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Title: DISCREPANCY IN CARBON DIOXIDE TURNOVER EXPLAINED

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Introduction To date no satisfactory explanation has been given for the observation that the time course of changes in the end expired carbon dioxide tension is considerably faster with a single step increase as compared to that with a decrease in ventilation.[1] This study was undertaken to determine whether this difference in turnover is due only to the magnitude of change in minute ventilation (VE) or is also related to an increase in metabolism during respiratory alkalosis.

Method Two groups, 10 dogs each, average wt 12 kg, were anesthetized with pentobarbital 30 mg/kg IV and maintained on an infusion of 0.2 mg/kg/min. The dogs were mechanically ventilated to a pHa of 7.4. Group I received room air and Group 2 a mixture of 3% CO_2, 21% O_2 and 76% N_2. After a control period of 2 hrs, respiratory alkalosis was induced for another 2 hrs either by a single step increase in $\dot{V}E$ (Group I) or by switching the inspired mixture to room air without altering VE (Group 2). A recovery period of 2 hrs was established in Group I by a single step decrease to original $\dot{V}E$ and in Group 2 by returning to the inspired mixture containing CO_2. Arterial and mixed venous samples were obtained for blood gas analysis at 0,1,2,3,5,7,10,15,30,60 and 120 min immediately on changing $\dot{V}E$ or inspired mixture. With the aid of a servo-spirometer, gas mass spectrometer and a digital computer, $\dot{V}E$ and CO_2 elimination was measured every minute and CO_2 production ($\dot{V}CO_2$), was calculated. Using the standard two compartment model CO_2 washout and washin were calculated from the CO_2 elimination data. Values are expressed as mean ± standard error of the mean. Statistics by analysis of variance.

Results Values obtained at the end of 1 hr of each period were similar to those obtained at the end of 2 hrs, signifying that a steady state was achieved and therefore CO_2 production equals CO_2 elimination as shown in table. Respiratory alkalosis increased $\dot{V}CO_2$ by 20% in both groups and the increase in $\dot{V}CO_2$ was proportional to the decrease in $PaCO_2$. In Group I, CO_2 washout was 2.44 ml/kg/Δ mmHg $PvCO_2$ with a turnover rate for the fast compartment (k_1) of 0.420 min^{-1} and the slow compartment (k_2) of 0.073 min^{-1}. The $PaCO_2$ and $PvCO_2$ half-times were 4 nd 10 min respectively. The CO_2 washin was 1.9 ml/kg/Δ mmHg P_vCO_2, and the turnover rates for the two compartments, k_1 0.701 min^{-1} and k_2 0.057 min^{-1}. The $PaCO_2$ and $PvCO_2$ half-times were 10 and 18 min respectively. In Group 2, when $\dot{V}E$ was kept constant but the inspired mixture was changed, CO_2 washout was 2.46 and washin 2.44 ml/kg/Δ mmHg $PvCO_2$. The turnover rates for the two compartment were k_1 = 0.420 and 0.421 min^{-1} and k_2 =0.074 and 0.073 min^{-1} for washout and washin respectively. The half-time in change for $PaCO_2$ was 4 min and for $PvCO_2$ was 9 min during both periods.

Discussion It has been shown that tissue production of CO_2 increases with increasing degree of respiratory alkalosis and that there is a statistically significant correlation between changes in $PvCO_2$ and tissue production of CO_2.[2] Therefore from the percentage change in $PvCO_2$, we calculated change in tissue CO_2 production during the unsteady period. By subtracting these values of tissue CO_2 production from CO_2 elimination, we obtained new CO_2 washout and washin rates. Following this correction for changing CO_2 production, CO_2 washout and washin in Group I was 2.69 and 2.68 ml/kg/Δ mmHg $PvCO_2$ respectively. However, the turn over rates for the two compartments were still significantly different k_1 = 0.462 and 0.277 min^{-1} during washout and k_2 = 0.069 and 0.051 min^{-1} during washin. In Group 2, CO_2 washout and washin were 2.68 and 2.67 ml/kg/Δ mmHg$PvCO_2$ and the turn over rates for the fast and slow compartments during washout and washin were not different k_1 = 0.466 and 0.460 min^{-1} and k_2 = 0.069 and 0.067 min^{-1} respectively. The study shows that even when the effect of the change in magnitude of ventilation is accounted for CO_2 washout and washin will be underestimated unless corrections are made for tissue production of CO_2 during these periods. With these corrections we note that the CO_2 washout and washin rates are the same; 2.69 and 2.68 ml/kg/Δ mmHg $PvCO_2$ for Group I and 2.68 and 2.67 ml/kg/Δ mmHg $PvCO_2$ for Group 2.

Conclusions Our data indicate that the differences in time constants of CO_2 turnover during single step increase and decrease in ventilation are not only due to the changes in the magnitude of ventilation but more important, due to changing tissue production of CO_2. When both these factors are taken into consideration CO_2 turnover is the same during washout and washin.

Table: Steady state values during CO_2 washout (alkalosis) and washin (recovery) at the end of 2 hrs.

Group I

	Control	Alkalosis	Recovery
pHa	7.39±0.01	7.66±0.01*	7.39±0.1
$PaCO_2$ mmHg	35.2±2.9	15.0±0.7*	34.6±1.4
$PvCO_2$ mmHg	39.1±1.0	17.7±0.9	38.7±1.6
$\dot{V}E$ l/kg/min	0.24±0.01	0.70±0.05*	0.24±0.1
$\dot{V}CO_2$ ml/kg/min	4.7±0.02	5.6±0.3*	4.6±0.1

Group 2

	Control	Alkalosis	Recovery
pHa	7.41±0.01	7.68±0.01*	7.40±0.02
$PaCO_2$ mmHg	32.0±2.1	14.0±0.05*	32.0±1.8
$PvCO_2$ mmHg	35.5±2.2	16.4±0.05*	34.0±2.0
$\dot{V}E$ l/kg/min	0.71±0.05	0.71±0.05	0.71±0.05
$\dot{V}CO_2$ ml/kg/min	5.8±0.2	6.8±0.2*	5.7±0.02

* $p < 0.01$ as compared to control and recovery.

References

1. Sullivan SF, Patterson RW, Papper EM: Arterial CO_2 tension adjustment rates following hyperventilation. J Appl Physiol 21:247-250, 1966
2. Khambatta HJ, Sullivan SF: Carbon dioxide production and washout during passive hyperventilation alkalosis. J Appl Physiol 37:663-669, 1974

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