Rapid inhalation induction with halothane-nitrous oxide for myasthenic patients

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Rapid inhalation induction (RII) was successfully employed for patients without myopathy. Inhalatory agents can be used for anaesthetic induction of myasthenics, avoiding the use of neuromuscular blocking agents. We studied the use of RII in 15 myasthenics (MG) and in 15 normal subjects (nMG), measuring induction time (TI), cardiorespiratory effects, complications, and evaluated the patient's reaction to RII. The patients were submitted to elective transsternal thymectomy (MG) and gynaecological or lower abdominal surgery (nMG). No premedication was used. After preoxygenation, RII was started using a mixture of 4% halothane and O_2:N_2O (1:2). They performed three vital capacity breaths, followed by normal spontaneous ventilation. The TI was assessed by timing the loss of verbal command (TLVC) and loss of eyelid reflex (TLER). Systolic and diastolic pressure, pulse oximetry, capnometry, respiratory rate (RR) and heart rate (HR) were measured during induction at each minute, for four minutes. After a postanaesthetic questionnaire only two normal subjects did not like the RII technique. Mean values for TLVC and TLER were 67 and 73 sec for MG and 64 and 69 sec for nMG, respectively. There was no change in HR for MG or blood pressure. The RR increased in both groups, but no change in $P_{ET}CO_2$ was observed; S_aO_2 was >97%. In conclusion, RII can be performed rapidly and safely in myasthenic patients and is a technique that should be considered for the induction of anaesthesia in myasthenic patients.

L'induction rapide par inhalation (IIR) a été utilisée avec succès chez des patients non myasthéniques. On peut administrer des inhalatoires pour l'induction de l'anesthésie chez le myasthénique et éviter ainsi d'utiliser des myorésolutifs. Nous avons comparé l'IIR chez 15 myasthéniques (MG) et 15 sujets normaux (nMG). Nous avons mesuré le temps d'induction (TI), le retentissement cardiovasculaire, les complications et la réaction du patient à ce type d'induction. Les MG ont subi une thymectomie programmée trans-sternale et les nMG une chirurgie programmée abdominale basse ou gynécologique. Aucun des patients n'a reçu de prémédication. Après préoxygénation, l'IIR est initiée avec un mélange d'halothane 4% et de O_2:N_2O (1:2). Les patients ont exécuté trois capacités vitales et poursuivi en respirant normalement. Le TI a été évalué par la perte de la réponse aux ordres et du réflexe palpébral. A l'induction, la TA systolique et diastolique, l'oxymétrie pulsée, la capnométrie, la fréquence respiratoire (Fr) et cardiaque (Fc) ont été mesurés à la minute pendant quatre minutes. Au questionnaire postanesthésique, deux des malades (nMG) seulement ont répondu qu'ils n'avaient pas aimé la technique de IIR. Les valeurs moyennes pour la perte de réponse aux ordres et du réflexe palpébral pour les MG étaient de 67 et 73 sec et pour les nMG, de 64 et 69 sec. La Fc et la TA n'ont pas changé dans le groupe MG. La Fr a augmenté dans les deux groupes, mais on n'a pas noté de changement de la $P_{ET}CO_2$; la SaO_2 était >97%. Pour conclure, la IIR est réalisée rapidement et en toute sécurité chez les myasthéniques et représente une technique qui mérite considération chez ces patients.

Key words
ANAESTHESIA: inhalation;
ANAESTHETICS, VOLATILE: halothane;
ANAESTHETIC TECHNIQUES: induction;
COMPLICATIONS: myasthenia gravis.

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Of the anaesthetic induction options available for myasthenic patients, a technique using only inhalational agents provides muscle relaxation and avoids complications associated with the use of neuromuscular blocking drugs in these patients.[1,2] It may also produce adequate anaesthesia depth for tracheal intubation.

Anticholinesterase treatment may complicate the anaesthetic management of myasthenics, and may increase

vagal responses.[2-5] From our experience of 132 myasthenic patients anaesthetized since 1983, we have observed that when we have used a classical inhalational anaesthetic induction technique, increasing the anaesthetic concentration gradually, it may take longer than ten minutes to produce anaesthesia of sufficient depth to allow tracheal intubation. Similar observations have been described by others.[6]

A rapid inhalational induction (RII) technique using 4% halothane, with or without nitrous oxide, has been described as safe, rapid and useful for patients without myopathy.[7-12] Our aim was to compare the use of RII in myasthenic patients with that in normal subjects by evaluating the anaesthesia induction time, the effects on the cardiorespiratory system and the incidence of undesirable effects.

Methods

After institutional Ethics Committee approval and patients' informed consent 30 adult subjects were studied, 15 myasthenic - myasthenic group (MG), and 15 non myasthenic patients - non myasthenic group (nMG). Sex distribution for MG was six males and nine females and for nMG was one and 14 respectively. They were scheduled to undergo elective thymectomy (MG) gynaecological or lower abdominal surgery (nMG).

Myasthenics were classified as Osserman's class IIA or IIB.[13] Six were class IIA myasthenics presenting with generalized mild muscle weakness and the remaining nine were class IIB complaining of generalized moderate weakness, and/or bulbar disfunction. All were receiving oral pyridostigmine (four patients, 240 mg per day; nine, 180 mg per day and two, 120 mg per day). Ten were receiving oral prednisone (six were taking 80 mg and four, 40 mg per day). Anticholinesterase and steroid drugs were withdrawn on the morning of surgery. Preoperative spirometry and arterial blood gas analysis were normal for all myasthenics. Patients of the nMG group were free of pulmonary disease and had normal thorax *x*-rays. No premedication was used, and no patient was receiving other medication. Before induction of anaesthesia, myasthenic patients received bolus hydrocortisone *iv* equivalent to the withdrawn oral morning steroid dose.

The induction technique was explained during the preanaesthetic visit. Before induction, all patients received preoxygen for three minutes with an O_2 flow of 10 $L \cdot min^{-1}$ using a separate circuit. Meanwhile, the circle system of the anaesthesia machine was saturated with an 8 $L \cdot min^{-1}$ flow of 4% halothane, and O_2–N_2O (1:2) mixture. Rapid inhalation induction was started by asking the patient to perform three vital capacity breaths (VCB), inhaling the anaesthetic mixture from the circle circuit through a well-fitted facial mask.[7-12]

TABLE I Time for loss of verbal command (TLVC) and time for loss of eyelid reflex (TLER), both in seconds, for myasthenic and non-myasthenic groups

	Non-myasthenic	*Myasthenic*
TLVC (sec)	64 (18)	67 (27)
TLER (sec)	69 (17)	73 (27)

Mean values (SD).

Respiratory rate (RR), heart rate (HR), non-invasive systolic (SBP) and diastolic blood pressure (DBP), pulse oximetry (SpO_2, Novametrix 550) and capnometry ($PETCO_2$, Novametrix 1260) were measured before (except for $PETCO_2$) and during induction, every minute, for four minutes. Induction time (TI) was assessed by measuring the time from the first of the three VCB, and the loss of response to verbal command (TLVC) and the loss of the eyelid reflex (TLER). The TLVC was evaluated by asking patients to open their eyes. The TLVC and TLER were assessed every ten seconds throughout the anaesthetic induction. At the same time, undesirable reactions, such as cough or airway obstruction, and the cardiorespiratory variables were recorded during the four minutes. After the fourth minute, the halothane concentration was decreased to 2%. The induction was completed by manual ventilation and the trachea was intubated after clinical assessment of jaw muscle relaxation. Anaesthesia was maintained with halothane, nitrous oxide and oxygen. On the day after surgery the patients answered an objective questionnaire to determine (1) how many of the three VCB they could remember; (2) the patients' evaluation of the anaesthetic induction; and (3) if the patients would accept the RII technique again. Data were analysed using ANOVA associated with Newman-Keuls test to compare, within each group, the cardiorespiratory variables obtained before RII with those recorded one, two, three and four minutes after RII. Unpaired t test and Fisher's exact test were used to compare parametric and non-parametric data, respectively.

Results

The mean values (SD) for age and weight were similar in both groups: 31.1 (7.1) yr and 54.9 (7.7) kg for nMG group, and 34.8 (11) yr and 63 (23.2) kg for MG group.

There were no differences in induction times between groups (Table I).

Haemodynamic variables

Non-myasthenics demonstrated a decrease in diastolic pressure at all four measurement times and a decrease in systolic pressure at three and four minutes. Heart rate increased at one and two minutes (Table II and Figure 1). Myasthenics showed a decrease of systolic pressure

TABLE II Haemodynamic data before and during RII for nMG patients

Time	SBP (mmHg)	DBP (mmHg)	HR (bpm)
Before RII	121.9	72.4	78.8
	(13.2)	(8.5)	(14.8)
+1 min	118.6	67.7†	90.2*
	(17.3)	(7.7)	(16.8)
+2 min	116.2	67.8†	89.0†
	(15.1)	(9.4)	(9.6)
+3 min	108.5*	66.4†	81.8
	(11.4)	(8.8)	(9.4)
+4 min	108.9*	64.3*	75.1
	(11.7)	(11.9)	(11.0)

Mean values (SD).
Systolic blood pressure (SBP), diastolic pressure (DBP) and heart rate (HR).
*$P < 0.05$ and † $P < 0.01$ compared with before RII.

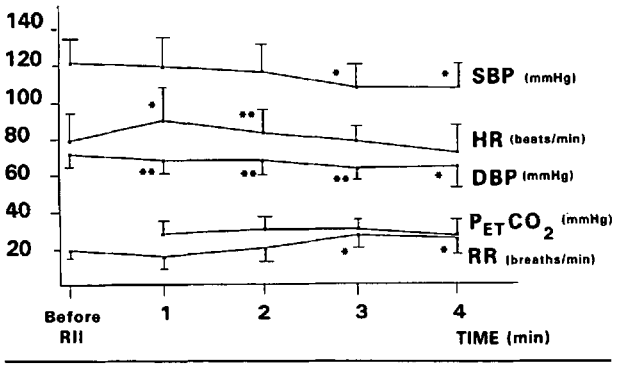

FIGURE 1 Haemodynamic and respiratory data befre and during RII for nMG patients. Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiratory rate (RR), and end tidal CO_2 ($PETCO_2$). *$P < 0.05$ and **$P < 0.01$ compared with before RII.

at three and four minutes of the study (Table III and Figure 2). No changes in heart rate were observed in myasthenics.

Respiratory variables

SpO_2 decreased in both groups at three and four minutes, although always remaining >97% (Tables IV and V). No changes in $PETCO_2$ were recorded in both groups (Tables IV and V). RR increased at three and four minutes for nMG and at two, three and four minutes for MG (Tables IV and V; Figures 1 and 2).

During the study five myasthenic and three non-myasthenic patients developed airway obstruction which required the use of a Guedel oropharyngeal airway. Coughing was observed in two myasthenic and in one non-myasthenic. In five patients (three myasthenic) apnoea (>15 sec without respiratory movements) was ob-

TABLE III Haemodynamic data before and during RII for MG patients

Time	SBP (mmHg)	DBP (mmHg)	HR (bpm)
Before RII	132.2	82.9	80.6
	(20.9)	(13.9)	(16.4)
+1 min	129.1	80.8	87.0
	(17.7)	(13.8)	(10.9)
+2 min	125.6	78.0	88.3
	(19.5)	(12.8)	(10.1)
+3 min	120.4*	74.0	84.8
	(19.0)	(19.7)	(14.1)
+4 min	118.0*	74.0	78.2
	(17.6)	(13.9)	(13.6)

Mean values (SD).
Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR).
*$P < 0.01$ compared with before RII.

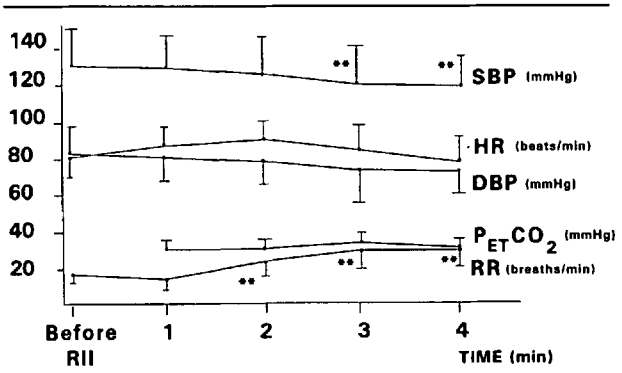

FIGURE 2 Haemodynamic and respiratory data before and during RII for MG patients. Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiratory rate (RR), and end tidal CO_2 ($PETCO_2$). **$P < 0.01$.

TABLE IV Respiratory data before and during RII for nMG patients. Respiratory rate (RR), oxygen arterial saturation (SpO_2) and end tidal CO_2 ($PETCO_2$).

Time	RR (bpm)	SpO_2 (%)	$PETCO_2$ (mmHg)
Before RII	18.0	99.6	-
	(3.7)	(0.6)	-
+1 min	14.5	99.5	27.0
	(5.5)	(0.8)	(6.3)
+2 min	17.8	99.2	30.7
	(5.3)	(1.1)	(6.1)
+3 min	25.4*	99.1†	29.3
	(5.6)	(0.8)	(5.9)
+4 min	24.0*	98.6*	25.7
	(7.7)	(1.0)	(5.0)

Mean values (SD).
*$P < 0.05$ and † $P < 0.01$ compared with before RII.

TABLE V Respiratory data before and during RII for MG patients Repiratory rate (RR), oxygen arterial saturation (SpO_2) and end tidal CO_2 ($PETCO_2$)

Time	*RR (bpm)*	*SpO_2 (%)*	*$PETCO_2$ (mmHg)*
Before RII	17.6	99.7	–
	(5.5)	(0.6)	–
+1 min	13.5	99.5	30.1
	(6.0)	(0.5)	(4.7)
+2 min	23.2*	99.4	30.1
	(8.5)	(0.5)	(5.2)
+3 min	28.0†	98.4†	33.2
	(9.5)	(1.1)	(4.9)
+4 min	29.5†	98.2†	30.2
	(9.9)	(1.5)	(5.5)

Mean values (SD).
†$P < 0.01$ compared to before RII.

TABLE VI Number of vital capacity breath (VCB) remembered

Number of VCB remembered	*Myasthenic*	*Non-myasthenic*
1	1	0
2	12	12
3	2	3

served. Excitatory movements of the extremities occurred in five myasthenic and in four non-myasthenic patients. None of these undesirable reactions precluded the completion of anaesthetic induction or of tracheal intubation. One myasthenic patient developed ventricular extrasystoles which reverted spontaneously to sinusal rhythm. This occurred after the fourth minute of the study, when halothane 2% was being used. All tracheal intubations were performed without difficulty, within five minutes after the fourth minute of the study. In all patients the trachea was extubated at the end of the procedure.

The number of remembered VCB is shown in Table VI. The median of the remembered inspirations was two in both groups. All myasthenics classified the anaesthetic technique as good and they would not oppose its use again. Twelve non-myasthenic patients classified RII as good, and three as bad. Of the latter, two would oppose its use again. No laryngotracheal complication was recorded at the post-anaesthetic visit.

Discussion

Unpredictable response to muscle relaxants administration is well recognized in patients with myasthenia gravis. Although atracurium has been used in *m gravis*, there is an absolute indication for careful neuromuscular transmission monitoring during surgery to titrate the dose of the neuromuscular blocking agent.[2] Baraka has described the use of a deep inhalation anaesthesia technique either for tracheal intubation or for the anaesthetic maintenance of myasthenics.[2]

A rapid inhalation induction anaesthetic technique was successfully described in subjects without neuromuscular disease. Two techniques of RII have been described, using one or three VCBs. They produced a deep level of anaesthesia rapidly for tracheal intubation, avoiding the unpleasant experience of inhaling increasingly higher concentrations of volatile agents.[7-12] We chose the three VCB method because it seemed to produce a more rapid induction.[9]

The analysis of the anaesthetic induction times (TLVC and TLER) indicates that the myasthenic patients reached a similar anaesthetic depth in a similar time as normal subjects. Both groups presented values of TLVC ad TLER similar to studies when RII was used in patients without myopathy.[7-11] When the classical inhalation technique was performed previously in myasthenics, using enflurane at increasing concentrations, the effects on heart rate and arterial blood pressure were almost negligible, and the observed period for anaesthesia induction, ranged from five to ten minutes.[6]

Both groups presented similar behaviour in respect to circulatory and respiratory variables. The RII provoked similar haemodynamic changes in both groups. The observed tendency towards a decrease in arterial blood pressure, although rendering normal mean values of blood pressure, is an expected side effect of halothane. Heart rate did not decrease in either group.

Florence *et al.* found when studying the effects of two intravenous anaesthetic drugs in myasthenic patients, that patients developed 54.6% of transient bradycardia. Approximately 30% of their patients presented arterial hypotension.[5] They stated that bradycardia and arterial hypotension were expected, as a low resting heart rate is common in myasthenic patients as a result of residual muscarinic action of the chronic anticholinesterase therapy. From our circulatory findings in the myasthenic group we suggest that, despite using high concentrations of anaesthetic agent, we did not find an interaction between halothane and chronic anticholinesterase therapy.

In both groups RR increased, but SaO_2 and $PETCO_2$ were within the normal range showing that gas exchange was not affected during the RII.

We do not consider the use of 4% halothane a hindrance for the use of the technique. In both groups, the median of the vital capacity breaths remembered while such a percentage was being used, was two. This is very close to the three VCB required by the technique.[9] Even with this high index of recall in patients in the high halothane concentration group, only 6.7% of patients (2 of 30) would oppose the use of RII to induce anaesthesia

if necessary. Both patients were from the nMG group. Myasthenic patients often consider thymectomy as the last chance for their cure. From this point of view, they could be more prone to accept the whole procedure, anaesthesia included, than the nMG patients.

Chronic anticholinesterase therapy can be associated with increase in salivary and bronchial secretion.[2-4] This could predispose to a larger incidence of cough or airway irritation during inhalatory technique. However, we observed no difference regarding these complications when we compared both groups.

Although both groups had a similar incidence of complications, in three myasthenic patients we found difficulty in the maintenance of the airway throughout the induction. All three were moderately obese and presented with cough and airway obstruction. Obesity can make the management of the airway difficult, imposing an obstacle to the establishment of a rapid and adequate depth of anaesthesia.

Halothane has a variable effect on the neuromuscular activity in MG patients. About one third of the MG patients presented no sign of muscular fading induced by halothane-N_2O anaesthesia.[14] For this reason, the speed of inducing muscle relaxation invariably in myasthenic patients is considered.

Recently sevoflurane has proved to be superior to halothane when RII was used in normal patients.[12] The onset is faster and less irritating than halothane and this may be another option for RII of patients with *m. gravis*.

In summary, we used the RII safely in myasthenic subjects for thymectomy, to avoid the risk of neuromuscular blocking agents. We did not find cardiorespiratory effects or pharmacological interaction between halothane and anticholinesterase therapy. The time for losing consciencness was within acceptable range. We believe that RII can be a technique to be considered for anaesthetic induction in myasthenic patients.

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