THE INFLUENCE OF PREMEDICATION WITH NARCOTICS AND BELLADONNA ON OXYGENATION IN CARDIAC SURGERY PATIENTS*

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PREMEDICATION with narcotics and/or belladonna drugs has been shown by some authors^{1,2,3} to lead to a significant decrease in arterial oxygen tension. Others have suggested that oxygenation is not compromised with combinations of barbiturate and belladonna⁴ (pentobarbital and atropine), barbiturate alone⁵ (pentobarbital) or narcotic and belladonna⁴ (morphine and scopolamine). Although some studies have shown that atropine caused no significant change in oxygenation in healthy volunteers,⁶ others have demonstrated that atropine decreased arterial oxygen saturation significantly.^{2,7} The present study is an attempt to re-evaluate the effects of narcotic and belladonna premedication on oxygenation in ambulatory patients prior to cardiac surgery, by measuring arterial oxygen tensions and alveolar-arterial gas tension gradients.

MATERIALS AND METHODS

Fifteen patients were studied. They were clinically free of chest disease or overt uncontrolled congestive heart failure, with the exception of one (case No. 7). Thirteen were candidates for coronary artery bypass graft procedures for refractory or intractable angina pectoris; one (No. 7) was a candidate for mitral and aortic valve replacement because of refractory congestive heart failure and the remaining one (No. 11) was a candidate for aortic valve replacement. The clinical details are shown in Table I.

All patients were seen 24 hours preoperatively. When the end-tidal carbon dioxide concentration had been constant for 10 to 15 minutes, blood samples were taken from the radial or femoral artery with the patient in the supine position. The patients breathed room air for 10 to 15 minutes, the samples were taken and the sequence was repeated using 100 per cent oxygen. The patients were premedicated on the day of operation with morphine (approximately 0.15 mg/kg) or meperidine (approximately 15 mg/kg) and either atropine or scopolamine as shown in Table I. Arterial samples were collected from brachial artery catheters one hour after premedication while the patients were awake and supine. They breathed room air for 10 to 15 minutes and then 100 per cent oxygen for 10 to 15 minutes. In all instances the end-tidal carbon dioxide concentrations were maintained for at least 10 to 15 minutes.

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TABLE I
DETAILS OF PATIENTS STUDIED

Patient	Age	Sex	Weight (Kg)	Premedication (mg)	Surgical Procedure
1	58	M	67.8	Morphine 15.0 + Atropine 0.6	Coronary Artery Bypass (CABG)
2	51	M	87.5	Morphine 15.0 + Atropine 0.6	CABG
3	56	M	70.3	Morphine 15.0 + Atropine 0.6	CABG
4	49	M	84.0	Morphine 15.0 + Atropine 0.6	CABG
5	51	M	71.5	Meperidine 100 + Atropine 0.6	CABG
6	10	M	80.0	Morphine 15.0 + Atropine 0.6	CABG
7	61	F	38.2	Morphine 15.0 + Scopolamine 0.4	Mitral & Aortic Valve Replace.
8	43	M	82.2	Meperidine 100 + Scopolamine 0.6	CABG
9	45	M	71.5	Morphine 15.0 + Scopolamine 0.4	CABG
10	47	M	66.6	Morphine 10.0 + Scopolamine 0.4	CABG
11	59	M	63.5	Morphine 10.0 + Atropine 0.6	Aortic valve replacement
12	54	M	63.5	Morphine 15.0 + Atropine 0.6	CABG
13	48	M	75.5	Morphine 15.0 and Atropine 0.6	CABG
14	40	M	73.8	Morphine 10.0 + Scopolamine 0.4	CABG & resect. ventric. aneurysm
15	61	M	68.0	Morphine 15.0 + Atropine 0.6	CABG
Means	50.4		70.9

FIGURE 1. Rahn-Otis End-Tidal Sampler (S) with Inspired (I) and Expired (E) collection bags and plastic tubing (T) which connects to the meters.

Collection of end-expiratory and mixed expiratory gas samples was done with a Rahn-Otis End-Tidal Sampler and a baffled (expiratory) 15-litre rubber bag as shown in Figure 1. Continuous measurements of the end-expiratory and mixed expired gases were obtained using a Beckman CO₂ Analyzer and a Beckman Oxygen Analyzer connected in series. A Beckman micro-catheter sample pump moved the 200 cc sample through a constant length of plastic tubing from the End-Tidal Sampler or expiratory bag through the meters. The meters were precalibrated with gases analyzed by the Scholander method.

TABLE II
ARTERIAL OXYGEN TENSIONS AT LOW AND HIGH ALVEOLAR OXYGEN LEVELS

Patient	PaO ₂ on Room Air (mmHg)		PaO ₂ on 100 per cent Oxygen (mmHg)	
	a	b	a	b
1	75.5	97.0	350	380
2	96.5	69.2	400	308
3	93.5	105.2	540	402
4	75.2	85.5	525	590
5	89.2	95.0	380	440
6	92.0	90.0	610	405
7	104.2	105.0	505	365
8	104.0	100.0	585	565
9	105.2	105.0	548	500
10	105.2	93.0	545	460
11	89.0	99.0	510	555
12	93.8	98.0	420	550
13	75.5	96.0	470	450
14	93.5	85.5	545	540
15	80.0	85.0	440	480

a = before premedication.

b = after premedication.

Tidal volumes were measured preoperatively with a Collins 9 litre spirometer while a Wright's Respirometer, precalibrated with the Collins spirometer, was used in the operating room.

Blood samples were taken in heparinized glass syringes, immediately iced and placed in a refrigerator at 4 degrees Centigrade ($^{\circ}$ C). Analysis was done within 30 minutes. Blood gas tensions and pH were measured with a Radiometer pH/Blood Gas Monitor and Microelectrode Unit at 37 $^{\circ}$ C. Calibration of this apparatus was done before and after each set of determinations. Severinghaus correction factors for body temperature and blood pH were utilized when determining per cent saturation of haemoglobin (SaO₂) from the arterial oxygen tension.⁸

The mean end-tidal oxygen and carbon dioxide concentrations of the respiratory cycle corresponding to the blood sampling period were assumed to equal the alveolar oxygen and alveolar carbon dioxide concentrations.⁹ These values were used to calculate the Alveolar-arterial oxygen gradients (A-aDO₂) and the arterial-Alveolar carbon dioxide gradients (a-ADCO₂) after allowance was made for ambient barometric and water vapour pressures. Dead space-tidal volume ratios (V_D/V_T) were based on the Riley modification of the Bohr equation¹⁰ substituting arterial carbon dioxide (PaCO₂) for the "ideal" alveolar Pco₂. The statistical evaluations were based on the paired two-tail t-test ("Student t-test").

RESULTS

Arterial oxygen tension was generally increased after premedication when the patients were breathing room air and 100 per cent oxygen, as shown in Tables II and III. There was wide individual variation (see Table II) in the PaO₂ when the patients were breathing 100 per cent oxygen. Alveolar-arterial oxygen gradients (A-aDO₂) of subjects breathing room air were decreased after premedication,

TABLE III
COMPARISON OF MEASUREMENTS MADE BEFORE AND AFTER PREMEDICATION AT LOW AND HIGH ALVEOLAR OXYGEN LEVELS

	P _A O ₂ mmHg	P _a O ₂ mmHg	SaO ₂ * %	A-aDO ₂ mmHg	P _a CO ₂ mmHg	P _A CO ₂ mmHg	a-ADCO ₂ mmHg	P _a H	V _D /V _T	V _T ml BTPS
(a) 20.95% oxygen (room air)										
i. before										
mean	112.7	90.8	97.15	21.8	34.2	31.5	2.70	7.418	36.5	689
(sd)	(3.66)	(2.84)	(0.42)	(4.62)	(1.52)	(1.43)	(0.76)	(0.015)	(2.5)	(80.1)
ii. after										
mean	112.7	94.0	97.0	18.0	38.4	35.6	2.85	7.373	36.1	601
(sd)	(2.78)	(2.55)	0.32	(4.08)	(1.10)	(0.95)	(0.71)	(0.009)	(2.6)	(58.9)
P	NS	0.01	NS	0.01	0.01	0.01	NS	0.01	NS	(0.01)
(b) 100% oxygen										
i. before										
mean	652.5	492.0	>98.8	160	34.9	33.0	1.90	7.418	45.8	739
(sd)	(10.3)	(20.7)	—	(22.2)	1.45	(1.43)	(0.55)	(0.011)	(2.2)	(77.7)
ii. after										
mean	634.1	466.0	>98.8	168	39.4	36.5	2.90	7.376	45.7	582
(sd)	(9.25)	(24.0)	—	(26.1)	(1.09)	(0.84)	(0.40)	(0.010)	(3.0)	(51.0)
P	0.01	0.01	—	NS	0.01	0.01	0.01	0.01	NS	0.01

*SaO₂-arterial oxygen saturation.

while A-aDO₂ remained the same with 100 per cent oxygen and premedication. Alveolar and arterial carbon dioxide tensions (PaCO₂ and PaCO₂ respectively) showed slight hyperventilation prior to premedication. Large tidal volumes (V_T) of 600 to 700 ml were the rule in this study. Arterial-alveolar carbon dioxide gradients (a-ADCO₂) were significantly increased with premedication and 100 per cent oxygen. Arterial pH (p_aH) was unchanged with changes in inspired oxygen but significantly decreased with premedication. Premedication was followed by PaCO₂ values within the range of normal (38.4 to 39.4 mm Hg) suggesting that ventilation was not depressed by the doses of narcotics used in these patients. Significant increases in dead space/tidal volume ratios (V_D/V_T) occurred with changes in inspired oxygen. Premedication itself did not significantly alter the V_D/V_T ratios.

DISCUSSION

The combination of narcotic and belladonna premedication has not been recently studied in cardiac surgery patients. The reason for this lack of study may be the possibility that atropine or scopolamine may cause detrimental arrhythmias and onset of angina or congestive cardiac failure.¹¹ Combinations of these drugs are commonly used in this hospital and a ready pool of subjects was available. Electrocardiographic monitoring revealed no arrhythmias 30 to 60 minutes after premedication, nor did any subject admit to any discomfort after premedication.

Ambulatory healthy volunteers given atropine intravenously do not get a significant decrease in PaO₂ or SaO₂.⁶ Other studies have shown hypoxaemia in patients given either subcutaneous or intramuscular atropine^{2,7} or narcotic-belladonna combinations.⁸ Some of these studies were based on measurement of oxygen saturation^{2,3} and omitted arterial samples prior to premedication. These two factors could yield significant errors. A more recent study including arterial samples 24 hours preoperatively showed a significant decrease in PaO₂ and SaO₂ when a combination of meperidine, promethazine and pentobarbital was used.⁶ Another recent study has shown the preoperative oxygenation was maintained when morphine and scopolamine were used.⁴ Pulmonary gas exchange was found adequate in this latter study⁴ and alveolar-arterial gas tensions were not assessed.

Significant hypoxaemia did not occur in this study. Possible causes of hypoxaemia in these subjects include changes in ventilation or physiological dead space, changes in perfusion, changes in the matching of ventilation to perfusion ($\dot{V}/\dot{Q}$) and changes in right-to-left shunting or venous admixture. The presence of a significant decrease of A-aDO₂ gradients on room air and the lack of an increase of A-aDO₂ gradients on 100 per cent oxygen effectively eliminates right to left shunts or venous admixture as a possible cause of hypoxaemia¹² after premedication. The presence of slight but significant ventilation-perfusion ($\dot{V}/\dot{Q}$) abnormalities is supported by the a-ADCO₂ gradients^{13,14} which were increased significantly above the accepted normal value of 1 mm Hg¹⁵ and the slightly increased alveolar oxygen tensions¹⁹ when the subjects were breathing room air. These gradients confirm that distribution of ventilation is changed with premedication, but the lack of increase in A-aDO₂ suggests that the magnitude of these $\dot{V}/\dot{Q}$ changes must be limited. Further support for the minimal changes in $\dot{V}/\dot{Q}$ is shown by the per-

sistence of the V_D/V_T ratio increase which occurs with 100 per cent oxygen¹⁷ despite the narcotic-belladonna premedication.¹⁸

The age distribution and the ambulatory status of the subjects in this study are important determinants of oxygenation. Narcotic and belladonna premedication in the older and/or bedridden patient may predispose to atelectasis and shunting secondary to inadequate "sighs," inadequate clearing of secretion and inactivity.^{19,20} All these factors may tend to increase atelectasis and give rise to increased shunting or $\dot{V}/\dot{Q}$ abnormalities with hypoxaemia as the end result.^{19,20,21} Large tidal volumes without "sighs," as seen in this study, tend to prevent atelectasis²⁰ and thus prevent shunting and hypoxaemia.

CONCLUSION

This study shows that combined narcotic-belladonna premedication in the ambulatory cardiac patient will maintain adequate arterial oxygen tension and unchanged arterial oxygen saturation despite slight increases in ventilation-perfusion abnormalities after premedication. Compromised oxygenation is probably uncommon in ambulatory cardiac patients premedicated with judicious doses of narcotic-belladonna combinations.

SUMMARY

The influence on oxygenation of premedication with mixtures of narcotic and belladonna drugs was assessed in 15 cardiac surgery patients. With the subjects breathing room air and then 100 per cent oxygen, comparisons were made of pre-operative measurements of arterial oxygen tension, carbon dioxide tension and pH. The same parameters were measured one hour after premedication using morphine 0.15 mg/kg or meperidine 1.5 mg/kg in combinations with atropine 0.6 mg or scopolamine 0.4 or 0.6 mg. End-tidal carbon dioxide and oxygen tensions were measured in all cases to evaluate alveolar-arterial oxygen ($A-aDO_2$) and carbon dioxide gradients ($a-ADCO_2$). The results show a significant increase in PaO_2 after premedication, with a slight decrease in pH and no significant change in arterial oxygen saturation. $A-aDO_2$ gradients did not increase significantly with premedication suggesting that increased right to left shunting did not occur. Changes in $a-ADCO_2$ ratios indicated slight but significant ventilation-perfusion changes but they were not large enough to decrease arterial oxygenation. Dead space tidal volume ratios (V_D/V_T) did not change after premedication but did alter markedly with increased oxygen. All subjects exhibited large tidal volumes and this may have been a factor in prevention of shunting by prevention of atelectasis. The ages and ambulatory status of this group were key factors.

This study shows that narcotic-belladonna premedication does not compromise oxygenation of the ambulatory cardiac surgery patient when used in judicious doses.

RÉSUMÉ

Nous avons évalué, chez 15 malades devant subir une chirurgie cardiaque, les effets de la prémédication aux narcotiques et à la belladone. Nous avons mesuré,

en cours d'opération, la tension d'oxygène artérielle, la tension de CO_2 et le pH alors que les malades respiraient l'air de la salle et, plus tard, de l'oxygène à 100 pour cent et nous avons comparé les données. Nous avons mesuré les mêmes paramètres une heure après la prémédication consistant en morphine 0.15 mgs/Kg ou en mepéridine 1.5 mgs/Kg associé l'atrophine 0.6 mgs scopolamine 0.4-0.6 mg. Nous avons mesuré les tensions d'oxygène et de CO_2 de fin d'expiration chez tous les malades pour évaluer les gradients d'oxygène et de CO_2 alvéolo-artériels ($A-a\text{DO}_2$) et ($A-\text{ADCO}_2$). Les résultats ont démontré une augmentation importante de la PaO_2 après la prémédication et une légère diminution du pH et peu de changement de la saturation artérielle en oxygène. Le gradient ($A-a\text{DO}_2$) n'a pas changé de façon importante après la prémédication faisant penser qu'il n'est pas survenu d'augmentation de shunt de droite à gauche. Les changements des rapports ($A-\text{ADCO}_2$) démontrent de légers mais significatifs changements mais pas assez importants pour diminuer l'oxygénation artérielle. Les rapports espace mort/air courant (V_D/V_T) n'ont pas changé après la prémédication, mais ils se sont modifiés de façon marquée avec l'augmentation de l'oxygène. Tous les sujets ont présenté un air courant augmenté et cela peut avoir été un facteur de prévention du shunt en prévenant l'atélectasie. Les facteurs importants chez ces malades ont été l'âge et l'état ambulatoire.

Cette étude démontre que la prémédication narcotique-belladone, employée à des doses judicieuses, ne compromet pas l'oxygénation du malade ambulant candidat à la chirurgie cardiaque.

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