Decreased Paradoxical Pulse from Increased Venous Return in Severe Asthma

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During severe asthma, paradoxical pulse may result from increased impedance to left ventricular ejection, mechanical impairment of left ventricular filling by ventricular interdependence or decreased pulmonary venous return augmented by hypovolemia. We studied the effect of reversible blood volume expansion by MAST inflation during severe attacks of asthma. Ten patients with clinically detectable paradoxical pulse of more than 20 mm Hg were studied. All had a history of reversible bronchial asthma with evidence of respiratory and circulatory failure. Standard therapy for asthma was started. We observed no difference in respiratory and heart rates during MAST inflation. Paradoxical pulse was consistently decreased during MAST inflation; paradoxical pulse returned to baseline values after MAST deflation. The decrease in paradoxical pulse was produced by an increased inspiratory systolic arterial pressure. We conclude that a reduction in pulmonary venous return is more important than ventricular interdependence in producing paradoxical pulse during severe asthma.

Paradoxical pulse is frequently associated with acute asthma and is considered an index of the severity of both airway obstruction and its cardiovascular consequences. Paradoxical pulse reflects a decreased arterial systolic pressure in inspiration and an increase during expiration and is defined as the maximum difference of systolic arterial pressure within a respiratory cycle.

Prior studies implied that the inspiratory fall is the major factor, and that it is caused by inspiratory decrease in LSVV due to three main mechanisms: (1) decreased pulmonary venous return, (2) enhanced ventricular interdependence and (3) increased left ventricle afterload.

Rapid volume expansion has never been evaluated as a treatment of circulatory failure in severe asthma. If the above mechanisms are correct, rapid filling therapy may result in the following hypotheses: (a) increased mean systemic venous pressure could possibly reduce respiratory variations of systemic venous return, (b) increased venous return and presumably increased RV volume could accentuate ventricular interdependence and tend to increase paradoxical pulse, (c) increased RV preload could partially compensate for the increased RV afterload and, increased mean pulmonary vascular bed volume and pressure could maintain a better LV preload throughout the respiratory cycle and reduce paradoxical pulse.

Since rapid fluid infusion in acute asthma could lead to possible beneficial or deleterious effects on hemodynamics, we have utilized the progressive inflation of MAST which provides a rapidly reversible filling. During MAST inflation, if paradoxical pulse were to decrease, hypotheses a and c would each or both be true and therefore rapid filling therapy could be of importance in acute asthma.

Patients and Methods

Patients

We prospectively studied all patients admitted to the hospital for asthma between August 1986 and January 1988. The following protocol was accepted by the ethical committee of our institution. To be included in the study, patients met the following criteria: (1) age between 15 and 65 years old; (2) no evidence of previous cardiac or renal disease; (3) a clear past history of reversible airway obstruction of allergic or idiopathic etiology; (4) evidence for actual episode of asthma; (5) no chest x-ray evidence of emphysema, chronic bronchopathy, interstitial or other restrictive pathology; (6) paradoxical pulse greater than 20 mm Hg using sphygmonanometry; (7) informed consent from patient or family for children. All patients were examined by a senior intensivist before entry in the protocol and admitted immediately to the intensive care unit. Standard therapy for asthma was initiated: nasal administration of humidified oxygen; intravenous hydrocortisone, 600 mg/24 h; and continuous salbutamol intravenous infusion at an initial dose of 0.25 mg/h and increased if no clinical improvement occurred. The protocol was started without delay. The total time for completing the protocol was less than 10 min. In all patients the standard therapy was effective and all recovered. One patient with a previous history of epilepsy needed transient mechanical ventilation because of an episode of grand mal seizure, 15 min after the MAST procedure.

Methods

Arterial pressure was monitored by radial cannulation and a

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Table 1—Main Characteristics of Patients

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<td>13.12</td>
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Hewlett-Packard transducer positioned at the radial artery level with atmospheric pressure as a zero reference level. Electrocardiogram and radial arterial pressure were recorded on a Siemens Mingograph multichannel recorder. An arterial sample was obtained for analysis of blood gas and lactate. The patient wore a MAST (Gladiator shock suit). Ten stable respiratory cycles were examined at three different periods: (1) baseline, (2) after MAST inflation and (3) after MAST deflation. We first inflated the bladders of the inflator for the legs to 40 mm Hg pressure and then inflated the bladder of the inflator for the abdomen to 30 mm Hg. The inflation procedure took less than 1 min. Stable respiratory cycles were selected and recorded. The bladders of the inflators for the abdomen and the legs were then simultaneously deflated. We measured for each of the ten respiratory cycles maximum (expiratory) and minimum (inspiratory) systolic and diastolic pressures. Pulse pressure at both expiration and inspiration was calculated: expiratory pulse pressure = maximum systolic minus minimum diastolic pressure; inspiratory pulse pressure = minimum systolic minus minimum diastolic pressure. Pressure variation between expiration and inspiration (delta pressure) was then calculated for each systolic, diastolic and pulse pressure using expiratory value minus inspiratory value of each pressure. We finally calculated means of each pressure for the ten respiratory cycles.

Statistical Analysis

Results are presented as mean ± standard deviation. Statistical analysis was made by nonparametric ANOVA for repeated measures. Where ANOVA revealed significant effects, Wilcoxon test was used to make appropriate comparisons. The p<0.05 was considered as significant to reject the null hypothesis. Bonferroni correction was used to compensate multiple comparisons.

INSPIRATORY RADIAL PRESSURES

![Figure 1: Effect of MAST inflation on radial artery expiratory pressure. There was no significant difference during MAST inflation for systolic, diastolic or pulse radial artery pressure before, during and after MAST. Mean systolic pressure: 150.1±23.4 mm Hg, 148.1±23.2 mm Hg, NS, 149.1±22.9 mm Hg. Mean diastolic pressure: 98.8±13.3 mm Hg, 97.7±14.6 mm Hg, NS, 97.8±12.4. Mean pulse pressure: 51.2±12.8 mm Hg, 50.0±11.8 mm Hg, NS, 51.32±12.3 mm Hg.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21606/ on 04/29/2017)
RESULTS

We included ten procedures for nine patients. A single patient was admitted twice in the same week for two distinct severe bronchial asthma episodes. All patients had evidence of respiratory and circulatory failure with alveolar hypoventilation, hypoxia, tachycardia and metabolic acidosis with hyperlactacidemia (Tables 1 and 2). No patient had hypotension (Fig 1) but during the inspiratory phase, five had systolic
pressure below 100 mm Hg and diastolic pressure less than 70 mm Hg. For these five patients the pulse pressure was below 30 mm Hg (Fig 2). We observed no difference in respiratory and heart rates during MAST inflation (Table 2). Radial systolic, diastolic and pulse pressures were not significantly changed by MAST inflation during the expiratory phase (Fig 1 and 2) but all three parameters significantly increased during the inspiratory phase (Fig 1 and 2) for each individual patient. Pressure variations between inspiration and expiration (delta pressures) were markedly decreased by MAST inflation (Fig 3); delta systolic (ie, paradoxic pulse): 44.3 ± 20.3 vs 27.5 ± 13.0 mm Hg; delta diastolic: 26.2 ± 9.4 vs 19.5 ± 7.4 mm Hg. Delta pulse pressure was also significantly decreased by MAST inflation (18.5 ± 11.8 vs 8.0 ± 6.5 mm Hg). After MAST deflation, all patients returned to baseline values.

The decrease in paradoxic pulse became significant after inflation of only the bladders of the inflaters for the legs (Fig 4). In three patients who were excluded from the protocol because of their refusal to wear the MAST, one liter of colloid fluid was infused rapidly for hypovolemia and it caused the same effect upon paradoxic pulse as wearing the MAST (Fig 5).

**DISCUSSION**

We demonstrated a constant and significant increase in inspiratory systolic, diastolic and pulse arterial pressures during MAST inflation while expiratory pressures remained unchanged. In consequence, delta systolic (paradoxic pulse), delta diastolic and delta pulse pressures all decreased. All pressures returned to baseline values in inspiration after MAST deflation.

Respiratory and heart rates were unchanged during the whole MAST procedure, suggesting that there had been no change in airway obstruction during the limited duration of the protocol.

**Criticism of Methodology**

The choice of MAST inflation for realizing a rapid filling test seems most appropriate in such patients. Indeed, this method has two advantages: (1) reversibility of volume loading in a situation in which vigorous fluid therapy may promote pulmonary edema, and (2) the possibility for a patient to be his own control: the short duration of the protocol and the reversibility allowed us to check for the absence of other causes (such as airway obstruction improvement) to explain the variations of arterial pressures.

The increased circulatory volume after MAST inflation is of debated importance. If we consider the mean of reported values, the translocated fluid volume from lower extremities and abdomen to the central circulation is about 10 ml/kg. However, there are considerable variations depending on circulating blood volume, baroreceptor activity and the protocol of MAST inflation, including the order of sequential inflation (first of the bladders of the inflaters for the legs and then of the bladder of the inflater for the abdomen) and pressure levels. Reported physiologic adaptation following MAST inflation includes progressive increase in atrial natriuretic factor and decrease in vasopressin and decrease in renin activity which may all alter the hemodynamic status of the patient. However, limited duration of the protocol and return of hemodynamic values to baseline after MAST deflation led us to consider these responses as negligible.

**FIGURE 4.** Decreased paradoxic pulse during MAST inflation: leg inflation = after only the bladders for the legs have been inflated. Total inflation = after the bladders of the legs of the abdomen have been inflated. *p<0.05, **p<0.01.

**FIGURE 5.** Decreased paradoxic pulse after rapid fluid infusion in three patients excluded from the study because they refused wearing MAST.
Decrease in Paradoxic Pulse due to an Inspiratory Increase in LVSV: The observed reduction in paradoxic pulse during MAST inflation paralleled the increase of inspiratory arterial pulse pressure. Theoretically, this may be due to either an increased inspiratory left ventricular stroke output or a decreased inspiratory systemic vascular distensibility. Our findings suggest a mechanism taking place only during inspiration and not during expiration. It is likely that MAST inflation would have acted on systemic arterial distensibility throughout the entire respiratory cycle. In addition, most of the clinical reports on hemodynamic consequences of MAST inflation at moderate pressure inflation, as used in our study, concluded that such external pressures only affect low pressure veins and not the high pressure arteries. This allows us to conclude that MAST inflation increases inspiratory left ventricular stroke output.

Inspiratory Increase in LVSV Secondary to Increase in PVR: Because left ventricular afterload and contractility are unchanged during MAST inflation, it is therefore likely that MAST inflation increases inspiratory left ventricular preload. An inspiratory increased left ventricular preload may be due to a decreased ventricular interdependence or an increased PVR. Ventricular interdependence tends to increase during MAST inflation. All investigators observed an increase in venous return and hence right ventricular volumes. This strongly argues against ventricular interdependence as the dominant mechanism for paradoxic pulse in asthma and allows to consider an inspiratory increase in PVR as the main effect of MAST inflation.

Inspiratory Increase in PVR as an Increase in RV Performance: An inspiratory increase in pulmonary venous return may result from one of the following: enhanced inspiratory RV performance or reduced inspiratory pulmonary venous pooling. The MAST inflation might increase the fraction of the lung in zone 3 and hence participate to increase the pulmonary venous flow for the same lung inflation. During our procedure there was no variation of the degree of airway obstruction, and possible modification of the lung zone characteristics may only be due to an increase in inspiratory RV output. Thus, even if an increased zone 3 may act as an amplifier, our findings are consistent with an inspiratory improvement of the RV performance.

Increased RV Performance as an Increase Preload: Theoretically, an increase in RV performance may be due to an increase in preload or a decrease in afterload, but during the study period there was no variation of the various factors known to overload the right ventricle during asthma: increased pulmonary resistance by pulmonary hyperinflation, hypoxia, hypercapnia and acidosis. Recently, Jardin et al highlighted the influence of the decreased extramural pressure in afterloading the RV, assuming that the pressure surrounding free wall of the RV (pleural pressure) was lower than the mean alveolar pressure surrounding intrapulmonary vessels. Regarding this mechanism, the abdominal compartment inflation of the MAST may increase intraabdominal pressure and consequently increase the pleural pressure by passive elevation of the diaphragm. We do not believe this phenomenon to be important because the inspiratory transdiaphragmatic pressure is very high during an asthmatic attack and would not be significantly affected by low pressure MAST inflation. In addition, most of the results were obtained solely after leg compartment inflation (Fig 4). This also is suggested in three additional patients, who exhibited the same trend of a decreased paradoxic pulse after 1L of rapid colloid infusion (Fig 5). For these patients we have no additional information regarding variation of pleural pressure due to eventual airway obstruction improvement. A decrease in paradoxic pulse was, however, observed after the very short time necessary to infuse 250 ml and no clinically detectable modification in the degree of airway obstruction was observed.

Paradoxic pulse is not a usual feature of hypovolemia. However, MAST may correct paradoxic pulse in asthma by increasing systemic venous return without modifying airway obstruction. Thus, we can state that paradoxic pulse in asthma is due to the combination of airway obstruction and insufficient systemic venous return, that may be absolute (true hypovolemia) or relative in face of increased right ventricular afterload. These findings are consistent with other reports in cardiac tamponade where a decreased systemic venous return was shown to be an important factor in the genesis of paradoxic pulse. The combined effects of asthma on systemic venous return, right heart, pulmonary capillary bed, pulmonary vein and left heart result in paradoxic pulse but the contribution of each specific effect is not known. In asthma, as in other situations of acute pulmonary hypertension, the stroke volume is preserved though enlargement of the RV (Frank-Starling mechanism). Several inconstant factors reported during an asthmatic attack may act as limiting factors for such a RV dilation: hypovolemia, tachycardia, lung hyperinflation, pericardial stretching by thoracic hyperinflation or inspiratory collapse of the IVC. The positive abdominal pressure during inspiration also may affect venous leg return. The cumulative effect of these factors might induce a fall of inspiratory RV ejection and stroke output. The MAST inflation may restore a more adequate preload against hyperinflated lung-induced RV overload. The inspiratory collapse of the IVC is not necessarily the major cause of inspiratory decrease in RV filling; MAST inflation may maintain IVC open
a longer period of time during inspiration by increasing leg and abdominal venous pressure.

**Therapeutic Consequences**

Our patients all had evidence of severe asthma with alveolar hyperventilation and presumably inadequate cardiovascular adaptation as shown by metabolic acidosis with hyperlactacidemia, marked tachycardia, large paradoxic pulse and reduced inspiratory pulse pressure. Hyperlactacidemia in status asthmaticus is of debated mechanisms,36-40 but a moderately increased cardiac output, insufficient in regard to hypoxemia and increased metabolic demands, has been reported.41 The filling test with MAST inflation improves cardiovascular adaptation during severe bronchial asthma. Nevertheless, increasing lung blood volume could potentially increase the pulmonary capillary pressure and the risk of bronchial or interstitial edema.9 Alveolar capillary bed is exposed to alveolar pressure. However, we know little about the mean intra-alveolar pressure during acute asthma.41,42 At inspiration, if air enters the alveolus in spite of bronchoconstriction, mean intra-alveolar pressure is obviously more negative than in the normal lung, but with hyperinflation, lung compliance decreases and then transpulmonary pressure (alveolar minus pleural pressures) becomes more negative. Thus, markedly negative pleural pressure might produce a strong pressure gradient between the capillary bed and LV promoting LV venous return rather than interstitial extravasation. However, it has been shown recently that patients with severe COPD and ischemic heart disease may exhibit LV failure that requires diuretics when LV is afterloaded by elevated transdiaphragmatic pressure (weaning from mechanical ventilation)41,42 and supports the hypothesis of an increased risk of pulmonary edema. In asthma, acute pulmonary edema has never been reported. Possibilities include the young age of these patients, the absence of prior LV diseases, and the high level of endogenous and exogenous \( \beta_{2} \)-agonists. The role of superimposed hypovolemia and the possibly increased transpulmonary pressure protecting capillary bed from extravasation further protects them against pulmonary edema. In our patients with presumably normal heart, the net effect of both increased transpulmonary and transdiaphragmatic pressure seems predominantly an impaired LV filling in spite of an increased LV afterload.

It also has been argued that coronary insufficiency may occur during severe asthma4-2 but this has not been substantiated in the literature. In our study, three patients had inspiratory diastolic radial pressure lower than 60 mm Hg and inadequate coronary blood flow might participate in cardiac dysfunction. We have no data regarding LV coronary perfusion pressure (ie, diastolic aortic pressure minus LV intramural diastolic pressure), but it is expected to be normal because of the negative LV intramural diastolic pressure during inspiration.43 In contrast, RV coronary perfusion may be more markedly impaired in the face of increased oxygen demand due to RV overload. In RV myocardial perfusion is both systolic and diastolic.44 The decrease in inspiratory stroke volume causes a more important decrease in systemic arterial pressure than in RV intramural systolic pressure so that RV systolic coronary perfusion pressure may decrease. In our study, MAST inflation was of too short duration to influence significantly coronary perfusion, but prolonged MAST inflation or fluid therapy could nevertheless increase RV coronary (and also diaphragmatic) systolic perfusion pressure in such patients.

In conclusion, the present study suggests that inadequate cardiac filling may be the predominant factor responsible for paradoxic pulse during a severe asthma attack. The finding is of therapeutic value in the presence of circulatory failure.

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