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Collagenase expressing mast cells accumulate in the walls of peripheral pulmonary arteries at the beginning of hypoxic pulmonary hypertension

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Chronic hypoxia results in pulmonary hypertension due to vasoconstriction and structural remodelling of peripheral lung blood vessels. We hypothesize that vascular remodelling is initiated in the walls of prealveolar pulmonary arteries by collagenolytic metalloproteinases (MMP) released from activated mast cells. Distribution of mast cells and their expression of interstitial collagenase, MMP-13, in lung conduit, small muscular, and prealveolar arteries was determined quantitatively in lungs of adult male rats exposed for 4 and 20 days to hypoxia (10% 0_2). Mast cells were identified using Toluidine Blue staining, and MMP-13 expression was detected using monoclonal antibody. Animals were humanely killed at the end of the experiment. After 4, but not after 20 days of hypoxia, a significant (ANOVA) increase in the number of mast cells and their MMP-13 expression was found within walls of prealveolar arteries. In rats with fully developed pulmonary hypertension after 20 days of hypoxia MMP-13 positive mast cells accumulated within the walls of conduit arteries and total number of mast cells was significantly higher than after 4 days exposure and in normoxic controls. These data support the hypothesis that perivascular pulmonary mast cells contribute to the vascular remodeling in hypoxic pulmonary hypertension by releasing interstitial collagenase.

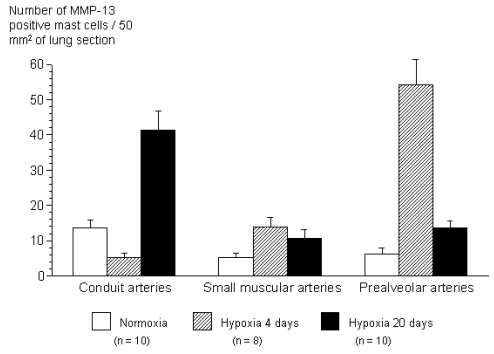

Figure 1.

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Where applicable, the experiments described here conform with Physiological Society ethical requirements.

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Pre-arrest administration of cell permeable ROS scavenger, Tempol, reduces warm ischaemic damage of lung function in non-heart-beating donors

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To use lungs retrieved from non-heart-beating donors (NHBD) in a safe way it is necessary to design an optimal method of their preservation during warm ischaemia. One of the most deteriorative effects of warm ischaemia is caused by ROS activity. Therefore we investigated a possible protective effect of cell permeable ROS scavenger, Tempol, on the function of NHBD grafts.

Four groups (n = 6) of Wistar male rats underwent experimental protocol of lung harvesting from NHBD. After pre-arrest administration of heparin, rats were humanely killed by an overdose of sodium pentobarbitone and then left untouched for 60 min (warm ischaemia) followed by 90 min of cold ischaemia provided by intrapleural in situ topical cooling. Group I: non-ventilated during warm ischaemia, group II: non-ventilated, Tempol (100mg/kg b.w.) added pre-arrestly intraperitonealy, group III: room-air ventilated, group IV: room-air ventilated, Tempol. Controls were: group V (n = 6) and group VI (n = 6) with Tempol added, in both lungs harvested immediately under anaesthesia by sodium thiopental (50mg/kg added intraperitonealy) without warm and cold ischaemia.

For functional assessment of all groups we used preparation of isolated ventilated rat lungs perfused with salt solution with Ficoll (4g/100ml) and meclofenamate (17 x 10exp-6 M). Perfusion pressure, lung weight gain and arterio-venous difference in oxygen partial pressure (dPO2) were measured in time periods of 30, 90 120 and 180 min after beginning of perfusion. To model in vivo conditions for oxygen transport, the perfusate was equilibrated with hypoxic gas mixture before entering the preparation.

For statistical evaluation we used ANOVA for repeated measures, Games/Howell post hoc test, $p<0.05$.

We did not find any differences between controls (group V and VI). Almost all lungs (5 of 6) retrieved from room-air ventilated rats without Tempol (group III) developed pulmonary oedema by 30 min of isolated lung perfusion, in contrast to 100% survival in all other groups. There were no differences in perfusion pressure between these groups. We found significant increase in weight gain in non-ventilated lungs (group I) compared with non-ventilated with Tempol (group II) or room-air ventilated with Tempol (group IV) - see Fig. 1. dPO2 was significantly lower in non-ventilated lungs (group I) than in controls (group V); in contrast, there were no differences in oxygen transport ability between non-ventilated, room-air ventilated and control groups with Tempol - see Fig. 2.

Pre-arrest administration of Tempol helps in protection of lung grafts retrieved from NHBD.

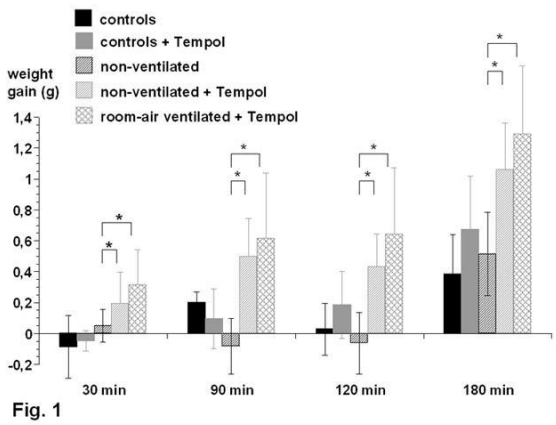

Figure 1.

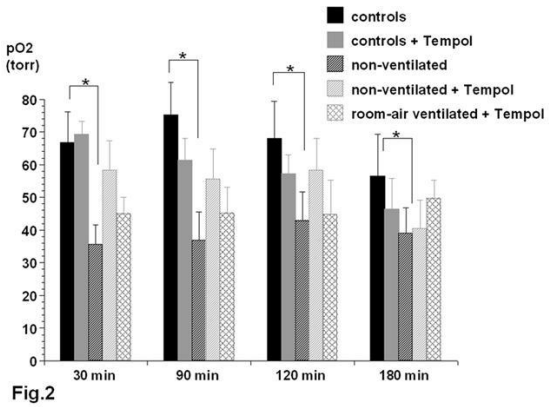

Figure 2.

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Where applicable, the experiments described here conform with Physiological Society ethical requirements.

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Ascorbic acid attenuates the oxidative stress of cigarette smoke on some vital organs in male rabbits

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This study was designed to investigate the effect of ascorbic acid on the degenerative effect of passive cigarette smoke on some vital organs in male rabbits.

A total of 16 male rabbits were used and the animals were divided into four groups of 4 rabbits each. Group A rabbits were exposed to passive cigarette smoke from 4 sticks of cigarette for 45-60 min daily while group B rabbits were exposed to cigarette smoke as described above but were also treated with 5mg/gm body weight of ascorbic acid. Group C animals were treated with ascorbic acid only and Group D rabbits were the untreated control group. The treatment went on for a minimum of 6 weeks. At the end of this period, the animals were humanely killed and various organs were neatly removed for histological investigation.

Photomicrographs showed that tobacco smoke had deleterious effects on the lungs, testes and kidneys while there were no significant changes in the liver. The brain and heart showed no abnormalities. It was also observed that ascorbic acid had some attenuating effect on inflammatory processes as observed in the lungs. Varying degrees of hypospermatogenesis was observed in the seminiferous tubules while the epididymis contained no spermatocytes in both groups A and B.

Despite the fact that ascorbic acid has some attenuating effect on inflammatory processes as observed in the lungs.It is also evident that ascorbic acid stops neither the inflammatory process (as seen in the lungs) nor the declining function as signified by hypospermatogenesis in the testes. Therefore, it is doubtful that the long-term effects of tobacco smoke can be prevented by the use of ascorbic acid.

Mc Cusker K (1992). Am J Med 93(suppl 1A), 195.

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