Title: HYPOXIC PULMONARY VASOCONSTRICTION IS POTENTIATED BY REPEATED INTERMITTANT HYPOXIA

Authors: Jonathan L. Benumof, M.D., Frank R. Trousdale

Affiliation: University of California, San Diego, Anesthesia Research Laboratory T-001
La Jolla, California 92093

INTRODUCTION: It has recently been shown that repeated intermittent hypoxic challenges to a lobe of the dog lung potentiates lobar hypoxic pulmonary vasoconstriction (HPV) over a time period of one - two hours. However, the experimental design consisted of instituting the repeated intermittent hypoxic challenges immediately after instrumentation of the lung lobe (cannulation of lobar bronchus, placement of circumferential flowprobes around lobar artery). It is possible, therefore, that a very recent past history of vessel manipulation prevented the vessels from responding to hypoxia normally (i.e. maximally) for a period of time and that if a waiting period had been interposed between vessel manipulation and the initiation of the repeated intermittent hypoxic challenges, then no potentiation of lobar HPV would have been observed. The purpose of this investigation was to test this hypothesis by allowing a period of two hours to pass after instrumentation of the test lobe, during which both the test lobe and the rest of the lung were ventilated with 100% oxygen and there were no further lung manipulations, and then exposing the test lobe to repeated intermittant challenges of nitrogen ventilation.

METHODS: Eight mongrel dogs weighing 17 - 29 kg were anesthetized with intravenous pentobarbital 25 mg/kg, intubated and ventilated with 100% O_2. Following a left 5th - 6th intercostal space thoracotomy, electromagnetic flow probes were placed around the main and left lower lobe (LLL) pulmonary arteries. LLL blood flow is expressed as a fraction of the cardiac output (Q_{LLL}/Q_t). Femoral artery, pulmonary artery and left atrial pressures were measured directly. The LLL bronchus was cannulated distal to a ligature and ventilated independently but synchronously with the rest of the lung with 100% O_2. Tidal volumes and external dead space in each ventilated compartment were manipulated to produce equal airway pressures and end-tidal CO_2 concentrations (5%). Respiratory rate was adjusted to achieve P_aCO_2=40 torr. Following the above operative period, both the LLL and rest of the lung were ventilated with 100% O_2 for two hours and no other manipulations were performed. Following this two hour waiting period the experimental sequence was begun and consisted of changing the ventilating gas mixture of the LLL from 100% O_2 to 95% N_2 + 5% CO_2 until a new (decreased) steady state Q_{LLL}/Q_t was obtained. Time to first achievement of the new decreased Q_{LLL}/Q_t plateau was noted. The LLL was then ventilated with 100% O_2 until a new (increased) steady state normoxic control Q_{LLL}/Q_t was achieved. The above ventilation and measurement sequence was repeated for a total of four intermittent hypoxic challenges in each dog. The LLL HPV response is expressed as the percentage reduction in Q_{LLL}/Q_t (% decrease Q_{LLL}/Q_t). All results are expressed as mean + SE and were analyzed by paired t analysis with $p<0.05$ considered significant.

RESULTS: The four LLL HPV responses (% decrease Q_{LLL}/Q_t) and time to achievement of a stable maximum LLL HPV response are shown in Figure 1. The first 3 LLL HPV responses significantly and progressively increased; the fourth LLL HPV response was not significantly different from the third LLL HPV. The first LLL HPV took significantly longer to reach a stable maximum plateau value than did LLL HPV responses 2-4; LLL HPV responses 2-4 displayed a progressive downward (shortening) response-time trend.

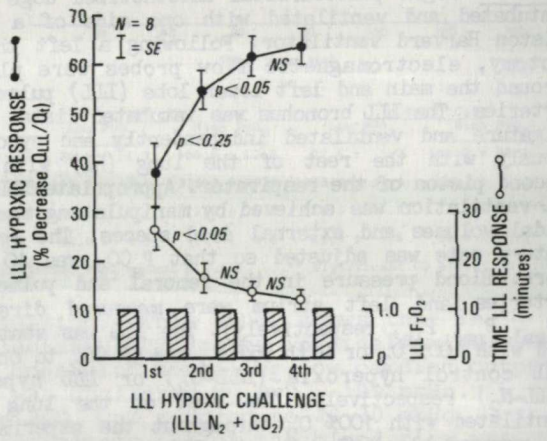

Figure 1

DISCUSSION: Our results demonstrate that regional HPV is potentiated by repeated intermittent hypoxic challenges. We found that lobar HPV increased rapidly and reached a stable plateau value after several hypoxic challenges. These intermittent HPV findings are in good agreement with previous quantitative whole lung (JAP 43:662,1977) and lobar (Anesthesiol 55:200,1981) results and qualitative single lung (Resp 38:185,1979) results. These present findings re-emphasize the conclusion that experiments concerned with the determinants of HPV should not use the first measured HPV response as a control response but rather a later, larger, and stable plateau HPV response. The potentiation of HPV by repeated intermittent hypoxia is compatible with the concept that the mechanism of HPV involves enzymatic processes that are inducible by repeated hypoxic challenges. The fact that the HPV responses also required less time to reach greater stable plateau values with repeated intermittant nitrogen exposures also implies an increasing efficiency of the HPV mechanism.

Downloaded from http://pubs.asahq.org/anesthesiology/article-pdf/57/3/A467/630676/0000542-198209001-00467.pdf by guest on 01 July 2022