Intensive Care Med (1982) 8:85 – 88

Intensive Care Medicine

Intravenous Nitroglycerin in Acute Respiratory Failure of Patients with Chronic Obstructive Lung Disease, Secondary Pulmonary Hypertension and Cor Pulmonale

F. Fourrier, C. Chopin, A. Durocher, D. Dubois and F. Wattel

Service d'Urgence Respiratoire et de Réanimation Médicale, Hôpital A. Calmette, Lille, France

Accepted: 3 February 1981

Abstract. We have studied the hemodynamic effects of an intravenous single dose of nitroglycerin in 13 patients with secondary pulmonary hypertension and Cor Pulmonale, during the acute course of respiratory failure and under assisted ventilation. We observed a significant decrease in systolic, diastolic and mean pulmonary arterial pressures, and in pulmonary resistance and systolic right ventricular work index, without any change in right or left pre-loads. The systolic arterial pressure decreased slightly, without any change in cardiac index or diastolic pressure. The arterial and mixed venous oxygen contents, and the pulmonary shunting (Qs/Qt) were unchanged. These results suggest that nitroglycerin may be a useful therapy in patients in the acute stages of pulmonary hypertension resulting from chronic lung disease and under assisted ventilation. In addition, the lack of change in cardiac index, intrapulmonary shunting and oxygen content suggests that this decrease in pulmonary resistance is not linked with any deleterious effect in oxygen transfer.

Key words: Secondary pulmonary hypertension – Nitroglycerin – Acute respiratory failure

Introduction

Recent clinical and hemodynamic studies have pointed out the usefulness of vasodilators in pulmonary hypertension. In chronic obstructive lung disease (COLD), the occurrence of acute respiratory decompensation is often linked with an exacerbation of right ventricular failure. So the possibility of decrease in pulmonary resistance and right ventricular systolic work could be a new way of treatment in these cases. Active vasodilation has been previously assessed with nifedipine [7], oral hydralazine [6] and sublingual nitroglycerin (NG) [5] and the effective decrease in pulmonary pressures and resistance is now well documented.

However in these studies, which have been done in spontaneously breathing patients, the consequences of active vasodilation on gas exchange and VA/Q ratios resulted in most cases in a fall of PaO_2. The increase in venous admixture could be a consequence of active vasodilation in poorly ventilated areas. In this way, vasodilation could be more dangerous than useful by suppressing the natural compensatory mechanism of hypoxic vasoconstriction.

To our knowledge, the assessment of pulmonary vascular reactivity has never been evaluated in patients with COLD during mechanical ventilation. The purpose of this study was to document the efficacy and consequences of intravenous NG in this situation.

Patients and Methods

Thirteen patients (eleven men, two women; mean age: 54 ± 12 years) admitted with acute respiratory failure were studied. In each case, the diagnosis of COLD had been made for three years or more. No patient had history or features of left heart failure, coronary artery disease or cardiac arrythmia. No patient required vasoactive drug infusion or digitalis therapy before the study.

The hemodynamic study was performed during the acute decompensation, between the third and the seventh day after admission. All patients were me-

0342-4642/82/0008/0085/$01.00

chanically ventilated using volumetric respirators[1]; PEEP was never used. In each case, arterial PCO_2 and pH were within normal ranges, and the working FIO_2 was choosen to obtain a normal PaO_2 (Table 3). Patients were in supine position. Prior informed consent was obtained appropriately.

After insertion of the right heart catheter[2] and of an arterial radial or femoral cannula under local anesthesia, and following a subsequent period of 5 min equilibration, the control hemodynamic and blood gas measurements were obtained. They included heart rate, systolic, diastolic, end-diastolic right ventricular pressures (RVP), systolic, diastolic and mean pulmonary pressures (PAP), mean pulmonary capillary wedge pressure (PCWP), systolic and diastolic arterial pressures. The cardiac output was obtained using the thermodilution method[3] (mean of three measurements). Cardiac index, pulmonary resistance, peripheral resistance, left and right systolic work index were calculated with standard formulae. Simultaneous arterial and mixed venous blood samples were analyzed immediately with standard electrodes for pH, PCO_2, PO_2, base excess, total CO_2 content, and SO_2. The O_2 contents were calculated from the standard equation:

$$O_2 \text{ content} = (Hb \times 1.35 \times SO_2) + (PO_2 \times 0.003) \text{ ml/100 ml}$$

The ratio of venous admixture to total blood flow (Qs/Qt) was calculated from the standard equation: $Qs/Qt = (Cc'O_2 - CaO_2)/(Cc'O_2 - CvO_2)$.

The capillary oxygen content was calculated from the formula: $Cc'O_2 = Hb \times 1.35 + [((FIO_2 \cdot (Pb - 47)) - (PACO_2/R) + (PACO_2 \cdot FIO_2 \cdot (1 - R/R)] \times 0.003$.

The respiratory quotient was presumed equal to 0.8 and $PACO_2$ to $PaCO_2$.

In each case the mean PAP was over 25 mmHg. The vascular pressures were measured during one respiratory cycle under mechanical ventilation. The end expiratory values were retained.

Nitroglycerin was then given intravenously. All patient weights were within 60 and 70 kg and the chosen injected dose was 1.5 mg in each case. According to the half-life of the drug, the hemodynamic and blood gas measurements were then repeated between 1 and 4 min after administration.

For statistical analysis of the results, Student's test for paired values was used. The mean values are expressed with standard deviation.

1 Monaghan M 251; Bennett MA2 B
2 Swan Ganz 7 F catheter – Bentley trantec M 800 transducer
3 Edwards Lab. M 9510 A – CO computer

Results

Hemodynamic Changes (Tables 1 and 2)

After intravenous administration of NG, the systolic PAP decreased significantly (44.15 ± 4.76 before vs 34.08 ± 3.55 after, $p < 0.01$), as the diastolic PAP (23.46 ± 2.82 vs 17.77 ± 3.03, $p < 0.01$), and the mean PAP (29.00 ± 2.57 vs 22.00 ± 2.48). In all cases but three, the decrease in systolic PAP was the most important so that the shape of the curve was changed. A significant decrease in pulmonary resistance (7.84 ± 0.95 vs 5.46 ± 1.20, $p < 0.05$) and in right venticular systolic work index was observed (15.59 ± 2.31 vs 9.59 ± 1.25, $p < 0.01$).

The end diastolic RVP and the PCWP were unchanged. The heart rate increased slightly and a reduction in systolic systemic arterial pressure was observed. There were no significant changes in cardiac index, stroke volume, peripheral resistance or diastolic blood pressure.

Blood Gas Changes (Table 3)

A slight but non-significant decrease in PaO_2 was observed (93.85 ± 1.66 before NG vs 90.92 ± 1.98 after). However the arterial and mixed venous O_2 contents, as the arterial-venous O_2 difference and the Qs/Qt remained unchanged. No difference could be observed in PaO_2, pH, base excess and total CO_2 content.

Comments

The hemodynamic changes observed after IVNG are consistent with the known pharmacological actions of the drug: slight increase in heart rate, decrease in PAP, pulmonary resistance and systolic work index.

However, no change could be observed in cardiac index, nor in right and left ventricular filling pressures. This surprising lack of change is not consistent with other studies (realised in spontaneous ventilation) where the reduction in right ventricular after-load was linked with a decrease in right ventricular filling pressure and/or in cardiac index [3, 5]. Several hypotheses may be forwarded.

It may be due to the previous existence of a severe alteration of myocardial contractility but the individual and mean values of end-diastolic ventricular pressures are not consistent with such a mechanism in our study.

The use of a high dose of NG in IV bolus could lead to exclusive arterial vasodilation with a further

Table 1. Hemodynamic changes in pulmonary circulation

Data	Before NG	After NG	Variation %	Stat. signif.
MEANRAP mmHg	4.46 ± 0.84	4.23 ± 1.19	− 5%	NS
S. PAP mmHg	44.15 ± 4.76	34.08 ± 3.55	−23%	$p < 0.01$
D. PAP mmHg	23.46 ± 2.82	17.77 ± 3.03	−21%	$p < 0.01$
MEAN PAP mmHg	29.00 ± 2.57	22.00 ± 2.48	−24%	$p < 0.05$
RV SWI g/mn/m^2	15.59 ± 2.31	9.59 ± 1.25	−38%	$p < 0.01$
PULM. RESIS. UI	7.84 ± 0.95	5.46 ± 1.20	−30%	$p < 0.05$

Table 2. Hemodynamic changes

Data	Before NG	After NG	Variation %	Stat. signif.
PCWP mmHg	10.77 ± 1.68	9.18 ± 1.26	− 5%	NS
SYST. B.P. mmHg	126.92 ± 4.72	109.23 ± 6.01	−14%	$p < 0.01$
DIAST B.P. mmHg	77.02 ± 3.29	73.08 ± 3.08	− 5%	NS
PERIPH RESIST. UI	30.16 ± 2.27	29.31 ± 2.09	− 3%	NS
C.I. l/mn/m^2	3.11 ± 0.26	2.90 ± 0.25	− 7%	NS
H.R. b/mn	90.31 ± 7.82	96.38 ± 5.84	+ 6%	NS

Table 3. Blood gas changes

Data	Before NG	After NG	Variation %	Stat. signif.
PaO_2	93.85 ± 1.66	90.92 ± 1.98	−3%	NS
CaO_2	17.62 ± 1.07	16.90 ± 1.13	−4%	NS
CvO_2	11.78 ± 1.52	12.05 ± 1.31	+2%	NS
$D(a-v)O_2$	5.10 ± 0.68	4.76 ± 0.44	−7%	NS
Qs/Qt	16.62 ± 0.92	17.69 ± 0.94	+6%	NS

increase in heart rate and contractility, with a paradoxical venoconstriction due to an adrenergic reaction. The slight increase in heart rate and the insignificant changes in peripheral resistance are however not consistent with such a postulate.

Finally, the lack of change in right ventricular filling pressure may be due to the action of mechanical ventilation on venous return, so that the effects of NG on venous pooling may be offset. These actions of mechanical ventilation are indeed now well documented and it is possible that in such conditions, NG has a direct effect on pulmonary vascular compliance producing a significant reduction of pulmonary vascular resistance without any change in venous return and consequently cardiac index [2].

The consequences of active vasodilation on gas exchange have been documented previously in spontaneously breathing patients: in the study of Mookerjee et al. [5], there was a fall in PaO_2 after oral NG with simultaneous increase in venous admixture and vd/vt ratio. The same decrease in PaO_2 was found by Fahmy [1] during surgical procedures and by Kopman et al. [4] in patients with coronary artery disease. It must be noted that these patients had normal PAP before administration of the drug. In the study of Konietzko et al. [3], NG was administered to patients with chronic restrictive lung disease and Cor Pulmonale. A small drop in PaO_2 was found with a simultaneous increase in O_2 alveolar-arterial gradient. These data were consistent with the "opening of actively occluded vessels in areas of hypoxic alveoli" with decrease in regional VA/Q ratio and resultant increase in venous admixture.

In our study, the fall in PaO_2 was very small and not significant and was not sufficient to produce any change in arterial oxygen content. Since the cardiac output itself was not altered, it can be presumed that the decrease in pulmonary resistance and pulmonary

pressures after NG was not linked with any further hypoxemia or decrease in O_2 transfer.

In fact, the consequences of active vasodilation on gas exchange could be very diverse, namely an increase of perfusion of poorly or unventilated areas; a decrease of perfusion in well ventilated areas by redistribution of blood flow towards previously vasoconstricted areas, and parallel increase in perfusion and ventilation after relaxation of bronchial and vascular musculature. In our study, where the patients were being ventilated and had normal blood gases, it can be presumed that hypoxic vasoconstriction was not present so that NG could produce active vasodilation in well as in poorly ventilated areas. This redistribution of pulmonary blood flow seemed to be quite homogenous and no change in $PaCO_2$ was found. It must be underlined, however, that a small increase in Vd/Vt with a dead space effect could have been offset by the high level of tidal ventilation.

On the basis of the results of this study, NG appears to be an active vasodilator by lowering pulmonary pressures and resistance without deleterious effect on oxygen transfer in patient with COLD who are being mechanically ventilated.

Acknowledgements. We are indebted to Ms. M. C. Bouche for technical assistance.

References

1. Fahmy NR (1978) Nitroglycerin as a hypotensive drug during general anesthesia. Anesthesiology 49:17 – 20
2. Kadowitz PJ, Higashida R, Hyman AL (1973) Effects of systemic vasodilatators on pulmonary venous tone. Am J Cardiol 43:405 – 408
3. Konietzko N, Schlehe H, Harisch B, Matthys H (1975) Effect of isosorbide dinitrate on hemodynamics and respiration of patients with coronary artery disease and of patients with Cor pulmonale. Respiration 32:368 – 377
4. Kopman EA, Weygandt GR, Bauer S, Ferguson JB (1978) Arterial hypoxemia following administration of sublingual nitroglycerin. Am Heart J 96: 444 – 447
5. Mookherjee S, Fuleihan D, Warner RA, Vardan S, Obeid AI (1978) Effects of sublingual nitroglycerin on resting pulmonary gas exchange and hemodynamics in man. Circulation 57:106 – 110
6. Rubin LJ, Peter RH (1979) The effects of oral hydralazine on rest and exercise hemodynamics in pulmonary hypertension secondary to chronic lung disease. Clin Res 27:793 A
7. Simonneau G, Escourrou P, Legrand A, Cerrina J, Duroux P, Lockart A (1980) Hemodynamic effects of Nifedipine in acute respiratory failure complicating chronic obstructive lung disease. Intensive Care Med 6:61 (Abstract)

F. Wattel
Service d'Urgence Respiratoire et de Réanimation Médicale
Hôpital A. Calmette
C.H.U.
F-59037 Lille Cedex, France