who received conventional protocol) was 3.5% whereas the rate of awareness in group(2) (who received alternative protocol) was (0.5%); the rate of awareness was lower in group (2) than in the group (1) however, the difference did not reach the statistical significance, (P=0.074). The rate of possible awareness in the group (1) was (4.5%) whereas in the group (2) it was (1.0 %), and the difference was statistically significant (P<0.05), furthermore, by comparing the none awareness rate I was significantly higher in group (2) than in group (1) ; (98.5%) and (92.0%), respectively, (P< 0.05), as shown in (table 2 and figure 2).

Table 2. Awareness and possibility of awareness according to type of anesthesia

Awareness	Group 1 n (%)	Group 2 n (%)	χ2	P
Aware	7 (3.5)	1 (0.5)	3.19	0.074
Possibly aware	9 (4.5)	2 (1.0)	4.58	0.0322
Not aware	184 (92.0)	197 (98.5)	7.96	0.0047
Total	200 (100.0)	200 (100.0)	-	-

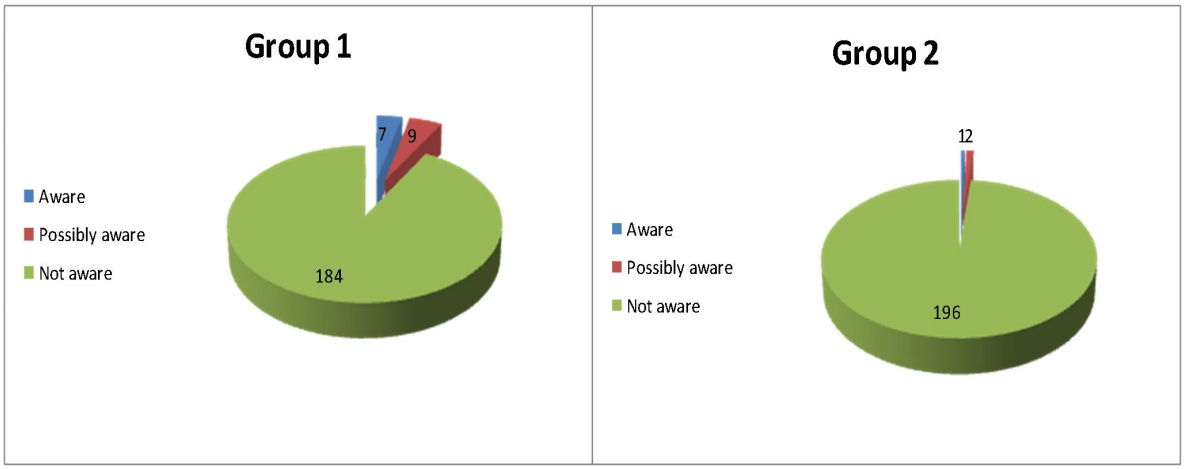

Figure 2: Awareness and possibility of awareness according to type of anesthesia

Association between possible risk factors and rate of awareness

No statistically significant association between age, gender, ASA stage, smoking, hypertension and diabetes mellitus from one side and awareness score from the other side had been found in both groups,, (P>0.05), (Table 3).

Table 3. Results of correlation tests between risk factors and awareness score in both groups.

Group	Factor*	Correlation indicators (Factors against Awareness score)	
		Correlation coefficient	P. value
Group 1	Age	0.053	0.44
	Gender	0.021	0.79
	ASA stage	0.032	0.66
	Hypertension	0.081	0.21
	Diabetes mellitus	0.011	0.83
	Smoking	0.064	0.34
Group 2	Age	0.011	0.92
	Gender	0.072	0.28
	ASA stage	0.051	0.44
	Hypertension	0.222	0.82
	Diabetes mellitus	0.034	0.66
	Smoking	0.020	0.77

* Spearman's correlation test used in all variables except age where Pearson's correlation test used,

Discussion

The main observation in the current study is that the use of dexmedetomidine was associated with significant reduction of the risk of awareness during anesthesia. Similar observation has been reported by other authors. Ghodki *et al.* [16] found dexmedetomidine reduced incidence of awareness during laproscopic surgery. In support of the present study, Elhakim et al. reported that the use of dexmedetomidine lead to prevention of awareness during anaesthesia, improvement of intraoperative oxygenation,decrease anesthetic drug requirement and improvement of postoperative analgesia [17]. Kasuya et al made a comparison of the sedative-effect of dexmedetomidine, and propofol utilizing (BIS) and the Observer's Assessment of Alertness and Sedation score, (OAA/S). The finding was that sedation was significantly lower with dexmedetomidine, than with propofol [18]. The probable reason is the potentiation of the anesthetic effect of anesthetic agents through an unknown mechanism and by this way it reduces the required amount of these agents like Des and fentanyl. Other, authors also reported the phenomenon of reduced doses of Des and fentanyl in patients undergoing liver transplantation, with comparable anesthetic depth [19] .It was pointed out by some authors that dexmedetomidine, offers the ability of producing both sedation and analgesia with no associted respiratory depression, hence it possess anesthetic-sparing advantage [20] . Patel *et al.* reported that dexmedetomidine, continuous infusion reduced the required dose of sevoflurane throughout general anesthesia [21]. The hemodynamic changes produced by dexmedetomidine sympatholytic effect were also proposed to explain the reduced need for anesthetic , agents [22] , and also it is suggested that sympathoadrenal reaction to tracheal intubation is attenuated following dexmedetomidine use [23] It is also documented that dexmedetomidine possesses analgesic potential and reduces visceral pain [24,25]. Similar observation regarding hemodynamic changes and reduced sympathoadrenal reaction to intubation is also reported by other studies [26].

REFERENCES

1. Lennmarken, C., & Sandin, R. (2004). Neuromonitoring for awareness during surgery.
2. surgery. The Lancet, (2004); **363**(9423): 1747-1748. https://doi.org/10.1016.
3. Sandin, R. H., Enlund, G., Samuelsson, P., & Lennmarken, C. (2000). Awareness during anaesthesia: a prospective case study. *The Lancet*, *355*(9205), 707-711. https://doi.org/10.1016/S0140-6736(99)11010-9.
4. Myles, P. S., Williams, D. L., Hendrata, M., Anderson, H., & Weeks, A. M. (2000). Patient satisfaction after anaesthesia and surgery: results of a prospective survey of 10,811 patients. *British journal of anaesthesia*, *84*(1), 6-10. https://doi.org/10.1093/oxfordjournals.bja.a013383.
5. Ghoneim, M. M., & Weiskopf, R. B. (2000). Awareness during anesthesia. *Anesthesiology: The Journal of the American Society of Anesthesiologists*, *92*(2), 597-597.
6. Ghoneim, M. M. (2007). Incidence of and risk factors for awareness during anaesthesia. *Best Practice & Research Clinical Anaesthesiology*, *21*(3), 327-343. https://doi.org/10.1016/j.bpa.2007.05.002.
7. Paech, M. J., Scott, K. L., Clavisi, O., Chua, S., Mcdonnell, N., & ANZCA Trials Group. (2008). A prospective study of awareness and recall associated with general anaesthesia for caesarean section. *International journal of obstetric anesthesia*, *17*(4), 298-303. https://doi.org/10.1016/j.ijoa.2008.01.016
8. Davidson, A. J., Huang, G. H., Czarnecki, C., Gibson, M. A., Stewart, S. A., Jamsen, K., & Stargatt, R. (2005). Awareness during anesthesia in children: a prospective cohort study. *Anesthesia & Analgesia*, *100*(3), 653-661. https://doi.org/10.1213/01.ANE.0000150604.73481.00
9. Malviya, S., Galinkin, J. L., Bannister, C. F., Burke, C., Zuk, J., Popenhagen, M., ... & Voepel-Lewis, T. (2009). The incidence of intraoperative awareness in children: childhood awareness and recall evaluation. *Anesthesia & Analgesia*, *109*(5), 1421-1427.
10. Myles, P. S., Leslie, K., McNeil, J., Forbes, A., Chan, M. T. V., & B-Aware Trial Group. (2004). Bispectral index monitoring to prevent awareness during anaesthesia: The B-Aware randomised controlled trial. *The lancet*, *363*(9423), 1757-1763. https://doi.org/10.1016/S01406736(04)16300-9
11. Sebel, P. S., Bowdle, T. A., Ghoneim, M. M., Rampil, I. J., Padilla, R. E., Gan, T. J., & Domino, K. B. (2004). The incidence of awareness during anesthesia: a multicenter United States study. *Anesthesia & Analgesia*, *99*(3), 833-839.
12. Ghoneim, M. M., Block, R. I., Haffarnan, M., & Mathews, M. J. (2009). Awareness during anesthesia: risk factors, causes and sequelae: a review of reported cases in the literature. *Anesthesia & Analgesia*, *108*(2), 527-535. https://doi.org/10.1213/ane.0b013e318193c634
13. Lennmarken, C., Bildfors, K., Enlund, G., Samuelsson, P., & Sandin, R. (2002). Victims of awareness. *Acta Anaesthesiologica Scandinavica*, *46*(3), 229-231. https://doi.org/10.1034/j.1399-6576.2002.t01-1-460301.x
14. Carollo, D. S., Nossaman, B. D., & Ramadhyani, U. (2008). Dexmedetomidine: a review of clinical applications. *Current Opinion in Anesthesiology*, *21*(4), 457-461. https://doi.org/10.1097/ACO.0b013e328305e3ef
15. Panzer, O., Moitra, V., & Sladen, R. N. (2011). Pharmacology of sedative-analgesic agents: dexmedetomidine, remifentanil, ketamine, volatile anesthetics, and the role of peripheral mu antagonists. *Anesthesiology clinics*, *29*(4), 587-605. https://doi.org/10.1016/j.anclin.2011.09.002
16. Szostakiewicz, K. M., Tomaszewski, D., Rybicki, Z., & Rychlik, A. (2014). Intraoperative awareness during general anaesthesia: results of the observational survey. *Anaesthesiology intensive therapy*, *46*(1), 23-28. https://doi.org/10.5603/ait.2014.0005
17. Ghodki, P. S., Thombre, S. K., Sardesai, S. P., & Harnagle, K. D. (2012). Dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery: An observational study using entropy monitoring. *Journal of anaesthesiology, clinical pharmacology*, *28*(3), 334. https://dx.doi.org/10.4103%2F09709185.98329
18. Elhakim, M., Abdelhamid, D., Abdelfattach, H., Magdy, H., Elsayed, A., & Elshafei, M. (2010). Effect of epidural dexmedetomidine on intraoperative awareness and post-operative pain after one-lung ventilation. *Acta Anaesthesiologica Scandinavica*, *54*(6), 703-709. https://doi.org/10.1111/j.13996576.2009.02199.x
19. Kasuya, Y., Govinda, R., Rauch, S., Mascha, E. J., Sessler, D. I., & Turan, A. (2009). The correlation between bispectral index and observational sedation scale in volunteers sedated with dexmedetomidine and propofol. *Anesthesia & Analgesia*, *109*(6), 1811-1815. https://doi.org/10.1213/ANE.0b013e3181c04e58
20. Sayed, E., & Yassen, K. A. (2016). Intraoperative effect of dexmedetomidine infusion during living donor liver transplantation: A randomized control trial. *Saudi Journal of Anaesthesia*, *10*(3), 288. https://dx.doi.org/10.4103%2F1658354X.174914
21. Afonso, J., & Reis, F. (2012). Dexmedetomidina: papel atual em anestesia e cuidados intensivos. *Revista Brasileira de Anestesiologia*, *62*(1), 125-133. https://doi.org/10.1590/S00347094201200010001 5.
22. Patel, C. R., Engineer, S. R., Shah, B. J., & Madhu, S. (2013). The effect of dexmedetomidine continuous infusion as an adjuvant to general anesthesia on sevoflurane requirements: A study based on entropy analysis. *Journal of anaesthesiology, clinical pharmacology*, *29*(3), 318. https://dx.doi.org/10.4103%2F09709185.117066
23. Gerlach, A. T., & Dasta, J. F. (2007). Dexmedetomidine: an updated review. *Annals of Pharmacotherapy*, *41*(2), 245-254. https://doi.org/10.1345%2Faph.1H314
24. Keniya, V. M., Ladi, S., & Naphade, R. (2011). Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. *Indian journal of anaesthesia*, *55*(4), 352. https://dx.doi.org/10.4103%2F00195049.84846

25. Cortinez, L. I., Hsu, Y. W., Sum-Ping, S. T., Young, C., Keifer, J. C., MacLeod, D., ... & Somma, J. (2004). Dexmedetomidine Pharmacodynamics: Part IICrossover Comparison of the Analgesic Effect of Dexmedetomidine and Remifentanil in Healthy Volunteers. *Anesthesiology: The Journal of the American Society of Anesthesiologists*, *101*(5), 1077-1083.
26. Feld, J. M., Hoffman, W. E., Stechert, M. M., Hoffman, I. W., & Ananda, R. C. (2006). Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery. *Journal of clinical anesthesia*, *18*(1), 24-28. https://doi.org/10.1016/j.jclinane.2005.05.009
27. Patel, C. R., Engineer, S. R., Shah, B. J., & Madhu, S. (2012). Effect of intravenous infusion of dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: A study with entropy analysis. *Indian journal of anaesthesia*, *56*(6), 542. https://dx.doi.org/10.4103%2F00195049.104571