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DOPAMINE MODULATES OXYGENATION OF THE JEJUNAL MUCOSA

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Dopamine increases blood flow to the mucosa and submucosa of the intestine. However the effects of this increase in regional oxygen transport on tissue oxygenation are unknown. The aim of this study was to investigate the influence of dopamine on mucosa and serosa oxygen tension and oxygen saturation.

Six fasted domestic pigs (31±1,3kg) were anesthesized, paralyzed (Sufentanyl, Midazolam, Vecuronium) and normoventilated. A small segment of the jejunal mucosa and serosa was exposed by a midline laparatomy and an antimesenteric incision. A venous catheter was inserted into the mesenteric vein. Two modified Clark-type multiwire oxygen electrodes (MDO) were placed on the surface of the exposed mucosa and serosa. An "Erlanger Micro Lightguide Spectrophotometer (EMPHO II)", based on the principles of remission spectrophotometry, was used for determination of intracapillary hemoglobin oxygenation. To study the influence of intestinal motility on regional oxygenation electromyogenic potentials (EMP) were recorded continuously. Following baseline measurements dopamine was infused in exponential steps (2,4,8,16,32,2µg/kgBW*min). Systemic oxygen transport (DO2sys) and consumption (VO2sys), extraction ratio of the gut (ERgut), serosa (pO2ser) and mucosa oxygen tension (pO2muc) and mucosa oxygen saturation (Hbsat) were determined at each step.

Results: Baseline DO2sys 10,8 ± 2,6 ml/kg*min; VO2sys 4,4 ± 0,5 ml/kg*min; ERgut (0,33 ± 3). Baseline tracings of pO2 muc (24,4 ± 8,5 torr) and HBsat (51,6 ± 13%) but not pO2ser (60 ± 19,5 torr) showed regular oscillations with a frequency of 4 to 5 cycles/min. There was no relation to the slow wave frequency of the EMP (9 to 14/min). Increasing dopamine resulted in a dose dependent increase in DO2sys (+40%) but no change in VO2sys. This was associated with an elevation of pO2muc (+50%) and Hbsat (+30%). ERgut decreased continuously to 50% of baseline. PO2ser and EMP frequencies remained unchanged. Po2muc and Hbsat oscillations increased in frequency and decreased in amplitude.

Conclusions: Dopamine modulates the microcirculation of the gut. Dopamine increases mucosa oxygenation in a dose dependent manner and has no effects on serosa pO2 and on jejunal motility.

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EFFICACY AND HEMODYNAMIC PROFILE OF INTRAVENOUS FENOLDOPAM IN PATIENTS WITH HYPERTENSIVE CRISIS

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Fenoldopam (F) acts through stimulation of post-synaptic dopaminergic DA1-receptors. It exerts no significant Alpha-, Beta- or presynaptic DA2-receptor agonist activity. These findings prompted us to assess the efficacy of F. to control acutely elevated blood pressure (BP > =200 mmHg syst., > =100 mmHg diast.) and to determine the hemodynamic profile of F. in these patients.

Immediately after obtaining baseline values (art. BP, PAP, PAOP, CO, HR), the therapy with F. was started with an initial dose of 0.2 mcg/kg/min. and increased every 10 min. by 0.1 mcg/kg/min. until blood pressure was controlled (< =170/100 mmHg) Blood pressure measurements and complete hemodynamics were performed in 10 min. intervals. F. decreased in all 12 pat. with hypertensive crisis the blood pressure to the desired level of 170/100 mmHg within 20-25 min. (range: 5 - 40 min.). The median dose to achieve blood pressure control was 0.3 mcg/kg/bw (range: 0.2 - 0.5 mcg/kg/bw). The most striking finding was a significant decrease in TPR (1853 to 1193 dyn. sec an-5), associated by a moderate, non significant increase of heart rate (80 to 86 min.-1), cardiac index (3.3 to 3.5 1/min/m2) and mixed venous oxygen saturation (75 to 78%). PAP remained unchanged, but pulmonary vascular resistance showed a trend towards lower values. PAOP tended to decrease as well, especially in those pat. with high filling pressure at study entry. F. was well tolerated. No clinical adverse event or laboratory abnormality occurred during the observation period.

We conclude that Fenoldopam is an effective intravenous agent for treatment of hypertensive crisis. Its high and reliable efficacy, linear dose-response relationship and rapid onset of action suggest that F. may have a role when perenteral treatment of severe hypertension is required.

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Pressure-support ventilation

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EFFECTS OF VARIATIONS OF EXPIRATORY TRIGGER SENSITIVITY (ETS) DURING PRESSURE SUPPORT VENTILATION (PSV) AT CONSTANT ALVEOLAR VOLUME.

Palo A., Iotti G., Brunner J. X., Smits T., Olivei M., Galbusera C., Raimondi F., Braschi A.

Variations in ETS during PSV have complex effects on patient's respiratory activity. We have revisited the problem by evaluating different ETS during PSV in a simplified experimental context. This was characterized by a constant alveolar volume (VA), the latter being defined by tidal volume minus series dead space.

Methods. The study included 10 patients in PSV for ARF. For each patient the ETS was ramdomly varied between 10, 25, 40 and 55 % of the peak inspiratory flowrate, while the VA was kept constant by close loop control of the PS level. The effects of the ETS variations were evaluated during steady state in terms of breathing pattern, gas exchange and indices of drive, effort and work.

Results. Mean values and level of significance of the parameters that showed major variations:

ETS	10%	25%	40%	55%	P(ANOVA)
Ti(s)	1.16	1.003	.856	.767	.0001
Ti/Ttot	.447	.39	.359	.328	.0001
Vt/Ti (ml/s)	.422	.465	.542	.607	.0001
PS (cmH2O)	14.369	15.78	17.293	19.974	.0002

Changes of Vt, Ttot, AutoPEEP, pH, PaO2, PaCO2, P0.1 and patient inspiratory work (WiPat) were minor and not significant. An increase of ETS, by decreasing the threshold for cycling to expiration, directly results in a reduction of Ti and duty cycle (Ti/Ttot). In our study this latter did not affect AutoPEEP and PaO2, both being probably more influenced by other factors that remained constant (Vt, Ttot, PEEP, FiO2). In order to keep a constant VA, the reduction of Ti had to be compensated by an elevation of the driving pressure. This compensation was performed by the machine by adequately increasing the PS level, so that no variations of patient's respiratory effort occurred, as witnessed by the absence of major changes of P0.1 and Wipat.

Conclusion. The Ti/Ttot of spontaneously breathing patients in PSV can be controlled by varying the ETS, without need for forcing fixed Ti and Te. No influence on patient drive and effort results, provided that the ventilatory pattern is maintained constant by adequate changes of the PS.

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NONINVASIVE, BREATH BY BREATH EVALUATION OF TOTAL EXPIRATORY TIME CONSTANT DURING PRESSURE SUPPORT VENTILATION (PSV).

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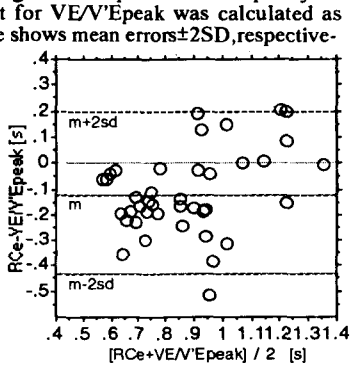
The expiratory time constant (RCe) of the unit represented by total respiratory system and ventilator defines, together with the expiratory time, the presence and the degree of dynamic hyperinflation and auto-PEEP. A continuous evaluation of RCe could be useful for adequately setting the ventilator, either manually or automatically. The assessment of RCe from measurements of resistance and compliance is difficult to be performed, specially during partial ventilatory support. For a continuous and noninvasive evaluation of RCe the ratio between the exhaled tidal volume (VE) and the peak expiratory flow (V'Epeak) can be suggested, being VE/V'Epeak a first approximation of the slope of the expiratory flow-volume curve. In order to investigate the accuracy of this approach and its possible dependance from the degree of respiratory muscle activity, we studied 8 non-COPD patients in PSV for ARF, at four different levels of pressure support (PS). In each condition, ventilator expiratory resistance (Rext), lung resistance (RL) and compliance (CL) were measured, while total compliance (Ctot) was calculated using chest wall compliance, this latter assessed during a final step of CMV and paralysis. Finally the reference measurement for VE/V'Epeak was calculated as RCe = (RL+Rext) * Ctot. The figure shows mean errors±2SD,respectively corresponding to -0.12 ±0.32 or -18.8±44.8%. VE/V'Epeak, although correlating well with RCe (R=0.757), tends to overestimate the low values. Considering the different conditions, the correlation is better in CMV and decreases with lower PS levels, i.e. with higher breathing activity. VE/V'Epeak allows a simple and noninvasive evaluation of RCe during both controlled and assisted ventilation, even if high degrees of respiratory muscle activity are associated with less accurate results.



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AUTOREGULATED INSPIRATORY SUPPORT VENTILATION

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In order to avoid the inconvenients related to available methods of weaning (risk of hypo and hyperventilation, lung hyperinflation, and necessity to modify settings frequently to meet the patient's needs), we propose a new mode of AutoRegulated Inspiratory Support ventilation (ARIS) whose main characteristics are : controlled tidal volume, decreasing inspiratory flow pattern, zero flow cycled, automatic regulation from spontaneous breathing to controlled ventilation according to patient's needs.

The principle for regulation uses the three fundamental parameters of ventilation : the minute ventilation (choosen by the doctor as the optimal level (V_{Eopt})), the minimum tidal volume (V_{Tmini}) and as a result, the maximum respiratory rate (RR) determined by RRmax = V_{Eopt} / V_{Tmini}. For maximum safety a value of maximum airway pressure is entered (Paw,max). Spontaneous mode of ventilation is maintained as long as patient's respiratory performance is compatible with the settings. On the contrary, the patient is given an inspiratory aid in order to meet both minimum V_T and optimum V_E or to decrease RR. Inspiratory support consists of an added markedly decreasing inspiratory flow as soon as inspiration starts. In the prototype, the flow was generated by discharging a pressurized tank into the patient's lung. The inspiration starts by testing the (zero-µ) flow level. It ends when the flow has reached the zero value subject to a minimum duration. The resultant flow is the sum of the flow given by the system and the flow spontaneously inspired by the patient through an additional valve. Expiration is a passive phenomena. The patient determines by himself VT, RR and inspiratory/expiratory ratio with respect to the settings.

An experimental protocol was instituted in the aim to compare the performance of the prototype with the conventional controlled ventilation. It included eight informed and consented adult patients without selection of pathology. Patients were submitted to controlled mode using a modern ventilator (CV) and then to the ARIS mode. With ARIS, the settings were chosen in order to obtain the same minute ventilation compared with CV. Blood gas samples were withdrawn after a 30 min stabilisation period.

From CV to ARIS mode, VE (l/min) remained identical (10.5±2.1 in CV vs 10.6±1.9 in ARIS). Level of Paw,mean was the same, but there was a significant difference in Paw,peak (cmH20) which was reduced from 36.2 ± 10.5 in CV to 26.5 ± 6.4 in ARIS. The value of T_I/T_{tot} was significantly modified from 0.28 ± 0.061 in CV to 0.354 ± 0.038. There was no significative difference on blood gas results.

These results confirmed that the prototype gives the patient a good and effective ventilation comparable to the CV mode using modern respirator and that the risk of barotrauma evaluated by peak airway pressure is considerably reduced. Long term clinical trials will be needed to establish efficiency and reliability of the ARIS ventilation and its interest compared to the current total or partial modes of ventilation.

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EFFECT OF PRESSURE INCREASE TIME AND TRIGGER THRESHOLD ON WORK OF BREATHING AND PRESSURE-TIME PRODUCT DURING PRESSURE SUPPORT VENTILATION

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Pressure support ventilation has been shown to facilitate the patient's efforts of breathing by reducing both the work of breathing (WOB) and the pressure-time product (PTP). In the pressure support mode of the EVITA ventilator (Dräger AG, Lübeck, Germany), the pressure increase time (the time to reach the preselected support level) and the trigger threshold (the inspiratory flow the patient has to generate to initiate ventilator support) can be varied to adapt to patient's requirements. The aim of this study was to determine the effects of pressure increase time (PIT) and trigger threshold on WOB and PTP. In 6 patients we combined PIT of 1.8 s and 0.3 s with TT of 3 l/min and 12 l/min respectively during weaning after coronary bypass surgery. WOB and PTP were measured with a Bicore CP-100 monitor (Bicore, Irvine, CA). Pressure support level was 10 cmH_2O with 5 cmH_2O PEEP.

	Pressure Increase Time (s)/Trigger Threshold (l/min)			
	1.8/3	0.3/3	1.8/12	0.3/12
WOBt (J/l)	1.1±0.2	1.2±0.2	1.1±0.2	1.2±0.2
WOBv (J/l)	0.5±0.03	0.8±0.04*	0.5±0.06	0.9±0.06*
WOBp (J/l)	0.6±0.02	0.4±0.02*	0.6±0.02	0.3±0.02*
PTP(cmH_2O s/min)	122±17	83±17*	120±21	81±25*

Mean±SD; WOBt=total work of breathing; WOBv=work of breathing ventilator; WOBp=work of breathing patient;*p<0.05, Wilcoxon-test.

Shortening the pressure increase time led to a significant reduction in patient's work of breathing and pressure-time product, indicating a decrease in patient's efforts of breathing. Trigger threshold variation had no effect on patient's work of breathing and pressure-time product.

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INDICATIONS OF NON INVASIVE PRESSURE SUPPORT VENTILATION (NIPSV) IN ACUTE RESPIRATORY FAILURE (COPD excluded).

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To delineate indications of NIPSV in non COPD pts with ARF, we looked at the result of NIPSV as an alternative to endotracheal intubation (ETI) in a group of 25 non COPD pts with ARF (Congestive heart failure:8,pneumoniae:7,laryngeal dyspnea:4,ARDS:2,chest wall impairement:4). Pts were connected via a face mask to a Puritan-Bennett 7200 ventilator set in the pressure support mode (PS).12 pts (48%) were successfully ventilated with NIPSV (S) while 13 (52%) failed (F) and required ETI 12 times. There was no difference between group S and F in term of age, Glasgow score, encephalopathy, radiologic score, nor in the level of PS, FiO2 and PEEP used. However, the 7 pts with pneumoniae failed (p < 0,02) while 9 of the 10 pts with post extubation ARF were successfully ventilated with NIPSV (p<0,01). The severity score (SAPS) was higher in pts who failed (18±7 vs 11±4, p<0,05) and 8 of the 13 pts who failed had a SAPS>16 (p<0,02). Gas exchange and RR before initiating NIPSV were significantly different between the two groups:

	SUCCESS	FAILURE	p
n	12 (48%)	13 (53%)	
RR (breaths/mn)	29 ± 9	42 ± 11	< 0,05
pH	7,36 ± 0,08	7,45 ± 0,08	< 0,05
PaCO2 (mmHg)	52 ± 22	33 ± 8	< 0,05
(A-a)PO2 (mmHg)	164 ± 81	296 ± 137	< 0,05

Conclusions: hypoxic pts with a high severity score failed to be ventilated with NIPSV. Pts with CO2 retention and post extubation ARF were successfully ventilated with NIPSV.

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NON-INVASIVE VENTILATION (PRESSURE SUPPORT) VIA FACIAL MASK IN THE HYPERCAPNIC FAILURE IN COPD PATIENTS

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COPD patients frequently show severe hypercapnia when respiratory failure develops. Hypercapnic encephalopathy, severe acidosis and respiratory muscle fatigue are the indicators for starting mechanical ventilation.

Objective: to test whether non-invasive ventilation via facial mask could reduce the need for tracheal intubation when mechanical ventilation must be initiated in COPD patients.

Material and methods: we have studied 12 COPD patients during 14 episodes of acute exhacerbation of chronic respiratory failure who failed to improve with intensive medical therapy and showed impairements in severe respiratory acidosis, hypercapnic encephalopathy and/or physical signs of respiratory muscle fatigue leading their attendant physicians to order mechanical ventilation. In these circumstances, a trial of pressure-support (PS) ventilation (Servo Ventilator 900C®) via facial mask (Vital Signs Inc.®) was performed. The level of pressure support was adjusted to obtain a tidal volume >400 ml. When high levels of autoPEEP were suspected, we tried to add external PEEP provided that there was no leakage around the mask. If the patient deteriorated, tracheal intubation and standard mechanical ventilation were performed.

Results (mean±SEM): a pressure-support level of 14±3 cmH_2O was used during a period of 8±4 hours.

	RR /min	pH	$PaCO_2$ mmHg	SaO_2 %
Admission	35±2	7.28±0.02	71±4	73±5
Pre-PS	32±2	7.18±0.02*	91±3*	86±3*
During PS	23±1*¡	7.31±0.01¡	67±3¡	92±1*¡

* p<0.05 compared with admission, ¡ p<0.05 compared with Pre-PS.
RR:respiratory rate, SaO_2:arterial hemoglobin saturation

Three patients needed tracheal intubation and one of them died.

Conclusions: Non-invasive ventilation (pressure-support) via face mask may reduce the need for tracheal intubation in the severe hypercapnic failure of COPD patients.

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