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Optimisation of positive end expiratory pressure for maximal delivery of oxygen to tissues using oesophageal Doppler ultrasonography

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Abstract

***Objective*—To assess oesophageal Doppler ultrasonography as a convenient means of optimising positive end expiratory pressure for maximal delivery of oxygen to tissues.**

***Design*—Measurements of blood flow, arterial oxygen saturation, and cardiac output by thermodilution (when available) at baseline and at 20-30 minutes after each incremental increase (2·5-5·0 cm H_2O) in positive end expiratory pressure to a maximum of 20·0 cm H_2O. If the cardiac output fell by more than 15% measurements were repeated after stepwise decreases in positive end expiratory pressure. No other manoeuvre such as endotracheal suction or changing ventilator settings, drug or fluid dosage, or the patient's position was performed for at least one hour before the start of the study or during it.**

***Setting*—Intensive care unit.**

***Participants*—10 Patients being mechanically ventilated for acute respiratory failure who had stable haemodynamic and blood gas values and required a fractional inspired oxygen concentration of $\geq$0·45. They were assessed on a total of 11 occasions.**

***Interventions*—Incremental increases in positive end expiratory pressure followed when indicated by stepwise decreases.**

***End point*—The positive end expiratory pressure providing maximal delivery of oxygen to tissues.**

***Measurements and main results*—Arterial oxygen saturation increased with positive end expiratory pressure in all patients by an average of 6·1%. In nine of the 11 studies, however, cardiac output fell by 15% to 30% after the second increment. On the two other occasions cardiac output and oxygen delivery rose by up to 54%. Positive end expiratory pressure was decreased on seven occasions; there was considerable individual variation in the time taken for cardiac output to rise and arterial oxygen saturation to fall. In six patients good agreement was seen between the results from Doppler ultrasonography and thermodilution, the mean of the differences being −0·3% with narrow limits of agreement (−14·4% to 13·9%).**

***Conclusions*—Oesophageal Doppler ultrasonography is a rapid, safe, and reliable technique for optimising positive end expiratory pressure to obtain maximal delivery of oxygen to tissues. The results show the need to consider haemodynamic consequences when altering positive end expiratory pressure.**

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Introduction

Positive end expiratory pressure is commonly used to increase the oxygenation of blood in patients who are being mechanically ventilated. The increased oxygenation, however, has to be offset against a depression of cardiac output, which occurs at varying positive end expiratory pressures in different patients[1-8] and with time in individual patients.[7] Factors such as left ventricular preload[4 5 7] and right ventricular function[9] play a part in determining when and to what extent this decrease in output occurs. Increasing positive end expiratory pressure will therefore alter unpredictably the equation of oxygen delivery=cardiac output× arterial oxygen content. The delivery of oxygen may even fall below the starting value and pass unrecognised without the monitoring of cardiac output; the perceived improvement in the oxygenation of blood may in fact disguise an appreciable drop in the delivery of oxygen to the tissues. Indeed, criticism has recently been voiced about the current trend of increasing positive end expiratory pressure without due regard to the haemodynamic consequences.[10]

Thermodilution is the main technique used in inten-

sive care units to measure cardiac output. Pulmonary artery catheterisation is not, however, without risk, the reported morbidity being 3·6-7·2%[11 12]; not all units are experienced in its use,[13] and it may not be deemed necessary in some patients who require positive end expiratory pressure. We previously described a new oesophageal Doppler system that accurately follows changes in cardiac output when compared with thermodilution.[14] Furthermore, by this technique alone volumetric cardiac output can be estimated with 85% accuracy. In view of its ease of use, safety, rapidity, and comparative non-invasiveness it should be a useful means of optimising positive end expiratory pressure to maximise the delivery of oxygen to tissues and to confirm that other indications of positive end expiratory pressure—for example, lowering inspired oxygen concentrations—do not have too deleterious an effect on oxygen delivery. We investigated this potential application of oesophageal Doppler ultrasonography, using thermodilution when available for comparison, to follow the percentage change in cardiac output on altering the positive end expiratory pressure.

Patients and methods

Patients being mechanically ventilated for acute respiratory failure were eligible for the study provided that they had stable haemodynamic and blood gas values and required an inspired oxygen concentration of ≥0·45. Those with abnormal blood clotting profiles or oesophageal disease were excluded. All were adequately sedated, and paralysed if necessary, for continuous mandatory ventilation with constant tidal volumes of 12-15 ml/kg delivered by either Veolar (Hamilton Medical, Rhazuns, Switzerland), Erica (Engstrom, Stockholm, Sweden), or Servo 900B ventilators (Siemens, Sunbury on Thames, Middlesex).

Physical manoeuvres such as endotracheal suction and turning the patient were not performed and ventilator settings, drug doses, and the administration of boluses of fluid were not changed for at least one hour before the start of the study. Similarly, no alterations were made during the course of the investigation other than changing the positive end expiratory pressure. The study was discontinued if another manoeuvre had to be performed that might have disturbed the steady state—for example, suction.

A 5·1 MHz continuous wave oesophageal Doppler transducer connected to a spectral analyser system (Doptek, Chichester, Sussex) was used. The transducer was inserted through the mouth to a depth of about 30-40 cm until blood flow was detected. It was focused on the midstream flow of the descending thoracic aorta by rotating the probe until velocity waveforms with minimal spectral dispersion were seen that were characteristic of midstream blood flow in the aorta.[14] The area of each waveform—the velocity-time integral or stroke distance—is a linear measure of the left ventricular stroke volume that passes through the descending thoracic aorta. The stroke distance and heart rate were computed semiautomatically by using a light pen and integral software. A minimum of five waveforms encompassing a respiratory cycle were measured and the results averaged to provide an index of total body cardiac output.

Haemoglobin concentration and arterial oxygen saturation were measured with an OSM2 Hemoximeter (Radiometer, Copenhagen, Denmark) in heparinised blood drawn from an indwelling radial or femoral line. Cardiac output was measured by thermodilution in patients with a pulmonary artery flotation cathether (American Edwards Labs, Santa Ana, California). Iced 5% dextrose (5 ml aliquots) was injected and cardiac output measured by a COM-1 computer (American Edwards Labs, Santa Ana, California). The average of three outputs falling within 10% of each other was taken.

The starting positive end expiratory pressure was noted and after baseline measurements were performed the pressure was increased by increments of 2·5-5·0 cm H_2O to a maximum of 20·0 cm H_2O. All measurements were repeated 20-30 minutes after each change. Positive end expiratory pressure was not increased further if the fall in cardiac output exceeded 15%, in which case it was reduced incrementally with

TABLE I—*Characteristics of patients studied*

Case No	Sex	Age (years)	Condition
1	M	53	Adult respiratory distress syndrome after intestinal obstruction
2	F	32	Lymphoma, cytomegalovirus pneumonitis, left ventricular failure secondary to cytotoxic treatment
3	M	57	Adult respiratory distress syndrome after trauma
4	M	56	Adult respiratory distress syndrome, sepsis
5	F	63	Pneumonia
6	M	59	Pneumonia, long term airflow limitation
7	M	29	Chickenpox pneumonia
8	F	65	Pneumonia
9	M	19	Adult respiratory distress syndrome after strangulation
10	M	29	Adult respiratory distress syndrome, pneumonia

TABLE II—*Positive end expiratory pressure (cm H_2O) and percentage changes in cardiac output and delivery of oxygen to tissues in 10 patients studied by oesophageal Doppler ultrasonography. Blank values indicate no change*

Case No	Positive end expiratory pressure	Cardiac output	Tissue oxygen delivery
1	0		
	5		
	10		+2
	15	+10	+16
	20	+17	+25
2	6		
	9	−2	
	12	+10	+15
	15	+40	+50
	18	+40	+54
2*	6		
	9	−13	−10
	12	−19	−8
	6	−19	−16
	6	−11	−11
3	6		
	9	−7	−6
	12	−29	−26
	6	−31	−28
	6	−5	−4
4	4		
	7	−17	−16
	10	−18	−18
	0	−12	−12
	0	−14	−13
5	5		
	7·5	−10	+2
	10	−15	−4
	7·5	−4	−19
	5	+2	+2
6	5		
	7·5	−9	−8
	10	−16	−15
	7·5	−6	−5
	5		
7	5		
	7·5	−8	−6
	10	−18	−5
	7·5	−15	−14
	5	−7	−7
8	0		
	5	−8	−7
	10	−15	−10
	0		+1
	0	+2	+3
9	0		
	5	−19	−15
	10	−29	−27
	10†	−11	−8
	10‡	+7	+9
10	0		
	4		+3
	8	−5	+2
	12	−15	−2
	10	−10	

*Five days later. †Colloid bolus of 200 ml. ‡Colloid bolus of 700 ml.

measurements once again repeated 20-30 minutes after each change.

An index of oxygen delivery was calculated from the formula (haemoglobin concentration × 1·34 × arterial oxygen saturation) × (stroke distance × heart rate).

The percentage change in cardiac output from baseline values measured by Doppler ultrasonography and thermodilution was compared according to the method described by Bland and Altman.[15]

The study was approved by the hospital district medical ethics committee.

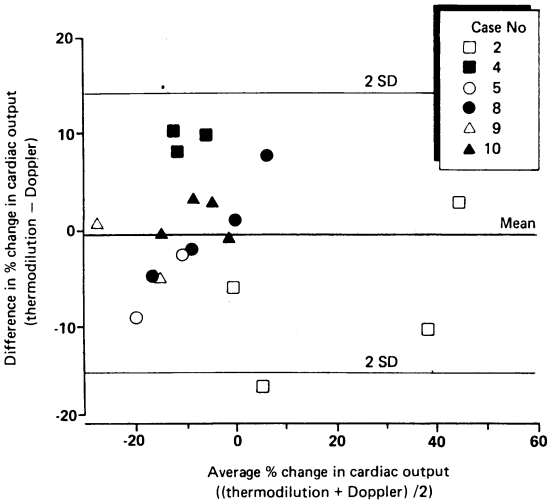
Results

Ten patients were studied on a total of eleven occasions, and their details are shown in table I.

Arterial oxygen saturation increased in all patients after increases in positive end expiratory pressure. The mean baseline saturation of 90·7% (SD 8·5%) rose to 96·2% (6·1%) at the highest value, an average increase of 6·1%. In all but two patients, however, the increase in positive end expiratory pressure resulted in reductions in cardiac output that exceeded 15% by the second increment (range −15% to −30%). Corresponding decreases of −2% to −25% were seen in the delivery of oxygen to the tissues (table II).

Increases in cardiac output and delivery of oxygen to the tissues of 40·4% and 53·5% respectively occurred in one patient with left ventricular failure (case 2) when positive end expiratory pressure was increased from 6 to 18 cm H_2O. The procedure was repeated five days later when the heart failure was controlled; on this occasion a fall in cardiac output of 19·3% was seen on increasing the pressure from 6 to 12 cm H_2O. One patient (case 9) became increasingly hypotensive and oliguric after positive end expiratory pressure was increased from 0 to 10 cm H_2O and recovered after having been given a colloid bolus of 700 ml.

Measurements after decreases in positive end expiratory pressure were obtained on seven occasions; we found considerable individual variation in the time taken for cardiac output to rise and arterial oxygen saturation to fall.



Comparison of percentage change in cardiac output with positive end expiratory pressure measured by thermodilution and oesophageal Doppler ultrasonography in six patients

Measurements from thermodilution and Doppler ultrasonography were obtained simultaneously in six patients. A total of 25 paired measurements were obtained, providing 19 changes from baseline values. The mean of the differences between the values obtained by the two techniques was −0·3% with narrow limits of agreement (−14·4% to 13·9%) (figure).

Discussion

Oesophageal Doppler ultrasonography may be used to show the variation in haemodynamic response to increasing positive end expiratory pressures both between patients and in the same patient over time. Large decreases in cardiac output may be easily recognised and, in conjunction with arterial blood sampling, the optimum pressure found for maximal oxygen delivery.

Positive end expiratory pressure is a useful means of improving the oxygenation of arterial blood. Through its use, however, the delivery of oxygen to tissues may actually fall, which may pass unrecognised. Whether oxygen delivery is the ideal variable for defining the best positive end expiratory pressure is debatable. Nevertheless, we are concerned that too large a depression of cardiac output by positive end expiratory pressure may prove deleterious, especially when oxygen consumption is dependent on delivery.[16] Even small positive end expiratory pressures may result in large falls in cardiac output. This was recognised soon after positive end expiratory pressure was first used,[1] and the importance of measuring oxygen delivery has been emphasised by several authors.[1-3 10] Multiple injections for thermodilution over short periods are, however, time consuming and may result in an undesirable fluid load. Furthermore, many British intensive care units use pulmonary artery catheterisation sparingly, if at all,[13] and this is probably reflected in many other countries.

Oesophageal Doppler ultrasonography thus provides a useful alternative means of determining the optimal positive end expiratory pressure for the maximal delivery of oxygen to body tissues. The transducer is easily inserted and excellent signals are uniformly obtained within one to two minutes. Because of the stability of the transducer the error in recording data is negligible; the transducer may either be left in situ for days without complication or be reinserted as necessary. The good agreement shown with thermodilution in our patients suggests that there are no large changes in the ratio of descending aortic flow to total cardiac output. This implies that positive end expiratory pressure does not appreciably redistribute regional cardiac output.

Apart from optimising the delivery of oxygen to the tissues oesophageal Doppler ultrasonography could be used to ensure that attempts to improve arterial blood oxygenation, reduce venoarterial admixtures, or lower inspired oxygen concentrations to non-toxic values by increasing positive end expiratory pressure do not have too deleterious an effect on the oxygen delivery. Furthermore, the efficacy of therapeutic manoeuvres such as fluid administration[3 8 16] given to restore the delivery of oxygen to tissues may be assessed.

In conclusion, oesophageal Doppler ultrasonography offers a reliable, safe, rapid, continuous, and comparatively non-invasive means of finding the optimal positive end expiratory pressure for the maximal delivery of oxygen to tissues in critically ill patients. It can be easily performed at regular intervals as any important change in haemodynamic state, either spontaneous or therapeutic, may alter the optimal positive end expiratory pressure. Increasing positive end expiratory pressure to improve the oxygenation of blood may result in major haemodynamic disadvantages, even at low values. Our results highlight the need to monitor circulatory changes occurring in consequence.

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Oral rehydration formula containing alanine and glucose for treatment of diarrhoea: a controlled trial

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Abstract

***Objective*—To determine whether adding L-alanine to the glucose based oral rehydration solution recommended by the World Health Organisation would improve its efficacy in treating acute diarrhoea.**

***Design*—Randomised double blind controlled trial of oral rehydration solution containing L-alanine and glucose.**

***Setting*—Inpatient service of a hospital treating diarrhoea.**

***Patients*—97 Male patients aged 6-59 years admitted to the hospital with acute and severe dehydration due to diarrhoea associated with *Vibrio cholerae* or enterotoxigenic *Escherichia coli*. Forty nine received the standard glucose based oral rehydration solution (control group) and 48 this solution with alanine added (study group).**

***Interventions*—All of the patients received rapid intravenous acetate solution for the initial four hours after admission, which fully corrected the signs of dehydration. They were then admitted to the study and randomised. Immediately after the intravenous treatment oral rehydration treatment was started. All of the patients received oral tetracycline for 48 hours, starting 24 hours after start of the study. If signs of dehydration reappeared during oral treatment patients were given rapid intravenous acetate solution until they were fully corrected and then continued to take the assigned oral rehydration solution.**

***End point*—Passage of the last watery stool.**

***Measurements and main results*—The median stool output/kg body weight during the initial 24 hours of oral rehydration treatment and until diarrhoea stopped was reduced in the study group compared with the control group from 309 ml to 196 ml and from 393 ml to 236 ml respectively. Intake of oral rehydration solution and intravenous acetate solution was reduced from 455 ml to 308 ml and from 616 ml to 425 ml respectively. Two patients in the study group compared with 18 patients in the control group required unscheduled rapid intravenous acetate solution to correct signs of dehydration during oral rehydration treatment.**

***Conclusion*—Oral rehydration solution containing L-alanine was considerably better than standard oral rehydration solution at reducing the severity of symptoms and the need for fluid of male patients with diarrhoea associated with *V cholerae* and enterotoxigenic *E coli*.**

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Introduction

Treatment with glucose based oral rehydration solution is effective for preventing and treating diarrhoea.[1-3] It does not, however, reduce the volume or frequency of stools or the duration of diarrhoea.[4,5] In 1984, encouraged by results from several clinical trials, the diarrhoeal diseases control programme of the World Health Organisation began supporting research projects on developing improved oral rehydration solution formulation.[6] Twenty eight such projects have been completed, are continuing, or are planned. Their aim is to compare the standard WHO oral rehydration solution with other formulations that have the same concentration of salts but may be more effective.[6] There are two types of alternative formulation. One type contains glucose or a glucose polymer and an amino acid or a peptide, or both, in varying concentrations[6]: this approach was stimulated by studies in children[7] and adults[8] that used formulations containing glucose and glycine. In the other type of formulation glucose is replaced by a staple food (cereals, legumes, or roots) as a source of starch and protein: this approach was based on studies that showed that a rehydration solution containing 50 or 80 g of rice powder per litre in place of glucose can reduce stool volume substantially.[9,10]

Alanine has been proposed as a component of an improved oral rehydration solution formulation.[11] Studies have shown that it enhances the absorption of sodium and water from the small intestine, the amount of absorption increasing with its concentration.[12] Alanine is a white, odourless, crystalline powder with a sweetish taste and is soluble in water; it is present in many foodstuffs and has been used as a dietary supplement.[13] Alanine 50 g each day orally in divided doses reversed hypoglycaemia and ketosis and reduced catabolism of muscle in obese subjects starved for two weeks.[14] A study of piglets with transmissible gastroenteritis showed that alanine with glucose caused a significantly greater absorption of sodium by the jejunal mucosa than either alanine or glucose alone.[15]

We report the results of a double blind randomised trial of an oral rehydration solution containing glucose and alanine.

Patients and methods

Male patients aged 6-59 years with a history of watery diarrhoea of 24 hours or less and clinical signs of severe dehydration were included in the study. Criteria for exclusion were: a history of treatment with anti-