Effect of partial pressures of end expiratory gases on voluntary breath holding time

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Abstract: INTRODUCTION - The break point of voluntary breath hold is believed to be brought about by multiple factors including partial pressures of arterial pCO2 and pO2. This study aims to look at the effect of partial pressures of arterial blood gases on voluntary breath holding time (BHT). MATERIALS AND METHODS - Breath holding time after 3 different maneuvers (normal, after re-breathing, after voluntary hyperventilation) were employed on 13 subjects to obtain their end expiratory partial pressures of gases before breath hold and at break point. RESULTS - The breath holding times for normal, re-breathing and voluntary hyperventilation were significantly different from each other (p less than 0.03 in all three comparisons). A negative correlation was observed between end expiratory pCO2 (eECO2) before breath hold and BHT (r equals -0.728, p less than 0.0001). A positive correlation was seen between end expiratory pO2 (eEO2) before breath hold and BHT (r equals 0.682, p less than 0.0001). Analysis of partial pressures of gases at break point revealed comparatively smaller deviations for end expiratory pCO2 than that of pO2. A three dimensional plot of eECO2 before breath hold, eEO2 before breath hold and BHT showed that all the data points fall along a straight line. CONCLUSION - Our experiments suggest a more significant role for arterial pCO2 than arterial pO2. Strong negative correlations between eECO2 before breath hold and BHT, and between eEO2 and eECO2 (r equals -0.965, p less than 0.0001) could have resulted in a positive correlation between eEO2 before breath hold and BHT.

Keyword: Breath holding time, break point, end expiratory partial pressures of oxygen and carbon dioxide, correlation

Introduction: Breath holding time (BHT) is the duration between the start of voluntary breath hold to the time when the subject starts to breathe due to the uncontrollable urge to do so. The mechanisms that bring about break point are not yet fully understood. Lung volume at the start of breath hold, awareness of breath holding, the subject’s motivation and the pCO2...
and pO₂ of the inspired gas had been shown to influence the duration of breath hold (1). The breath holding duration has also been shown to increase with repeated trials performed on the same subject (2). Here we investigated the relationship between the arterial blood gas partial pressures before breath hold and the breath holding time. **Materials and methods:** 13 healthy adult subjects of both genders (9 males and 4 females) were recruited. Subjects were asked to breathe through a custom made mouth piece. The air through the mouth piece was sampled at 100 ml/min using a gas analyzer (CWE, Inc, USA, Gemini gas analyzer). The analog output for both pCO₂ and pO₂ from the analyzer was sampled at 500 Hz with 2 different channels and digitized and stored in a computer through CMCdaq data acquisition system. Data were analyzed using CMCdaq, Igor pro (version 5.0) and Microsoft excel. The subjects were instructed to hold their breath after 3 different maneuvers which would alter the partial pressures of alveolar gases.

1. **After normal breathing:** The subjects were asked to breathe normally for a few cycles through the mouth piece, exhale completely, inhale to total lung capacity (TLC) and then hold their breath as long as possible. At the end of this cycle they were asked to hold their breath at the total lung capacity (TLC) after exhaling completely.

2. **After re-breathing into a closed bag:** As soon as the normal end expiratory partial pressures of gases were obtained, the subjects were asked to re-breathe into a closed bag for a period of one minute. At the end this period they were made to inflate their lungs to TLC by inspiring the air within the bag and hold their breath.

3. **After voluntary hyperventilation:** After obtaining the normal end expiratory partial pressures of gases, the subjects were asked to hyperventilate by increasing the depth and rate of breathing. They were instructed to hold their breath at TLC, when they felt dizzy. The air sampled during the last expiration before breath hold was used to obtain the end expiratory partial pressures of O₂ and CO₂ before breath hold. The subjects were instructed to exhale completely through the mouth-piece, when they felt the uncontrollable urge to expire. The sample of air thus obtained was used to assess the end expiratory partial pressures of gases at break point.

Figure 1B: Breath holding after 1 min of re-breathing into a bag. Increase in inspired air pCO₂ and the end expiratory pCO₂ after each breath is shown by arrows.
Figure 1C: Breath holding after voluntary hyperventilation. Note the decrease in end expiratory pCO2 during voluntary hyperventilation.

Statistical methods: Data are represented as mean ± SD. Breath holding time between the three different maneuvers were tested for statistical significance using Wilcoxon signed rank test. Correlation between end expiratory pCO2 and breath holding time, end expiratory pO2 and BHT, and between end expiratory pCO2 and pO2 were tested using Pearson’s correlation. P-value of <0.05 was considered significant.

Results: The breath holding times with three different maneuvers employed in our experiment were significantly different from each other. (Table 1 and 2)

Normal vs hyperventilation 0.027
Re-breathing vs hyperventilation <0.001

Table 2: Comparison of breath holding times during different maneuvers. Relationship between end expiratory pCO2 (eECO2) before breath hold and breath holding time As shown earlier by others (3) a negative correlation was observed between the end expiratory pCO2 (eECO2) before breath hold and breath holding time. The dispersion of eECO2 before breath hold with different maneuvers was narrow as suggested by the small standard deviations (Figure 2, left tracing), while the variation in breath holding time (BHT) was large during all maneuvers within the subjects. In spite of this large variation in BHT, when individual trends were analyzed they showed a negative relation between eECO2 before breath hold and breath holding time in 11 out of 13 subjects (Figure 4A). A scatter plot of all data with a best line fit (Figure 5A) proves the negative correlation described above. The Pearson’s correlation coefficient was found to be -0.728 with a p-value of less than 0.0001 (Figure 5-table).

Figure 2: Relationship between end expiratory partial pressures of O2 and CO2 before breath hold and breath holding time, shown as mean ± SD. Note the negative correlation between eECO2 vs breath holding time; and the positive correlation between eEO2 vs breath holding time. (n = 13)

Relationship between end expiratory pO2 (eEO2) before breath hold and breath holding time A significant positive correlation (Figure 5D, r = 0.682, p<0.0001) was observed between end expiratory pO2 (eEO2) before breath hold and breath holding time (Figure 2, right tracing). Figure 5B shows this positive correlation with a best line fit through the eEO2-BHT scatter plot. The alveolar gas equation relates the alveolar pCO2 and pO2 (4–6). This well-known negative correlation was also observed in our analysis with eECO2 and eEO2 before breath hold (r = -0.965; p<0.0001) (Figure
A negative correlation between $eE$-CO$_2$ before breath hold and BHT, a positive correlation between $eEO_2$ before breath hold and BHT and a negative correlation between $eEO_2$ and $eECO_2$ have thus far been shown. When three data sets are taken, a good correlation between any two of these pairs would make the other pair also correlated. It is therefore logically appropriate to consider that negative correlations between $eECO_2$ before breath hold and BHT, and $eEO_2$ and $eECO_2$ could have led to the positive correlation observed between $eEO_2$ and BHT. Or a positive correlation between $eEO_2$ and BHT, and a negative correlation between $eEO_2$ and $eECO_2$ could have resulted in a negative correlation between $eECO_2$ before breath hold and BHT. Since the correlation between alveolar pCO$_2$ and pO$_2$ is well established the third possibility is not considered. To identify which of these scenarios is true we analyzed the end expiratory partial pressures of gases at break point.

End expiratory partial pressures of gases at break point
The analysis of the end expiratory partial pressures of gases at break point is shown in figure 3. It can be noted from the magnitude of the error bars, that the standard deviation of $eECO_2$ is smaller than that of $eEO_2$. We also calculated the coefficient of variation for $eECO_2$ and $eEO_2$ at break point, considering the fact that mean and standard deviation of pO$_2$ would have a larger magnitude than those of pCO$_2$. These results are given in table 3. Accounting for the fact that the standard deviations and coefficient of variations for $eECO_2$ were less than those of $eEO_2$, it can be hypothesized that arterial pCO$_2$ is the important determinant among the blood gases. It was also observed that the break point $eECO_2$ after voluntary hyperventilation was significantly lower than the other two interventions ($p < 0.05$ with both comparisons using Wilcoxon signed rank test). Similarly, break point $eECO_2$ after re-breathing was found to be significantly higher than the other two maneuvers ($p < 0.05$ with both comparisons using Wilcoxon signed rank test). This suggests that there exists a factor other than arterial pCO$_2$ which causes the break point to be reached at a comparatively lower paCO$_2$ in longer breath holding times. A reasonable explanation for this observation could be the inward elastic recoil tendency of the respiratory system that exists at TLC, which was the chosen lung expansion while breath holding in our experiments. The inspiratory muscles which counteract this inward force might undergo fatigue with longer breath holding durations, causing the break point to be attained at relatively lower paCO$_2$.

Figure 3: Breakpoint partial pressures of O2 and CO2. pO2 is plotted on x-axis and pCO2 is plotted on y-axis. The data values obtained from all the subjects for various maneuvers are shown as open circles. The solid squares represent mean ± SD of each maneuver (Normal – Red; Re-breathing – Blue; Hyperventilation – Green) (n = 13). The black solid square shows the mean ± SD of all interventions (n = 39). The mean, SD and coefficient of variation of each data set is shown in the table 3.
The breath holding times with three different maneuvers employed in our experiment were significantly different from each other. (Table 1 and 2)

<table>
<thead>
<tr>
<th>Normal</th>
<th>Re-breathing</th>
<th>Voluntary</th>
<th>Hyperventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>56.98</td>
<td>33.54</td>
<td>83.05</td>
</tr>
<tr>
<td>SD</td>
<td>24.45</td>
<td>15.40</td>
<td>32.01</td>
</tr>
</tbody>
</table>

Table 1: Mean ± SD of breath holding times during three different maneuvers. 
$p$ value with Wilcoxon signed rank test

| Normal vs Re-breathing | 0.005 |
| Normal vs hyperventilation | 0.027 |
| Re-breathing vs hyperventilation | <0.001 |

Table 2: Comparison of breath holding times during different maneuvers.

Relationship between end expiratory pCO$_2$ (eECO$_2$) before breath hold and breath holding time

<table>
<thead>
<tr>
<th>Normal pCO$_2$</th>
<th>Normal pO$_2$</th>
<th>Re-breathing pCO$_2$</th>
<th>Re-breathing pO$_2$</th>
<th>Voluntary Hyperventilation pCO$_2$</th>
<th>Hyperventilation pO$_2$</th>
<th>All Maneuver pCO$_2$</th>
<th>All Maneuver pO$_2$</th>
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<tbody>
<tr>
<td>Mean</td>
<td>51.193</td>
<td>86.306</td>
<td>53.974</td>
<td>73.806</td>
<td>45.786</td>
<td>83.421</td>
<td>50.32</td>
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<tr>
<td>SD</td>
<td>4.803</td>
<td>12.711</td>
<td>4.241</td>
<td>0.741</td>
<td>5.728</td>
<td>18.782</td>
<td>5.932</td>
</tr>
</tbody>
</table>

Coefficient of variation

Table 3: Mean, SD and coefficient of variation of partial pressures of gases taken at break point.

Figure 4A: Three dimensional plot of end expiratory gases before breath hold and breath hold time obtained from 13 different subjects. Each set of colored markers represents a single subject. Each of the three identical markers denotes: left – hyperventilation, middle – normal; right – re-breathing. The dotted black line suggests the trend in relationship between the three axes. (n = 13) Figure 4B and 4C: (B) In the three dimensional plot of eECO$_2$ before breath hold, eEO$_2$ before breath hold and breath holding time, all the data points are seen clustered within a narrow 3 dimensional region. (C) Rotating the 3D plot about the axis shown in panel B reveals that the data points are clustered along a straight line directed away from the viewers’ perspective. (n = 13)
Interrelationship between end expiratory pCO$_2$ (eECO$_2$) before breath hold, end expiratory pO$_2$ (eEO$_2$) before breath hold and breath holding time A three dimensional plot was constructed using eECO$_2$ before breath hold, eEO$_2$ before breath hold and breath holding time to understand the interplay between these parameters (Figure 4A). It can be observed that the data points from all the experiments are confined to a narrow three dimensional space (Figure 4B). This when viewed from an appropriate perspective shows that the data points are clustered along a straight line (Figure 4C).

Discussion:
Multiple factors have been reported to influence the duration of voluntary breath hold. In this study, we sought to understand the role of partial pressures of arterial blood gases on the break point after voluntary breath hold. This has been achieved indirectly through the analysis of relationship between breath holding time and the partial pressures of end expiratory O2 and CO2 before breath holding and at break point. Oxygen tension of the arterial blood is principally sensed by the carotid bodies located in the bifurcation of the common carotid artery. Central chemoreceptors situated diffusely throughout the brain stem are believed to monitor the carbon dioxide tension or the pH of its environment (7, 8). An increase in paCO$_2$ or a decrease in paO$_2$ can logically result in breaking of voluntary breath hold. Increase in BHT with reduction in initial pCO$_2$ has been reported by Kelman et al (3) and increase in pO$_2$ of the air mixture has been shown to increase the breath hold duration (1). Whereas, resection or denervation of carotid body did not prolong BHT to unconsciousness. This led to the supposition that there are diaphragmatic chemoreceptors which respond to hypoxia (9).
Figure 5: Relationship between end expiratory pCO₂ (eECO₂), end expiratory-pO₂ (eEO₂) and breath holding time. (A) Correlation between eECO₂ before the breath holding and breath holding time. The best fit line (slope = -0.25805; y-intercept = 53.384) is shown as a dotted line. (B) Correlation between eEO₂ before breath holding and breath holding time. The best fit line (Slope = 1.0654; y-intercept = -59.465) is also shown. (C) Correlation between eEO₂ before breath holding and eECO₂ before breath holding. The best fit line (slope = -0.5338; y-intercept = 97.238) is shown. The correlation parameters of each pair depicted in panels A, B and C are shown in the table above. (n = 39)

Our experiments showed a negative correlation between the initial end expiratory pCO₂ (eECO₂) and breath holding time, and a positive correlation between the initial end expiratory pO₂ (eEO₂) and breath holding time. But, the relatively lesser deviation of break point eECO₂ about the mean compared to that of eEO₂, suggests that pCO₂ influences the voluntary breath hold break point more than pO₂. The teleological reason behind this may lie in the associated outcomes of low pO₂ and high pCO₂. While in low pO₂ conditions the cellular requirements can be met through anaerobic metabolism, high pCO₂ would result in derangement of the acid-base balance, which is incompatible with life.

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References:


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