Oral clonidine versus gabapentin as premedicant for obtunding hemodynamic response to laryngoscopy and tracheal intubation

Suresh K. Singhal,

Kiranpreet Kaur,

Promila Arora

Department of Anaesthesiology and Critical Care, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India

Address for correspondence:
Dr. Kiranpreet Kaur,
52/9 J, Medical Enclave,
Rohtak - 124 001, Haryana, India.
E-mail: kiranpreet72@rediffmail.com

ABSTRACT

Background: We compared the effects of oral clonidine and gabapentin as premedicant in obtunding hemodynamic response to laryngoscopy and intubation in normotensive patients undergoing elective surgery. **Methods:** A total of 100 patients of either sex enrolled in the study were randomly divided into two groups of 50 each. Group A patients received oral clonidine 200 μg and Group B patients received oral gabapentin 900 mg, 90 min prior to induction of anesthesia. **Results:** Both groups were matched for age, sex weight and intubation time. Anxiety score and sedation scores before induction were significantly better in Group A as compared with Group B. Heart rate rise was obtunded in Group A except at 1 min, as compared with Group B in which tachycardia persisted even at 3 and 5 min following intubation. Mean arterial pressure was maintained below baseline at all times in Group A as compared with Group B in which significant rise ($+7.55\%$, $P < 0.001$) was seen at 1 min after intubation. **Conclusion:** Oral clonidine provided good attenuation of hemodynamic response to laryngoscopy and intubation as compared with oral gabapentin.

Key words: *Gabapentin, oral clonidine, pressor response*

INTRODUCTION

Laryngoscopy and endotracheal intubation are potent stimuli that can induce increased sympathetic activity leading to tachycardia, hypertension and dysrhythmias. It may have deleterious respiratory, neurological and cardiovascular effects.[1,2] These responses are more marked in hypertensive patients.[3,4] In patients with coronary artery disease, leaking abdominal aneurysm, intracranial aneurysm and recent myocardial infarction these transient changes can result in potentially deleterious effects such as myocardial ischemia, left ventricular failure and cerebral hemorrhage.[4-6]

Vasodilators such as nitroprusside,[7] hydralazine[8] and nitroglycerine[9] have been used to attenuate these hemodynamic responses with varying degree of success. Calcium channel blocker,[10] beta blockers[11,12] and opioids such as alfentanil,[13] fentanyl[14] and remifentanil[15] have also been used in different dosage regimens to attenuate hemodynamic response to laryngoscopy and intubation.

Clonidine is a α_2 adrenergic agonist, stimulates α_{2A} subtype of α_2 adrenergic receptors in the brainstem resulting in a reduction in sympathetic outflow from central nervous system thus causing lowering of arterial pressure by an effect on both cardiac output and peripheral resistance. By its central sympatholytic action, it tends to attenuate the hemodynamic response to any surgical nociceptive stimulus and to improve overall perianesthetic cardiovascular stability.[16]

Similarly, gabapentin which is a structural analogue of the neurotransmitter gamma-aminobutyric acid (GABA) is being used as an anticonvulsant drug is also effective in controlling neuropathic pain. It acts by selective activation of heterodimeric $GABA_B$ receptors. Gabapentin has been used in randomized controlled trials to treat acute post-operative pain and to reduce post-operative opioid requirements.[17] The mechanism by which gabapentin attenuates the pressor response to laryngoscopy and

Access this article online

Quick Response Code:

Website:
www.saudija.org

DOI:
10.4103/1658-354X.130692

intubation is unknown, the drug inhibits membrane voltage-gated calcium channels, thus acting in the manner similar to calcium channel blockers.[18]

The aim of the present study was to evaluate and to compare the effect of clonidine and gabapentin in obtunding hemodynamic response to laryngoscopy and intubation in normotensive patients undergoing elective surgery.

METHODS

The study was approved by hospital ethical committee and informed consent from all the participants was obtained. A total of 100 adult patients of either sex between the age group of 20 and 50 years, having physical status of Grade-I and Grade-II according to American Society of Anesthesiologists, scheduled for elective surgery under general anesthesia with endotracheal intubation were enrolled in the study. Patients with anticipated difficult intubation, obesity, hypertension and bronchial asthma were excluded from the study.

Study design
It was a prospective, randomized and double-blind study. Randomization was performed by keeping 100 coded slips in the box and observer as well as the person giving the drug was blinded.

All patients were examined pre-operatively and details regarding clinical history, general physical examination were recorded and all routine investigations were carried out. They were kept fasting for 6 h prior to surgery and tablet alprazolam 0.25 mg on the night before surgery was given as pre-medication. Patients were randomly allocated to two groups of 50 each. Group A ($n = 50$) patients received oral clonidine 200 μg and Group B ($n = 50$) patients received oral gabapentin 900 mg, 90 min prior to induction of anesthesia with a sip of water. In the operating room, standard monitoring consisting of electrocardiogram (ECG), pulse oximetry SPO_2 and non-invasive arterial blood pressure was established. After the placement of intravenous line injection thiopentone sodium 5 mg/kg was used for induction followed by injection succinylcholine 2 mg/kg for intubation. All patients were manually ventilated using oxygen 33%, nitrous oxide 67% and halothane 0.5% for 90 s. Intubation was performed with size 7 mm internal diameter (ID) endotracheal tube (ETT) in female and 8 mm ID ETT in male patients. Laryngoscopy and intubation was performed by the trained observer in all cases for consistency of observations.

In the pre-anesthetic room, the Sedation Score,[19] Anxiety Score[20] was noted under:

Anxiety score
0 = Point – patient quiet and comfortable
1 = Point – patient uneasy
2 = Point – patient worried or anxious
3 = Point – patient very worried or very upset
4 = Point – patient frightened or terrified.

Sedation score
1 = Point – wide awake
2 = Point – sleeping comfortably but responding to verbal commands
3 = Point – deep sleep but arousable
4 = Point – deep sleep but not arousable.

Hemodynamic parameters were noted just before the drug (basal-B_1) and after the administration of drug on the operation Table (B_2). Thereafter mean arterial pressure (MAP) and heart rate (HR) were recorded before intubation (T_0) 1, 3 and 5 min after intubation (T_1, T_3 and T_5). ECG was continuously monitored for any dysrhythmias during this period. Duration of laryngoscopy and endotracheal intubation was also recorded. Side-effects pertaining to clonidine and gabapentin were noted pre-operatively as well as post-operatively.

At the end of the study decoding was performed and data was compiled and analyzed using independent *t*-test (paired and unpaired) for quantitative data and for non-quantitative data and association between groups with respect to various characteristics Chi-square test was applied. A $P < 0.05$ was considered significant, <0.001 highly significant and >0.05 insignificant.

RESULTS

Table 1 shows the distribution of age, weight and sex in two groups, which were comparable statistically. Anxiety score and sedation score were compared before and after administration of the drug. The difference was statistically significant ($P < 0.001$) in both the groups [Table 2]. However, anxiety score and sedation score were significantly better in clonidine (Group A) as compared with gabapentin (Group B) ($P < 0.05$) [Table 3]. Mean duration of laryngoscopy and endotracheal intubation in Group A and Group B was also comparable (11.18 ± 1.063 and 11.38 ± 1.210 min respectively).

Table 1: Demographic profile of patients

Parameters	Group A (*n*=50)	Group B (*n*=50)	P value
Age in years (mean±SD)	33.44±8.80	32.14±8.58	0.456 (*P*>0.05)
Weight in kg (mean±SD)	55.82±8.82	54.86±8.24	0.575 (*P*>0.05)
Sex (male/female) (*n*)	19/31	18/32	0.84 (*P*>0.05)

SD : Standard deviation

Hemodynamic parameters HR and MAP are shown in Tables 4 and 5 and represented graphically in Figures 1 and 2. HR in Group A (clonidine group) remained below baseline at all times except at 1 min following intubation when transient rise of 5.33% was observed. Whereas in Group B (gabapentin), the HR rise persisted until the end of the study period and was statistically highly significant at all times as compared with Group A.

Similarly MAP was also attenuated in Group A and it remained below baseline throughout the study period. Although, this fall in MAP was significant but it did not warrant any active intervention. In Group B also fall in MAP was observed at all times except at 1 min following intubation when rise in MAP (7.55%) was observed, which was highly significant ($P < 0.001$) when compared with Group A but MAP returned to below baseline value at 3 and 5 min.

Side-effects pertaining to clonidine and gabapentin were noted pre- and post-operatively. 68% of the patients in Group A complained of dry mouth pre-operative as well as post-operatively and bradycardia was observed in 2-4% cases, which did not warrant any treatment. Similarly in Group B, there were minor complaints of headache, drowsiness and dizziness [Table 6].

DISCUSSION

The sympathoadrenal activation associated with laryngoscopy and tracheal intubation causes the rise in arterial blood pressure, tachycardia and dysrhythmias.[1-4] The achievement of a smooth induction with minimal reflex hemodynamic response during laryngoscopy and endotracheal intubation remains an important anesthetic goal. Several strategies have been evolved to blunt this undesirable hemodynamic response to laryngoscopy and endotracheal intubation, but each method has its own advantages and disadvantage.[18]

Clonidine and gabapentin are drugs under intense investigation as an adjunct to anesthesia in various forms.[21,22] Clonidine originally introduced as antihypertensive drug, has analgesic, sedative and

Table 2: Distribution of anxiety score and sedation score within the two groups

Group	Anxiety score					P value
	0	1	2	3	4	
Group A (n=50)						
Baseline (B_1) (%)	17 (34)	30 (60)	3 (6)	0	0	$3.101×10^{-8}$ ($P<0.001$)
Before induction (B_2) (%)	44 (88)	6 (12)	0	0	0	
Group B (n=50)						
Baseline (B_1) (%)	13 (26)	35 (70)	2 (4)	0	0	$1.065×10^{-5}$ ($P<0.001$)
Before induction (B_2) (%)	35 (70)	15 (30)	0	0	0	

Group	Sedation score				P value
	0	1	2	3	
Group A (n=50)					
Baseline (B_1) (%)	45 (90)	5 (10)	0	0	$5.604×10^{-6}$ ($P<0.001$)
Before induction (B_2) (%)	24 (48)	23 (46)	3 (6)	0	
Group B (n=50)					
Baseline (B_1) (%)	46 (92)	4 (8)	0	0	0.009 ($P<0.05$)
Before induction (B_2) (%)	36 (72)	14 (18)	0	0	

Table 3: Comparison of anxiety score and sedation score in-between the two groups before induction (B_2)

Group	Anxiety score					P value
	0	1	2	3	4	
Group A (n=50)	44	6	0	0	0	0.0271 ($P<0.05$)
Group B (n=50)	35	15	0	0	0	

Group	Sedation score				P value
	0	1	2	3	
Group A (n=50)	24	23	3	0	0 ($P<0.001$)
Group B (n=50)	36	14	0	0	

Anxiety score was significantly better in clonidine (Group A) as compared with gabapentin (Group B) ($P<0.05$)

Table 4: Changes in heart rate compared with baseline in two groups at various time intervals (percentage)

Groups	Before induction (B_2)	Just before intubation (T_0)	After intubation		
			1 min (T_1)	3 min (T_3)	5 min (T_5)
Group A (n=50)	†−3.71**	†−4.64**	+5.33**	−1.30	††−7.58**
P value	$3.736×10^{-5}$ ($P<0.001$)	$2.505×10^{-5}$ ($P<0.001$)	$9.765×10^{-10}$ ($P<0.001$)	0.068 ($P>0.05$)	$1.101×10^{-12}$ ($P<0.001$)
Group B (n=50)	+0.24	−1.780*	††+15.682**	††+7.243**	+0.804
P value	0.698 ($P>0.05$)	0.0212 ($P<0.05$)	$1.873×10^{-23}$ ($P<0.001$)	$9.229×10^{-12}$ ($P<0.001$)	0.3860 ($P>0.05$)
P value (inter group)	0.0031 ($P<0.05$)	0.014 ($P<0.05$)	$1.091×10^{-10}$ ($P<0.001$)	$1.981×10^{-8}$ ($P<0.001$)	$4.325×10^{-8}$ ($P<0.001$)

+ − Increase, − − Decrease. P value within the group *<0.05 (significant), **<0.001 (highly significant) and in between group †<0.05 (significant), ††<0.001 (highly significant)
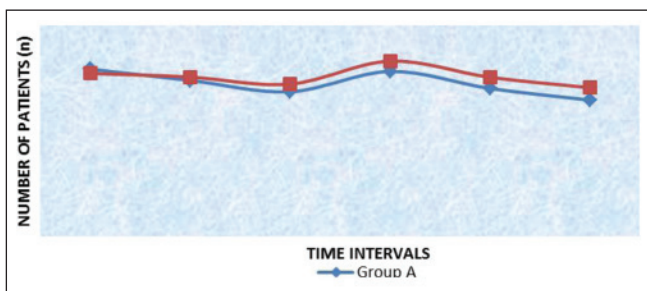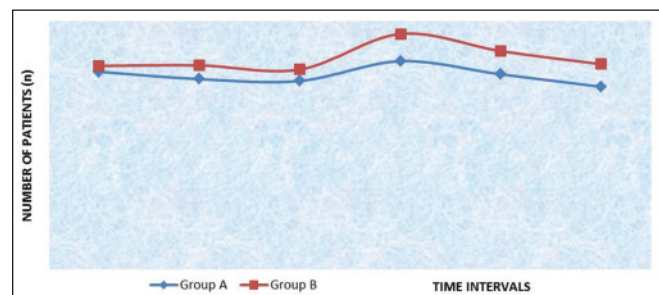
Table 5: Changes in mean arterial pressure compared with baseline in two groups at various time intervals (percentage)

Groups	Before induction (B_2)	Just before intubation (T_0)	After intubation		
			1 min (T_1)	3 min (T_3)	5 min (T_5)
Group A ($n=50$)	−6.725**	−13.56**	−1.34	††−11.55**	††−18.55*
P value	4.551×10^{-14} ($P<0.001$)	2.256×10^{-17} ($P<0.001$)	0.157 ($P>0.05$)	9.558×10^{-16} ($P<0.001$)	6.851×10^{-23} ($P<0.001$)
Group B ($n=50$)	−2.26*	−6.62**	††+7.55**	−2.39*	−8.79**
P value	0.0034 ($P<0.05$)	4.149×10^{-9} ($P<0.001$)	2.878×10^{-12} ($P<0.001$)	0.014 ($P<0.05$)	1.233×10^{-11} ($P<0.001$)
P value (inter group)	0.224 ($P>0.05$)	0.2406 ($P>0.05$)	2.604×10^{-5} ($P<0.001$)	3.307×10^{-5} ($P<0.001$)	6.423×10^{-7} ($P<0.001$)

+ – Increase; − − Decrease. *P* value within the group *<0.05 (significant), **<0.001 (highly significant) and in between group †<0.05 (significant), ††<0.001 (highly significant)

Table 6: Comparison of side-effects in two groups

Side-effects	Dry mouth	Hypotension	Bradycadia	Headache	Drowsiness	Dizziness
Pre-operative side-effects (percentage)						
Group A ($n=50$) (%)	34 (68)	0	1 (2)	0	0	0
Group B ($n=50$) (%)	0	0	0	2 (4)	2 (4)	0
Post-operative side-effects (percentage)						
Group A ($n=50$) (%)	34 (68)	5 (10)	2 (4)	0	0	0
Group B ($n=50$) (%)	0	0	0	2 (4)	6 (12)	2 (4)

Figure 1: Changes in mean arterial pressure between two groups

Figure 2: Changes in heart rate between two groups

anxiolytic properties. It improves the quality of induction, maintenance and recovery from anesthesia. By its central sympatholytic action, it tends to attenuate the hemodynamic response to any surgical nociceptive stimulus and improve overall perianesthetic cardiovascular stability.[16] Prevention of tachycardia in response to laryngoscopy and endotracheal intubation and the slowing of the HR induced by clonidine share a complex underlying mechanism. It consists of different components, centrally the activation of α_2 adrenoceptors causes both a reduction in peripheral sympathetic tone and an increase of vagally induced reflex bradycardia, peripherally stimulation of presynaptic alpha adrenoceptors leads to diminished release of nor epinephrine from the nerve endings toward the vasculature and to a reduction in peripheral sympathetic tone toward the heart.[23] Similarly, gabapentin most recently has been evaluated as analgesic, anti-hyperalgesic or both perioperatively.[17] Role of gabapentin in obtunding hemodynamic response has been highlighted by Fassoulaki *et al.* and Memiş *et al.*[18,21] We evaluated and compared oral clonidine and gabapentin in abolishing the hemodynamic response to laryngoscopy and endotracheal intubation.

In our study, both groups were comparable regarding age, weight and sex distribution. Our reason for studying the patients up to 50 years of age was that elderly patients more often are on drugs such as antidepressants, hypnotics and anti-hypertensives and also exhibit increased sensitivity to drugs.

Premedication with opioids like morphine and large induction dose of thiopentone sodium, propofol, which can largely increase the depth of anesthesia can indirectly influence this hemodynamic response to laryngoscopy and intubation.[18,22] In our study, no additional premedication was given and fixed dose of thiopentone 5 mg/kg was used for induction in both groups to avoid this bias. It is known that response to laryngoscopy is dependent on the duration of laryngoscopy, peaking at 45 s.[9,10] In this study, the mean duration of laryngoscopy and intubation did not exceed 11.35 s and was comparable in both groups.

Pre-operative anxiolysis and sedation are the main objective of premedication and both involve a number of possible mechanisms of action implicating central gamma amino butyric acids.[17] The sedation effect of clonidine may be due to decreased tonic activity of locus coeruleus, which modulates the stimuli arriving in the central nervous system and adrenergic receptor.[16] Raval and Mehta in their study comparing oral clonidine (200 μg) with diazepam (0.2 mg/kg) and a placebo group observed that clonidine produces significant sedation and analgesia, but when compared in-between group diazepam faired better.[20] The anxiolytic effect of gabapentin in patients with a variety of psychiatric disorder has been demonstrated in several clinical trials. Significantly lower pre-operative visual analog scale anxiety score ($P < 0.001$) has been seen with gabapentin as compared with placebo in patients undergoing knee surgery.[24] Rorarius *et al.* found that 1200 mg gabapentin was less effective in inhibiting pre-operative anxiety as compared with oxazepam (15 mg), which was used as active placebo in the control group.[25]

We observed that both clonidine and gabapentin showed anxiolysis and sedation in a significant proportion of subjects. The anxiolytic and sedative effect was significantly more with clonidine than gabapentin. Our results are similar to the study of Faheim *et al.*[23] who used 600 mg of gabapentin and 300 μg clonidine orally.

In the present study, baseline hemodynamic parameters HR and MAP were comparable in both groups. Raval and Mehta[20] stated that clonidine (200 μg) results in persistent fall in MAP, but decreases HR only before and after induction. After intubation, HR increased marginally which is less marked and persisted for a very short period. The effect of clonidine (200 μg) on MAP and HR in our study was similar to the observations of Raval and Mehta gabapentin was used as premedicant by Memiş *et al.*[21] and they observed complete attenuation of MAP and HR with 800 mg gabapentin when given 1 h prior to surgery. While Fassoulaki *et al.*[18] observed that even higher doses of gabapentin, i.e., 1600 mg had no effect on the MAP and HR at 0-24 h after operation. In our study, we observed that 900 mg gabapentin ameliorates MAP, but not HR response. Faheim *et al.*[23] and Marashi *et al.*[26] after comparative evaluation of the two drugs reached an inference that both gabapentin and clonidine are equally effective in attenuating blood pressure response to laryngoscopy and intubation and further stated that in fact gabapentin was more superior. Our results are in contrast to the studies of Faheim *et al.*[23] and Marashi *et al.*[26]

Both clonidine and gabapentin have certain adverse effects inherent to their structure. Most common side-effects with clonidine are dry mouth and sedation documented in almost 50% of patients and less common are sexual dysfunction, hypotension and marked bradycardia.[16] The most frequent side-effects reported with gabapentin are somnolence, dizziness, ataxia, uncontrollable back, fatigue, unsteadiness, nystagmus, headache, tremors, diplopia and nausea,[21] but depression, irritability and mood changes can also be there.[17] It is also pertinent to mention here that these side-effects are transient and usually abolish on their own.[18]

High incidence of dryness of mouth (68%) was reported with clonidine in our study, which is associated with the effect of drug on pre-synaptic alpha-adrenoceptors in the brainstem as well as on parasympathetic nerves, which supplies the salivary glands.[23] Hypotension (10%) and bradycardia (2%) were the other associated side-effects observed with the use of clonidine. We also observed few cases of drowsiness (12%), headache (4%) and dizziness (4%) with gabapentin in our study, which clinically did not warrant any treatment.

CONCLUSION

We conclude that oral clonidine 200 μg when given 90 min before anesthesia, provides good attenuation of hemodynamic response to laryngoscopy and intubation as compared with oral gabapentin (900 mg), which also fairly obtunded the hypertensive response, but not the tachycardiac response. Clonidine also provided better sedation and anxiolysis when compared with gabapentin.

REFERENCES

1. Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon the heart. Surg Gynecol Obstet 1940;70:157-62.
2. King BD, Harris LC Jr, Greifenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology 1951;12:556-66.
3. BURSTEIN CL, Lopinto FJ, Newman W. Electrocardiographic studies during endotracheal intubation. I. Effects during usual routine technics. Anesthesiology 1950;11:224-37.
4. Forbes AM, Dally FG. Acute hypertension during induction of anesthesia and endotracheal intubation in normotensive man. Br J Anaesth 1970;42:618-24.
5. Abou-Madi MN, Keszler H, Yacoub JM. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous doses of lidocaine. Can Anaesth Soc J 1977;24:12-9.
6. Safwat AM, Reitan JA, Misle GR, Hurley EJ. Use of propranolol to control rate-pressure product during cardiac anesthesia. Anesth Analg 1981;60:732-5.
7. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. Anesth Analg 1979;58:116-9.
8. Davies MJ, Cronin KD, Cowie RW. The prevention of hypertension at intubation. A controlled study of intravenous hydrallazine on patients undergoing intracranial surgery. Anesthesia 1981;36:147-51.

9. Fassoulaki A, Kaniaris P. Intranasal administration of nitroglycerine attenuates the pressor response to laryngoscopy and intubation of the trachea. Br J Anaesth 1983;55:49-52.
10. Puri GD, Batra YK. Effect of nifedipine on cardiovascular responses to laryngoscopy and intubation. Br J Anaesth 1988;60:579-81.
11. Coleman AJ, Jordan C. Cardiovascular responses to anesthesia. Influence of beta-adrenoreceptor blockade with metoprolol. Anesthesia 1980;35:972-8.
12. Cucchiara RF, Benefiel DJ, Matteo RS, DeWood M, Albin MS. Evaluation of esmolol in controlling increases in heart rate and blood pressure during endotracheal intubation in patients undergoing carotid endarterectomy. Anesthesiology 1986;65:528-31.
13. Miller DR, Martineau RJ, O'Brien H, Hull KA, Oliveras L, Hindmarsh T, et al. Effects of alfentanil on the hemodynamic and catecholamine response to tracheal intubation. Anesth Analg 1993;76:1040-6.
14. Ghignone M, Quintin L, Duke PC, Kehler CH, Calvillo O. Effects of clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. Anesthesiology 1986;64:36-42.
15. O'Hare R, McAtamney D, Mirakhur RK, Hughes D, Carabine U. Bolus dose remifentanil for control of haemodynamic response to tracheal intubation during rapid sequence induction of anesthesia. Br J Anaesth 1999;82:283-5.
16. Westfall TC, Westfall DP. Adrenergic agonist and antagonist. In: Bruton LL, Lazo JS, Parker JS, editors. Goodman and Gilman's the Pharmacological Basis of Therapeutics. 11th ed. USA: McGraw-Hill; 2006. p. 255-6.
17. Taylor CP. Gabapentin mechanism of action. In: Levy RH, Mattson RH, Meldrun BS, Percucca E, editors. Antiepileptic Drugs. 5th ed. Philadelpheia: Lippincott Williams & Wilkins; 2002. p. 320-34.
18. Fassoulaki A, Melemeni A, Paraskeva A, Petropoulos G. Gabapentin attenuates the pressor response to direct laryngoscopy and tracheal intubation. Br J Anaesth 2006;96:769-73.
19. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: Study with intravenous midazolam. J Clin Psychopharmacol 1990;10:244-51.
20. Raval D, Mehta M. Oral clonidine premedication for attenuation of haemodynamic response to laryngoscopy and intubation. Indian J Anaesth 2002;46:124-9.
21. Memiş D, Turan A, Karamanlioğlu B, Seker S, Türe M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol 2006;23:686-90.
22. Denlinger JK, Ellison N, Ominsky AJ. Effects of intratracheal lidocaine on circulatory responses to tracheal intubation. Anesthesiology 1974;41:409-12.
23. Faheim SM, Hassanin M, Hafez AA. Gabapentin versus clonidine oral premedication for attenuation of pressor response to laryngoscopy and endotracheal intubation. Tanta Med Sci J 2008;3:12-20.
24. Ménigaux C, Adam F, Guignard B, Sessler DI, Chauvin M. Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. Anesth Analg 2005;100:1394-9.
25. Rorarius MG, Mennander S, Suominen P, Rintala S, Puura A, Pirhonen R, et al. Gabapentin for the prevention of postoperative pain after vaginal hysterectomy. Pain 2004;110:175-81.
26. Marashi SM, Ghafari MH, Saliminia A. Attenuation of hemodynamic responses following laryngoscopy and tracheal intubation — Comparative assessment of clonidine and gabapentin premedication. Middle East J Anesthesiol 2009;20:233-7.

New features on the journal's website

Optimized content for mobile and hand-held devices
HTML pages have been optimized of mobile and other hand-held devices (such as iPad, Kindle, iPod) for faster browsing speed.
Click on **[Mobile Full text]** from Table of Contents page.
This is simple HTML version for faster download on mobiles (if viewed on desktop, it will be automatically redirected to full HTML version)

E-Pub for hand-held devices
EPUB is an open e-book standard recommended by The International Digital Publishing Forum which is designed for reflowable content i.e. the text display can be optimized for a particular display device.
Click on **[EPub]** from Table of Contents page.
There are various e-Pub readers such as for Windows: Digital Editions, OS X: Calibre/Bookworm, iPhone/iPod Touch/iPad: Stanza, and Linux: Calibre/Bookworm.

E-Book for desktop
One can also see the entire issue as printed here in a 'flip book' version on desktops.
Links are available from Current Issue as well as Archives pages.
Click on View as eBook