disposable equipment and machine dispensing are modern trends which may reduce the opportunities for teaching. Hospital maternity units will need to consider this point, and the domiciliary midwife (or health visitor) at a later stage will carry even more responsibility for ensuring that mothers have the information, that they understand it, and that they act accordingly.

The investigation shows that in the artificial feeding of babies the mothers who used the hypochlorite method of sterilization of bottles and teats produced significantly better results. This finding may have been due to the continuing action of traces of the agent during its transport to the laboratory, but evidence in support did not reach statistically significant proportions in the one area where this was tested. Mothers adopting this method, however, were more inclined to clean the utensils better beforehand, and they stored them in solution, thus avoiding subsequent contamination.

Undoubtedly, many factors are involved in achieving satisfactory results by either method—social class, educational level, mothercraft advice obtained, and so on. It may even be that (in the words of one of the doctors involved in the project) “a ‘method of sterilization,’ presumed to be based on chemistry, is followed more carefully and thoroughly than the use of a ‘procedure’ (boiling) which is regarded more as a domestic activity.” Over one-fifth of babies had suffered from diarrhoea and vomiting that was usually serious enough

for the mother to consult her doctor. This can be taken as evidence that gastroenteritis is not entirely a thing of the past, even though the consequences may be less serious than in former days.

The basic problem highlighted by this study is that so many mothers failed to carry out sterilization procedures effectively in spite of the fact that they had received “health education” in this field. Information of how to do it and why it should be done had been put across but the resultant behaviour did not seem to reach the necessary standard. This is a fundamental problem of health education—the communication of ideas is insufficient in itself and must be associated with a desire to change habits. There would seem to be a need for (a) straightforward yet effective health education materials, and (b) professional backing so that mothers adopt a routine which gives protection to their babies. Why are the results so bad when effective methods are readily available?

While it is not possible to indicate individually the many people who willingly co-operated in this study, we would like to express our gratitude and indebtedness to them. The study would obviously have been impossible without the joint effort of doctors, health visitors, and technicians in the local authority and public health laboratory services.

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Comparison of Effect of Salbutamol and Isoprenaline on Spirometry and Blood-gas Tensions in Bronchial Asthma

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Summary: The effect of the aerosol inhalation of 200 µg. of salbutamol and 1,000 µg. of isoprenaline on spirometry and blood-gas tensions was compared in the same 11 asthmatic subjects. Both drugs significantly reduced airway obstruction, and the extent of the reduction did not differ for periods of up to 30 minutes. After isoprenaline tachycardia and a small significant fall in arterial oxygen tension occurred, whereas after salbutamol there was no change in pulse rate and the arterial oxygen tension did not fall.

Introduction

Salbutamol is a new type of sympathomimetic bronchodilator drug which is claimed to act selectively on β_2 -adrenergic receptors in bronchial muscle without significant stimulation of β_1 -receptors in the myocardium. In asthma it has been shown to produce bronchodilatation without increasing pulse rate, blood pressure (Choo-Kang *et al.*, 1969; Kennedy and Simpson, 1969), or cardiac output (Kelman *et al.*, 1969). Isoprenaline, on the other hand, is a powerful stimulator of β -receptors in both bronchial and cardiac muscle, so that in addition to relaxing smooth muscle in the bronchi it also increases cardiac output (Aviado and Schmidt, 1957; Kelman *et al.* 1969). Probably as a direct result of its action on the cardiovascular system, hypoxaemia may become worse after isoprenaline even though airway obstruction is diminished (Field,

1967; Palmer and Diament, 1967). There is evidence that salbutamol in relieving airway obstruction does not lead to a fall in lowered arterial oxygen tension (P_{aO_2}) (Palmer and Diament, 1969a, 1969b), and that its action lasts longer than that of isoprenaline (Choo-Kang *et al.*, 1969). Because of the known variability of the response of asthmatic patients to bronchodilator drugs it is important to compare the response to salbutamol and isoprenaline in the same patient. We report here the effect of these drugs on spirometry and arterial blood-gas tensions in the same asthmatic patients.

Patients and Methods

Eleven asthmatic outpatients (seven men and four women) were investigated. The nature of the experiment was explained to them and all gave their consent. Their mean age was 46 (± 12.7) years, height 62.5 (± 2.86) in. (159 (± 7.26) cm.), and weight 151.3 (± 19.4) lb. (68.6 (± 8.8) kg.) All had long attacks of airway obstruction. Seven had positive scratch tests to various allergens and nine had sputum and/or blood eosinophilia. They attended the laboratory on three separate occasions when arterial blood-gas tensions, dynamic lung volumes, pulse, and blood pressure were measured before and at intervals of up to 30 minutes after either the aerosol-inhalation of 1,000 µg. of isoprenaline or 200 µg. of salbutamol. Blood samples were obtained in a heparin-lubricated syringe from the brachial or radial artery when the patient was breathing air, and P_{aO_2} , P_{aCO_2} , and pH were measured in duplicate with electrodes manufactured by Radiometer, Copenhagen. The standard deviation of a single measurement in our hands was 1.7 mm.Hg for the oxygen electrode and

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TABLE I.—Effect of Isoprenaline and Salbutamol on Mean ($\pm$ S.D.) Dynamic Lung Volumes (% Predicted), Arterial Blood-gas Tensions (mm.Hg), and pH, Blood Pressure, and Pulse Rate in 11 Asthmatic Subjects

	Isoprenaline					Salbutamol				
	Control	5 Min.	10 Min.	15 Min.	30 Min.	Control	5 Min.	10 Min.	15 Min.	30 Min.
% Pred. F.E.V. ₁	67.4($\pm$ 24.8)	78.8($\pm$ 26.4)*	79.6($\pm$ 26.3)*	80.8($\pm$ 26.5)*	79.4($\pm$ 26.8)*	67.6($\pm$ 26.1)	77.6($\pm$ 27.0)*	79.8($\pm$ 27.5)*	81.7($\pm$ 27.7)*	83.1($\pm$ 27.6)*
% Pred. F.V.C.	92.6($\pm$ 22.7)	99.3($\pm$ 22.6)†	101.2($\pm$ 21.7)*	102.7($\pm$ 20.5)*	101.4($\pm$ 22.3)†	93.2($\pm$ 24.4)	103.3($\pm$ 21.8)*	103.5($\pm$ 21.2)*	106.2($\pm$ 19.8)*	106.9($\pm$ 20.8)*
F.E.V. ₁ % F.V.C.	59.4($\pm$ 12.8)	65.0($\pm$ 13.4)*	64.4($\pm$ 13.6)*	64.5($\pm$ 14.3)†	64.2($\pm$ 14.3)†	59.3($\pm$ 12.8)	61.1($\pm$ 13.9)	62.8($\pm$ 14.1)	63.0($\pm$ 14.9)	63.3($\pm$ 14.0)
Pao ₂	75.2($\pm$ 12.1)	75.0($\pm$ 12.1)	71.9($\pm$ 12.1)*	71.9($\pm$ 12.1)*	73.9($\pm$ 11.4)	73.9($\pm$ 11.4)	73.9($\pm$ 11.4)	76.0($\pm$ 12.2)	76.0($\pm$ 12.2)	76.0($\pm$ 12.2)
Paco ₂	38.7($\pm$ 3.3)	38.7($\pm$ 3.3)	38.5($\pm$ 3.3)	38.5($\pm$ 3.3)	38.1($\pm$ 3.1)	38.1($\pm$ 3.1)	38.1($\pm$ 3.1)	37.6($\pm$ 3.7)	37.6($\pm$ 3.7)	37.6($\pm$ 3.7)
pH	7.42($\pm$ 0.03)	7.42($\pm$ 0.03)	7.42($\pm$ 0.03)	7.42($\pm$ 0.03)	7.42($\pm$ 0.03)	7.42($\pm$ 0.03)	7.42($\pm$ 0.03)	7.43($\pm$ 0.03)	7.43($\pm$ 0.03)	7.43($\pm$ 0.03)
Pulse rate	81.5($\pm$ 9.1)	90.4($\pm$ 14.1)†	90.4($\pm$ 14.1)†	88.7($\pm$ 13.5)†	84.5($\pm$ 12.0)	82.2($\pm$ 9.6)	82.4($\pm$ 9.9)	82.4($\pm$ 10.2)	82.5($\pm$ 9.9)	82.2($\pm$ 10.0)
Systolic B.P.	124.3($\pm$ 13.5)	127.0($\pm$ 14.8)	125.8($\pm$ 15.3)	124.7($\pm$ 14.3)	122.7($\pm$ 13.3)	125.5($\pm$ 17.2)	124.1($\pm$ 15.7)	123.7($\pm$ 14.9)	123.4($\pm$ 14.5)	122.9($\pm$ 13.9)
Diastolic B.P.	74.8($\pm$ 10.5)	73.9($\pm$ 10.2)	73.1($\pm$ 10.0)	72.5($\pm$ 9.6)†	72.5($\pm$ 9.6)†	75.5($\pm$ 10.4)	74.7($\pm$ 10.1)	74.5($\pm$ 10.0)	74.0($\pm$ 9.4)	73.7($\pm$ 9.1)
Pulse pressure	49.5($\pm$ 7.0)	53.1($\pm$ 8.5)†	52.7($\pm$ 8.5)	52.3($\pm$ 7.3)	50.3($\pm$ 6.0)	49.9($\pm$ 7.9)	49.4($\pm$ 6.9)	49.2($\pm$ 6.4)	49.4($\pm$ 6.2)	49.2($\pm$ 5.9)

* $P < 0.001$. † $P < 0.005$. ‡ $P < 0.05$. Other changes were not significant.TABLE II.—Comparison between Mean Change ($\pm$ S.D.) in Dynamic Lung Volumes (% Predicted), Arterial Blood-gas Tensions (mm.Hg), and pH, Blood Pressure, and Pulse Rate in 11 Asthmatic Subjects after Aerosol Isoprenaline and Salbutamol

	Control Values		Change After 5 Min.		Change After 10 Min.		Change After 15 Min.		Change After 30 Min.	
	Isoprenaline	Salbutamol	Isoprenaline	Salbutamol	Isoprenaline	Salbutamol	Isoprenaline	Salbutamol	Isoprenaline	Salbutamol
% Pred. F.E.V. ₁	67.4($\pm$ 24.8)	67.6($\pm$ 26.1)	+11.4($\pm$ 5.0)	+10.0($\pm$ 7.4)	+12.3($\pm$ 6.7)	+12.2($\pm$ 8.2)	+13.5($\pm$ 6.7)	+14.1($\pm$ 8.4)	+12.1($\pm$ 5.3)	+15.4($\pm$ 9.6)
% Pred. F.V.C.	92.6($\pm$ 22.7)	93.2($\pm$ 24.4)	+6.7($\pm$ 5.9)	+10.1($\pm$ 7.2)	+8.5($\pm$ 5.1)	+10.3($\pm$ 5.8)	+10.1($\pm$ 6.3)	+13.0($\pm$ 7.1)	+8.8($\pm$ 8.4)	+13.8($\pm$ 6.7)
F.E.V. ₁ % F.V.C.	59.4($\pm$ 12.8)	59.3($\pm$ 12.8)	+5.8($\pm$ 4.2)	+1.8($\pm$ 7.3)	+5.1($\pm$ 5.0)	+3.5($\pm$ 7.3)	+5.1($\pm$ 5.2)	+3.7($\pm$ 7.0)	+4.8($\pm$ 5.1)	+3.9($\pm$ 6.1)
Pao ₂	75.2($\pm$ 12.1)	73.9($\pm$ 11.4)					-3.3($\pm$ 2.2)	+2.1($\pm$ 3.5)*		
Paco ₂	38.7($\pm$ 3.3)	38.1($\pm$ 3.1)					-0.2($\pm$ 1.6)	-0.5($\pm$ 1.0)		
pH	7.425($\pm$ 0.030)	7.422($\pm$ 0.029)					+0.002($\pm$ 0.009)	+0.004($\pm$ 0.005)		
Pulse rate	81.5($\pm$ 9.1)	82.2($\pm$ 9.6)	+8.9($\pm$ 7.7)	+0.2($\pm$ 1.9)†	+8.9($\pm$ 8.3)	+0.2($\pm$ 1.7)†	+7.3($\pm$ 8.7)	+0.4($\pm$ 2.3)†	+3.6($\pm$ 6.6)	0.0($\pm$ 2.7)†
Systolic B.P.	124.3($\pm$ 13.5)	125.5($\pm$ 17.2)	+2.7($\pm$ 6.4)	-1.4($\pm$ 3.6)	+1.5($\pm$ 5.8)	-1.7($\pm$ 4.5)	+0.5($\pm$ 4.1)	-0.1($\pm$ 4.3)	-1.5($\pm$ 6.4)	-2.5($\pm$ 5.2)
Diastolic B.P.	69.4($\pm$ 10.5)	75.5($\pm$ 10.4)	-0.9($\pm$ 3.5)	-0.8($\pm$ 2.2)	-1.7($\pm$ 2.9)	-1.0($\pm$ 2.0)	-2.4($\pm$ 3.2)	-1.5($\pm$ 3.1)	-2.4($\pm$ 2.4)	-1.8($\pm$ 3.5)
Pulse pressure	49.5($\pm$ 7.0)	49.9($\pm$ 7.9)	+3.6($\pm$ 5.3)	-0.5($\pm$ 2.8)†	+3.3($\pm$ 5.4)	-0.7($\pm$ 3.6)	+2.8($\pm$ 4.7)	-1.5($\pm$ 3.2)	+0.8($\pm$ 3.2)	-0.7($\pm$ 3.3)

* $P < 0.001$. † $P < 0.005$. ‡ $P < 0.05$. Other differences were not significant.

1.2 mm.Hg for the carbon dioxide electrode. Forced expiratory spirometers were obtained and from the best of three attempts the forced vital capacity (F.V.C.), the forced expiratory volume in 1 second (F.E.V.₁), and the F.E.V.₁ as a percentage of F.V.C. (F.E.V.₁%) were calculated. The measurements were recorded in litres A. T. P. S. (ambient temperature and pressure saturated with water vapour) and expressed as a percentage of predicted normal values to allow for differences in age, sex, and height, the data of the Committee on Rating of Mental and Physical Impairment (1965) being used for the normal values. Pulse and blood pressure were recorded sitting.

Results

The mean ($\pm$ S.D.) of the spirometric findings, arterial blood-gas tensions, pH pulse rate, and blood pressure before and after the drugs is shown in Table I. At the beginning of the experiment the F.V.C., F.E.V.₁ and F.E.V.₁% were all reduced and there was hypoxaemia without hypercapnia—findings typical of asthma of moderate severity. After isoprenaline there was a significant rise in spirometric measurements and pulse rate for 30 minutes but a significant fall in Pao₂ of 3.3 ($\pm$ 2.2) mm.Hg at 15 minutes. After salbutamol there was also a significant rise in all the spirometric measurements but no change in cardiovascular measurements and a slight though insignificant rise in Pao₂ of 2.1 ($\pm$ 3.5) mm.Hg.

It can be seen from Table II that there was no difference in the mean control values before the drugs and that the extent of the rise in dynamic lung volumes did not differ after isoprenaline or salbutamol. There was a significant rise in pulse rate ($P < 0.005$) and fall in arterial oxygen tension ($P < 0.001$) after isoprenaline.

Discussion

Airway obstruction was significantly reduced both by isoprenaline and salbutamol in these asthmatic subjects though the extent of the reduction for 30 minutes after the drug did not differ significantly. After isoprenaline, however, tachycardia and some rise in systolic blood pressure occurred, whereas after salbutamol there was no change in the cardiovascular measurements. After isoprenaline there was a significant

fall in Pao₂, whereas after salbutamol there was a small, though insignificant, rise in Pao₂. Salbutamol, therefore, because of its selective β_2 -stimulant action leads to reversal of asthmatic airway obstruction without undesirable falls in Pao₂—most probably because it does not cause cardiovascular stimulation and thereby an increase in cardiac output leading to worsening of disturbed ventilation/perfusion ratios in the lung. That isoprenaline leads to falls in Pao₂ by this mechanism is supported by the observation that when β_1 -receptors in the myocardium are selectively blocked bronchodilatation follows the administration of isoprenaline without a concomitant fall in Pao₂ (Palmer *et al.*, 1969).

We did not find any difference in bronchodilator activity between salbutamol and isoprenaline, but our subjects were studied for only 30 minutes. Salbutamol has been shown to have a bronchodilator action up to five hours in the dosage we used, whereas a worth-while bronchodilator action of isoprenaline lasted only one-and-a-half hours (Choo-Kang *et al.*, 1969). Orciprenaline has less action on the cardiovascular system and has a longer bronchodilator action than isoprenaline, but in both these respects it is slightly inferior to salbutamol (Kennedy and Simpson, 1969). It seems clear, therefore, that because of its effectiveness in producing bronchodilatation, its long duration of action, its lack of cardiovascular stimulant action, and its lack of tendency to produce falls in Pao₂, salbutamol is the most effective drug at present available by aerosol inhalation for the relief of asthmatic airway obstruction.

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