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Early effects of inhalation injury on lung mechanics and pulmonary perfusion *

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Abstract. We investigated the early effects of a rather large amount of cotton-smoke on lung mechanics and pulmonary perfusion. Under halothane anesthesia 18 ewes were intubated with a double-lumen tube. In 6 sheep the left lung was exposed to smoke, in another 6 the right lung. A sham group of 6 sheep was insufflated with air instead of smoke. Prior to and 30–45 min following the smoking- (sham-) procedure the following parameters were determined for the smoke- (sham-) exposed and the contralateral lung: static compliance, inspiratory airway resistance, and physiologic dead space ratio. In addition MAP, MPAP, WP, and CO were recorded. The data indicate that inhalation of large amounts of smoke has no major direct effects on pulmonary mechanics and perfusion in the early post-injury period. Only an increase in airway resistance of the smoke exposed lungs was found, which must be attributed to a local reflex mechanism.

Key words: Inhalation injury – Sheep – Lung mechanics – Pulmonary perfusion

A chemically induced tracheobronchitis is the pathophysiological hallmark of inhalation injury. The formation of mucous casts and subsequent bronchial obstruction not only induces airway closure and impairment of lung mechanics and pulmonary gas exchange but also, in combination with a loss of ciliary clearance activity, predisposes to the development of bronchopneumonia. On admission to the emergency room, however, the respiratory function of inhalation injury patients often is unimpaired and the diagnosis is only made after fiberoptic inspection of the major airways [3, 4]. This is in contrast with several animal studies in which a marked decrease in lung compliance [5] with increased work of breathing [2] and pulmonary vasoconstriction with increased dead space ventilation [7, 8] were observed within the first 30 min after smoke exposure of the lungs. However, significant decreases of lung compliance were only observed in open chest models and increases of dead space ventilation only in the presence of a severely depressed cardiac output. It was the objective of this study to investigate the early effects (within 45 min) of a rather large amount of smoke on pulmonary perfusion and lung mechanics in a closed chest model and in the absence of cardiopulmonary depression due to carbonmonoxide intoxication. For this purpose a sheep model was developed in which only one lung was exposed to smoke.

Materials and methods

Eighteen adult range ewes of Merino or Suffolk breed weighing 38–52 kg were instrumented in a cutdown procedure: an arterial line was placed in the common carotid artery, and a thermistor tipped, flow-directed pulmonary artery catheter was passed into the pulmonary artery from the external jugular vein. Under halothane anesthesia the sheep were placed in the prone position and intubated with a double-lumen tube. We used a commercially available double-lumen tube (Broncho-Cath 35 Fr.-Left, Mallinckrodt Inc., Argyle, NY) that had been modified to meet the sheep anatomy. Under bronchoscopic control the tip of this catheter was introduced into the left main bronchus and the bronchial cuff was inflated just below the carina. Two Siemens Servo 900 C ventilators (Siemens Elema AB, Sweden) operating in a synchronized mode were con-

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nected to the double-lumen tube, each machine ventilating one lung. The respirator ventilating the lung that was not to be exposed to smoke triggered the other ventilator. This ventilator was also equipped with a halothane vaporizer and anesthesia was maintained by adding halothane to the inspiratory gas delivered by this machine.

The ventilator setting was as follows: FiO_2 0.21, controlled ventilation without sigh mechanism, PEEP 5 cm H_2O, continuous inspiratory flow, inspiratory time 25%, and inspiratory pause 10% of the respiratory cycle time. The tidal volumes of both ventilators were adjusted in such a way, that their sum equaled 15 ml/kg body-weight, and inspiratory pause pressures were the same in both lungs, thus adjusting tidal volume for each lung according to its size. The respiratory frequency was set between 8 and 10/min in order to maintain a stable $paCO_2$ in the range between 30 and 40 mmHg. The gas exchange was considered to be at an equilibrium when the $paCO_2$ did not change within 10 min. When this equilibrium was achieved the following parameters were determined (time-point "PRE"): mean arterial blood pressure (MAP), mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (WP), heart rate (HR), cardiac output (CO), pulmonary vascular resistance (PVR), arterial oxygen tension (p_aO_2), arterial carbondioxide tension (p_aCO_2), and mixed venous oxygen tension (p_vO_2). The following parameters were determined for each lung separately: effective static compliance (C), inspiratory airway resistance (R), and physiologic dead space (V_d/V_t). Smoke was produced by filling the combustion chamber of a modified bee smoker [9] with 40 g of ignited cotton toweling. The smoke was delivered by depressing the bellows of the bee smoker. For the actual insufflation procedure the respirator ventilating that lung was disconnected from the tube while the ventilation of the contralateral lung was maintained at an unchanged pattern. The charged bee smoker was connected to the tube by a 30 cm adapter containing a thermistor probe. The temperature of the delivered smoke never exceeded 40 °C. The amount of delivered smoke was adjusted to achieve a carboxyhemoglobin level of 50%. For this purpose carboxyhemoglobin plasma levels were determined intermittently. Thirty to forty-five minutes following the smoking procedure the same parameters were determined again (time-point "POST").

Each of the 18 sheep was randomly assigned to one of three groups: in 6 sheep the right lung was insufflated with smoke (RLI-group), in another 6 sheep the left lung (LLI-group). Six animals underwent a sham procedure in which the bee smoker was substituted by a manual resuscitator and the lung was insufflated with air (SHAM-group).

Cardiac output was determined by means of the thermal dilution technique using a 9520A Cardiac Output Computer (American Edwards Laboratories, Irvine, Calif). For each measurement 10 ml of iced 5%-glucose solution were injected centrally as a bolus using the proximal lumen of the pulmonary artery catheter. For each determination of CO three measurements were obtained and averaged. Intravascular pressures (MAP, MPAP, WP) were measured using pressure transducers (Gould P 23, Gould, Oxnard, Calif). A horizontal plane 5 cm above the sternum was taken as a zero reference. Pressure traces and digital readings were displayed on a physiological recorder (EforM series OM, Electronics for medicine – Honeywell Inc., Pleasantville, NY). The PVR was calculated as the quotient of pressure differences between MPAP and WP, and the cardiac output. Tidal volumes were measured in the inspiratory line of the respiratory circuit utilizing the inspiratory flow transducer of the ventilator. The accuracy of the volume detection by the ventilators electronic unit was confirmed with a Wright respirometer. Airway pressures (IPP, PEEP) relative to the atmospheric pressure were measured at the site of the endotracheal tube connectors using a differential pressure transducer (Statham PM 131TG) and the physiological recorder. Pressure traces were recorded on the monitors strip chart recorder. Effective static compliance (C) was determined utilizing the "inspiratory pause hold" mode of the ventilators. Inflation of both lungs was maintained until the airway pressure plot reached a stable plateau (inspiratory plateau pressure (IPP)). C was calculated by dividing the pressure difference between IPP and PEEP into the tidal volume. Inspiratory airway resistance (R) was calculated by dividing the pressure difference between peak inspiratory pressure and pause pressure into the inspiratory flow. Calculations were performed by a lung mechanics calculator 940 (Siemens Elema AB, Sweden), processing the calibrated airway pressure and flow signals of the ventilator. The physiological dead space/tidal volume ratio was determined using the Bohr equation in its modification by Enghoff. Mixed expiratory CO_2 concentration ($FECO_2$) was measured by means of an microprocessor controlled infrared absorption system employing a fixed volume mixing chamber (Beckman MMC Horizon System, Beckman Inst. Inc., Anaheim, Calif). Averages of $FECO_2$ were obtained over time periods of 5–8 min. During each period the partial pressure of carbon dioxide in the arterial blood was measured. Blood gas samples were analysed at 37 °C (IL 1302, Instrumentation Laboratory Inc., Lexington, Mass) and data were corrected for body temperature. Carboxyhemoglobin concentrations were determined using a spectrophoto-

Table 1. Hemodynamic parameters and blood gas tensions before (PRE) and 30–45 min after (POST) (sham-) smoke-exposure of one lung

		Sham-group	RLI-group	LLI-group
MAP (mmHg)	PRE	87.7±2.3	98.7±2.9	93.3±5.9
	POST	88.5±2.8	98.8±2.7	92.8±5.1
MPAP (mmHg)	PRE	18.2±0.9	17.0±0.6	16.8±0.8
	POST	18.5±0.5	17.7±0.8	17.3±1.0
WP (mmHg)	PRE	10.5±0.8	7.8±0.6[a]	9.0±0.6
	POST	10.8±0.5	8.2±0.6[a]	9.8±0.8
CO (l/min)	PRE	4.0±0.5	4.6±0.3	3.9±0.3
	POST	4.2±0.5[b]	5.2±0.3[b]	4.6±0.5[b]
PVR (dynes s cm^{-5})	PRE	161±20	164±9	161±15
	POST	153±16[b]	150±6[b]	132±10[b]
P_aCO_2 (mmHg)	PRE	33.8±1.3	34.7±0.8	32.8±1.4
	POST	32.7±1.0	36.1±0.6	34.2±1.2
P_aO_2 (mmHg)	PRE	104±3.0	105±3.0	105±3.5
	POST	105±2.8[b]	93±6.4[b]	97±4.1[b]
P_vO_2 (mmHg)	PRE	47.2±1.5	44.8±2.8	43.2±1.8
	POST	45.8±1.4	26.0±2.1[c]	26.8±4.3[c]

Data are mean ± SE.
[a] Compared to SHAM-group, $p \leq 0.05$; [b] compared to PRE, when all three groups are pooled, $p \leq 0.05$; [c] compared to PRE

Table 2. Lung mechanics and physiologic dead space before (PRE) and 30–45 min after (POST) (sham-) smoke-exposure of one lung

		Sham-group		RLI-group		LLI-group	
		left	right	injured	contralat	injured	contralat
C (ml/cmH_2O)	PRE	38.3±1.4	43.3±1.5	43.5±2.1	32.3±2.1	32.5±2.5	40.3±4.0
	POST	37.8±1.5	44.7±1.6	37.2±3.2	32.5±2.3	32.3±2.8	41.8±4.3
R ($cmH_2O/l/s$)	PRE	10.3±1.1	10.8±0.5	11.3±0.3	11.3±0.8	10.3±1.0	10.7±0.6
	POST	11.0±1.2[a]	11.0±0.4[a]	13.0±0.9[a]	11.7±0.7[a]	13.7±0.4[a]	11.8±1.4[a]
V_d/V_t	PRE	47.3±2.4	51.7±3.9	44.0±4.4	51.4±2.3	45.7±1.9	37.0±6.1
	POST	46.7±2.7	50.7±3.2	45.6±4.2	49.8±3.8	43.7±1.5	35.0±6.1

Data are mean ± SE.
[a] Compared to PRE, when all three groups are pooled, $p \leq 0.05$

meter (IL 282 CO-Oximeter, Instrumentation Laboratory).

All data are expressed as mean ± standard error of the mean (SE). Data were analysed as two factor factorial design with repeated measures. Factors are defined as group and time (repeated measure factor). Statistically significant differences were accepted at $p \leq 0.05$.

Results

In the SHAM-group a carboxyhemoglobin-level of 5.5±0.2% was measured immediately following the sham-smoking procedure. The injury produced COHb-levels of 50.8±5.4% (RLI) and 49.2±4.4% (LLI), indicating that both groups had sustained a comparable injury. Despite this severe carbonmonoxide intoxication the cardiovascular system was not depressed in this model (Table 1). Statistical analysis indicated no significant differences between groups at either time-point for MAP, MPAP, CO, and PVR. Only WP is significantly lower at both time-points in the RLI-group, when compared with the SHAM-group. But this difference is practically unimportant as it is only about 2.5 mmHg. Looking at differences between the time-points PRE and POST no statistically significant changes were found for MAP, MPAP, and WP. Only CO increased and PVR decreased significantly from PRE to POST when all three groups are pooled together. This tendency is most pronounced in the two smoke-groups. With no change in MAP, this must be attributed to a decrease in systemic vascular resistance.

Blood gas tensions are summarized in Table 1. In the smoke-exposure groups p_aCO_2 was slightly increased at time-point POST without reaching the level of statistical significance. p_aO_2 was decreased after smoke exposure. However, this decrease is only statistically significant when all three groups are pooled together. p_vO_2 decreased significantly from PRE to POST in the smoke-exposure groups.

Data for static compliance (C), inspiratory airway resistance (R), and physiologic dead space to tidal volume ratio (V_d/V_t) are summarized in Table 2. Statistical analysis of the static compliance data indicated

no significant differences between groups at the two time-points and no significant changes between the two time-points.

Inspiratory airway resistance (R) data are relatively high. This is due to the small diameter of the double-lumen tube in combination with its length of 70 cm (the teeth-carina distance is about 50 to 60 cm in adult sheep). Statistical analysis of R data indicated no significant differences between the groups at the two time-points. But when all groups are pooled a significant increase from PRE to POST is detected. As can be seen from Table 2 this increase in R is predominantly due to an increase of R in the smoke-exposed lungs. In a preliminary study, in which anesthesia was maintained by continuous intravenous infusion of sodium pentobarbital, R increased in the smoke exposed-lungs from 13.8 ± 1.7 to 29.8 ± 4.9 $cmH_2O/l/s$ ($n = 4$). This indicates a more pronounced bronchospastic reaction towards smoke under pentobarbital anesthesia than under halothane anesthesia.

As can be seen from Table 2 no statistically significant differences could be found for V_d/V_t between groups at the two time-points and no significant changes between the two time-points.

Discussion

With aggressive treatment of burn shock and infections the presence or absence of inhalation injury has become a major determinant of mortality in burn patients. Due to the variability in smoke composition the injury is not well defined. Upon clinical admission patients may present with pulmonary edema, e.g. after hyperbaric trauma [6] or after inhalation of special hydrocarbons [1]. In the majority of cases, however, lung function is unimpaired upon admission, inhalation injury will only be diagnosed by fiberoptic inspection of the airways, and a deterioration of lung function will only develop later in the clinical course. This course is characteristic of inhalation injury with cotton or wood smoke, both materials combusting to give considerable concentrations of aldehydes [11] which cause a tracheobronchitis.

In this model a rather large amount of cotton-smoke (120 ± 9 breaths) was administered to one lung. This amount is well above the dose that results in the death of the animals 24 to 48 h after exposure when both lungs are exposed. In spite of this large amount of smoke no cardiovascular depression due to hypoxia was found in this model.

Hypoxia inducing phenomena are at least threefold in inhalation injury. First of all the environment contains less oxygen, which is consumed by the fire. In this model, this effect was attenuated by ventilating the contralateral lung with room air during the smoking procedure. Secondly, incomplete combustion results in the formation of carbonmonoxide which readily reduces the oxygen transport capacity by combining with hemoglobin. In this study, oxygen transport capacity was roughly one half of the baseline value after smoke-exposure, with 50% of hemoglobin being transformed to carboxyhemoglobin. Thirdly, carbonmonoxide as well as cyanide interfere with oxygen utilization at the electron transfer level. A 50%-reduction in oxygen transport capacity results in a 50%-reduction of oxygen delivery with no change in cardiac output. This is reflected by the decrease in p_vO_2, which also is roughly one half of the baseline value after smoke-exposure. The minor decreases in p_aO_2 can be attributed to this decrease in p_vO_2, which will decrease p_aO_2 in the presence of venous-to-arterial intrapulmonary shunting.

An increase of physiologic dead space in the early phase after inhalation injury was found in two previous animal models and has been attributed to an increase in pulmonary vascular resistance [8] and regional pulmonary vasospasm [7], suggesting a vasospastic reaction towards smoke. However, the increased physiologic dead space could as well be the result of a decreased cardiac output with hypoperfusion of the non-dependent lung areas. Stephenson et al. [8] reported an increase of V_d/V_t from 0.43 to 0.58 30 min after wood smoke inhalation while cardiac output decreased from 3.5 to 1 l/min in a dog model. Robinson et al. [7], utilizing the multiple inert gas technique, found that ventilation to high ventilation/perfusion and dead-space compartments was increased over control levels 6 h after wood smoke injury. No cardiac output data were reported in this rabbit study. The data presented here do not support the concept of vasospasm due to smoke inhalation. In the presence of a moderately elevated cardiac output the physiologic dead space ratio was unchanged from baseline 30–45 min after injury in the smoke-exposed lungs. In addition, calculated PVR did not increase in this model after injury, but was somewhat smaller when compared to baseline. However, only major reductions of the pulmonary vascular area in the injured lungs would have been indicated by an increase in PVR.

A pronounced decrease of lung compliance immediately following wood smoke inhalation has been observed in open-chest dog models. Nieman et al. [5] reported a reduction of lung compliance from a control value of 76.4 to 36.0 ml/mmHg which endured for at least 2 h. Clark et al. [2] found dynamic lung compliance to be reduced from 26 (control) to 10 ml/min/cm H_2O 5 min after smoke exposure. These authors observed the development of gross atelectasis after a few breaths of smoke despite the presence of

5 cm of PEEP and found a severely compromised surfactant activity in the lung extract following smoke exposure. These pronounced reductions of lung compliance in the open-chest preparations could not be reproduced in this closed-chest model. Only a minimally decreased compliance was measured in the smoke-exposed lungs, a finding which is consistent with the observations of Stephenson et al. in their closed chest dog model [8]. It must be concluded, that the immediate impairment of surfactant activity by smoke particles as described by Nieman, Clark, and coauthors does not have the sudden impact on the pulmonary microstructure that is seen in the open-chest preparation when the chest is intact. It is possible that alveoli do not collapse as easily in the intact chest.

Pulmonary airway resistance increased in the smoke-exposed lungs. As airway resistance remained essentially unchanged in the contralateral lungs and in the SHAM-experiment lungs this must be attributed to a local reflex mechanism. These data are in contrast to the findings of Widdicombe et al. [10] who reported that charcoal dust induced increases of pulmonary airflow resistance could be prevented by blocking conduction in the cervical vagosympathetic nerves, suggesting a centrally mediated reflex in this cat model. Clearly, this discrepancy in data deserves further investigation. As the bronchoconstrictory response towards smoke is modulated by other factors, such as type of anesthesia, no conclusions can be drawn for the degree of smoke-induced bronchospasm in the unanesthetized human being. In summary, we conclude that the inhalation of rather large amounts of cotton smoke has no major direct effects on pulmonary function in the early post-injury period.

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