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Treatment of Intraoperative Bronchospasm with Nebulized Isoetharine

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Administration of a metered dose of nebulized isoproterenol to the anesthetized patient with bronchospasm is frequently a useful therapeutic measure.[1,2] This method of administration of isoproterenol is preferred to the parenteral route because it results in a greater concentration of bronchodilator at the bronchial smooth muscle site, allows greater predictability of the bronchodilator effect, and decreases systemic cardiovascular effects of isoproterenol.[3,4] However, the use of nebulized isoproterenol may still be hazardous for certain patients who cannot tolerate the systemic absorption of isoproterenol that occurs.

Isoetharine, one of the newer bronchodilators that produce greater effects on β_2-adrenergic receptors in bronchial smooth muscle than on β_1-receptors in myocardium, has been used extensively in the preoperative and postoperative periods and has been found to be a potent, rapidly-acting bronchodilator with fewer side effects than isoproterenol.[5–7] This study reports the respiratory and cardiovascular effects of an isoetharine preparation (Bronkometer) nebulized in metered doses for the treatment of bronchospasm during anesthesia.

MATERIALS AND METHODS

Sixteen patients in whom bronchospasm developed during general endotracheal anesthesia were studied. The patients were diversified with respect to sex, age, physical status, medical history, surgical procedure, preoperative medication, and anesthetic management. The primary anesthetic used was halothane (nine cases), nitrous oxide–narcotic (six cases), or enflurane (one case). Ventilation was controlled at an appropriate fixed volume for each patient by means of a mechanical ventilator. All patients were monitored continuously with a precordial or esophageal stethoscope and an electrocardioscope.

Isoetharine, as the commercially available preparation of isoetharine and phenylephrine (Bronkometer), was administered to each patient after the development of bronchospasm. The diagnosis of bronchospasm was made on the basis of an increase in peak airway pressure associated with the occurrence of expiratory wheezing. In all cases, before treatment was undertaken, an attempt was made to rule out and correct, if necessary, the presence of inadequate anesthetic depth, unusual surgical stimulation, and mechanical airway problems. The isoetharine preparation was administered by means of a plastic adaptor[9] in which the Bronkometer cartridge was placed; this adaptor was interposed between the Y-piece of the circle system and the endotracheal tube. Two doses of isoetharine (340 μg isoetharine and 70 μg phenylephrine per dose) were administered at the onset of an inspiration that was held at end-inspiration for 3 seconds. The administration of isoetharine was repeated at 5-minute intervals provided that 1) wheezing persisted, 2) the prior dose had improved ventilation, and 3) vital signs were stable.

Severity of wheezing, peak airway pressure, tidal volume, heart rate, and blood pressure were recorded immediately prior to and at 5-minute intervals after the administration of isoetharine. The electrocardiogram was continuously monitored during the observation period. Arterial blood gases were analyzed prior to and 5 minutes after isoetharine in six cases. Wheezing was graded from 1 to 4 in order of increasing severity, as judged by the observer.

RESULTS

The severity of wheezing and peak airway pressure decreased in every patient after the initial administration of isoetharine (table 1). Wheezing disappeared completely in four cases and decreased by variable amounts in the other 12 cases. Peak inspiratory airway pressures decreased an average of 3.2 ± 2.2 cm H_2O, mean ± SD (table 2).

Of the 12 patients who needed a second administration of isoetharine, further clinical alleviation of the severity of bronchospasm was observed in ten (table 1). Wheezing disappeared completely in seven, decreased in three, and remained unchanged in two patients. In this group, peak inspiratory airway pressures decreased an average of 1.3 ± 1.4 cm H_2O (table 2), decreasing in ten and remaining unchanged in two patients.

Three patients needed a third administration of isoetharine (table 1). Further improvement occurred in one of these patients; wheezing disappeared and peak airway pressure decreased 1 cm H_2O in this patient. No change in the severity of wheezing or peak airway pressure was observed in the two other patients.

No consistent change in pulse or blood pressure

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TABLE 1. Effects of Isoetharine on Wheezing, Peak Airway Pressure, Blood Pressure, and Pulse

Patient	Treatment	Wheezing		Before			After			Tidal Volume (ml)
		Before	After	Peak Airway Pressure (cm H_2O)	Blood Pressure (torr)	Pulse (Beats/Min)	Peak Airway Pressure (cm H_2O)	Blood Pressure (torr)	Pulse (Beats/Min)	
1	First	IV	II	31	124/85	115	28	120/82	112	700
	Second	II	0	28	120/82	112	25	120/76	118	
2	First	IV	III	42	110/60	90	39	105/55	95	900
	Second	III	II	39	105/55	95	36	105/52	96	
	Third	II	II	36	105/52	96	36	100/50	104	
3	First	II	I	35	115/75	84	33	115/80	86	875
	Second	I	0	33	115/80	86	32	110/74	94	
4	First	III	0	40	125/80	100	34	120/76	100	750
5	First	III	I	35	110/80	95	33	112/80	95	800
	Second	I	0	33	112/80	95	31	100/74	100	
6	First	III	0	45	90/55	76	36	100/60	82	900
7	First	III	0	38	125/80	104	34	120/80	104	850
8	First	II	I	35	115/60	80	33	114/60	80	850
	Second	I	I	33	114/60	80	33	110/55	92	
9	First	III	II	38	130/85	100	36	130/85	98	900
	Second	II	0	36	130/85	98	35	122/78	105	
10	First	IV	II	42	145/95	95	40	145/95	95	850
	Second	II	0	40	145/95	95	39	140/88	98	
11	First	II	I	34	120/90	100	32	120/90	100	800
	Second	I	I	32	120/90	100	32	118/86	104	
12	First	III	II	33	130/85	110	32	130/85	110	750
	Second	II	I	32	130/85	110	32	126/80	110	
	Third	I	0	32	126/80	110	30	120/76	116	
13	First	II	0	37	100/60	90	35	100/65	90	800
14	First	III	I	38	122/78	82	34	125/80	84	900
	Second	I	0	34	125/80	84	34	125/80	88	
15	First	III	II	33	110/70	85	32	110/70	85	800
	Second	II	I	32	110/70	85	31	108/70	90	
	Third	I	I	31	108/70	90	31	105/65	98	
16	First	III	II	38	130/80	72	32	135/75	72	800
	Second	II	0	32	135/75	72	28	138/78	70	

was observed after the initial administration of isoetharine; however, with repeated administrations a tendency for the pulse rate to increase and blood pressure to decrease was found (table 2). No dysrhythmia or significant change in arterial blood gases was found.

Discussion

Although not a common problem, bronchospasm during anesthesia can seriously compromise ventilation, and thus requires immediate treatment.[10,11] Occasionally, this treatment consists of simple changes in anesthetic technique, *e.g.*, adjustment of the position of the endotracheal tube, elimination of reflexes induced by surgical traction, increase in the depth of anesthesia, or change of anesthetic agent. However, often these measures are not indicated or desirable. When such is the case, the optimal approach to the relief of airway constriction would seem to be the administration of an adrenergic β-stimulant such as isoproterenol. Unfortunately, the use of isoproterenol as a bronchodilator has serious disadvantages, primarily because its action is nonselective; bronchodilatation is usually accompanied by cardiac stimulation and vasodilation.[3] These disadvantages have been minimized by the

TABLE 2. Mean Differences in Peak Airway Pressure, Blood Pressure, and Pulse after Administration of Isoetharine

Treatment	Number of Patients	Mean Difference ± SD			
		Peak Airway Pressure (cm H_2O)	Systolic Pressure (torr)	Diastolic Pressure (torr)	Pulse (Beats/Min)
First	16	−3.2 ± 2.2	0 ± 3.9	0 ± 3.2	0.6 ± 2.2
Second	12	−1.3 ± 1.4	−3.2 ± 4.0	−3.8 ± 3.2	4.4 ± 3.8
Third	3	−0.7 ± 1.2	−4.6 ± 1.5	−3.6 ± 1.5	7.3 ± 1.2

delivery of precise therapeutic doses of isoproterenol via a metered-dose nebulizer.[1,2,9] However, because isoproterenol-induced side effects still can occur, the use of an agent with more selective actions on bronchial muscle would seem advisable; this would appear to be indicated particularly in management of patients who have cardiac irritability and during the administration of anesthetics that lower the threshold for catecholamine-induced dysrhythmias.

Isoetharine is representative of a group of newer bronchodilators that were synthesized when compounds with more optimal ratios of bronchodilatation to cardioacceleration were being sought.[12] Although isoetharine is a structural analog of isoproterenol, it has a preferential affinity for β_2-adrenergic receptor sites of bronchial musculature and a lower order of affinity for β_1-adrenergic receptors of myocardium. This favorable bronchodilatation to cardioacceleration ratio, in addition to its relatively rapid and long action, has made isoetharine a useful adjunct in the treatment of increased bronchomotor tone.[5–7]

The cardiovascular effects of isoetharine administered intravenously during cyclopropane anesthesia in man without bronchospasm were studied by Shulman *et al.*[8] They observed reductions in systolic and diastolic pressures and an increase in heart rate after 1–15 μg/kg, iv. Dysrhythmias were not found, except for the development of nodal beats or rhythm in seven of the 14 patients studied. These investigators concluded that the observed cardiovascular effects were minimal compared with those produced by isoproterenol and epinephrine, and suggested that isoetharine was a safe drug to administer during cyclopropane anesthesia. No other study of the effects of isoetharine on the anesthetized patient has been reported.

The current study indicates that, for the treatment of intraoperative bronchospasm, isoetharine is an effective bronchodilator that produces minimal cardiovascular side effects when administered by metered-dose nebulization. In all patients, isoetharine increased compliance and decreased wheezing without inducing cardiac dysrhythmias or marked changes in heart rate or blood pressure. This lack of an effect on cardiovascular indices can be explained both by the use of relatively small doses and by minimal systemic absorption. The metered-dose nebulization of the drug directly to the airway allows the use of a smaller dose of isoetharine than otherwise would be necessary, and the inclusion of phenylephrine in the preparation minimizes the systemic concentration via vasoconstriction in the bronchial mucosa.

The lack of change in blood gases following isoetharine suggests that the reported occurrence of reduced Pa_{O_2}'s following use of other bronchodilators[13,14] may not be a feature of isoetharine therapy. However, since this phenomenon may depend on both the inspired oxygen concentration[15] and the severity of the pulmonary dysfunction,[13] the present limited blood-gas data need to be expanded.

The data obtained in this study support the conclusion that metered-dose nebulization of isoetharine is a useful technique for the treatment of bronchospasm occurring during anesthesia, and that since its use results in few cardiovascular actions, it may be preferable to isoproterenol. The latter particularly may be the case in management of patients who have pre-existing myocardial irritibility.

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