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Pulmonary oxygen toxicity in saturation dives with PO_2 close to the lower end of the toxic range – A quantitative approach

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ABSTRACT

Pulmonary oxygen toxicity (POT) has been extensively described at partial pressures of oxygen (PO_2) ≥ 1 bar, but much less so at lower PO_2. We proposed the *POT index* [$K = t^2 \times (PO_2)^{4.57}$] as a means of evaluating the severity of POT, expressed either as reduced lung function or the incidence of POT in a group of divers. In the exponential recovery process ($e^{-\frac{1}{2}[-0.42 + 0.384 \times (PO)_{ex}] \times tr}$), the time constant increases linearly from 0.0024 to 0.54 h^{-1} for a PO_2 of 1.1 to 2.5 bar. A linear relationship was demonstrated between the incidence of POT and the *POT index*, given by the equation: POT incidence % = 1.85 + 0.171 × K. In saturation diving, PO_2 is kept close to the lower end of the toxic limits for POT, which is approximately 0.5 bar. We suggested that at this low range of PO_2, the two processes of cumulative toxicity and recovery operate simultaneously. For one example of saturation diving, we show that a recovery time constant of 0.0135 h^{-1} yields the measured incidence of POT. We therefore propose the formula $K = t^2 \times PO_2^{4.57} \times e^{-0.0135 \times t}$ for calculation of the *POT index* in further analyses of POT in saturation diving.

1. Pulmonary oxygen toxicity

Pulmonary oxygen toxicity (POT) has been extensively described at partial pressures of oxygen (PO_2) ≥ 1 bar, but much less so at lower PO_2. We proposed the *POT index* K as a means of evaluating the severity of POT, expressed either as reduced lung function or the incidence of POT in a group of divers (Arieli, 2019; Arieli et al., 2002). A rise in the calculated *POT index* will be indicative of increasing severity of POT. The appropriate equations are:

For the cumulative toxic effect:

$$K = t^2 \times PO_2^{4.57} \quad (1)$$

where K is the *POT index*, t is the time in h, and PO_2 is the partial pressure of oxygen in bar.

During recovery, breathing a non-toxic gas mixture:

$$K' = K \times e^{-\frac{1}{2ex}[-0.42 + 0.384 \times PO] \times tr} \quad (2)$$

where tr is the recovery time in hours, K' is the value after the recovery time, K is the value following the previous hyperbaric oxygen exposure, and PO_{2ex} is the PO_2 in bar for the previous exposure to hyperbaric oxygen. The time constant of recovery (contained within the squared brackets in the exponent) increases linearly from 0.0024 h^{-1} to 0.54 h^{-1} when the PO_2 preceding recovery was 1.1 and 2.5 bar, respectively. We suggested that if it is to replace the unit pulmonary toxic dose (UPTD), the *POT index* should not exceed 250 (Arieli, 2019).

The percentage incidence of POT in three reported studies (16 different exposures) at a PO_2 of 1.3 or 2 bar, with or without periods of recovery (Shykoff, 2014, 2015; Shykoff and Florian, 2018), is plotted in Fig. 1 as a function of our calculated *POT index*. A linear relationship may be seen between incidence of POT and the *index* according to the equation:

$$\text{POT incidence \%} = 1.85 + 0.171 \times K. \quad (3)$$

$r^2 = 0.88$

Regardless of the PO_2 during exposure and between recovery periods, the *POT index* will determine the incidence of POT.

2. PO_2 in saturation diving

In saturation diving, divers live in a pressurized habitat at working depth, remaining there for up to several weeks until they are decompressed to surface pressure after completing the work in hand. By limiting the number of decompressions in this way, the risk of decompression sickness is significantly reduced, and the time spent decompressing is kept to a minimum.

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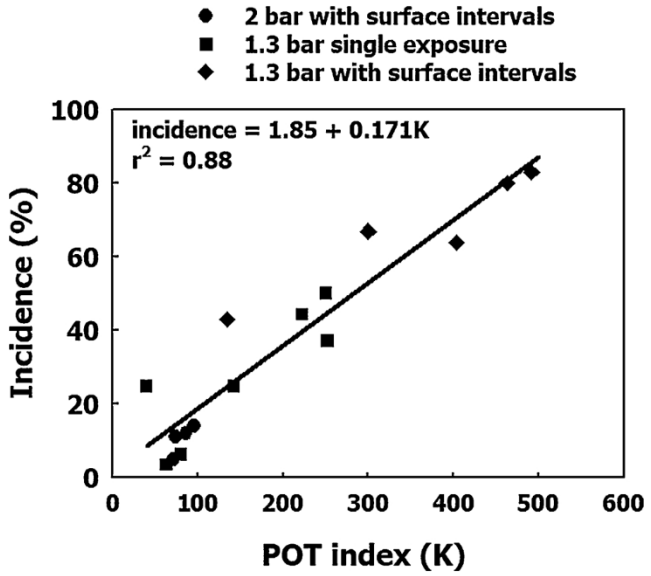

Fig. 1. Incidence of POT (references in the text) plotted as a function of the *POT index* calculated for each of the 16 different exposures. Regression line is also shown.

Most saturation diving is carried out using heliox breathing mixtures in which the partial pressure of oxygen is kept around 0.40–0.48 bar, close to the upper limit for long-term exposure (U.S. Department of the Navy, 2018). Although diving bell and lockout operations may also be conducted with a PO_2 of between 0.4 and 0.6 bar, in practice these often employ a PO_2 between 0.6 and 0.9 bar. This serves to attenuate the effect of pressure variations due to excursions away from the holding pressure, thereby reducing the probability and amount of bubble formation which may ensue (Staff, 2011). Recently received information has attested to saturation holding set typically at a PO_2 of 0.4 bar, and a PO_2 usually somewhere between 0.6–0.8 bar during diving and 0.4–0.5 bar in the bell, although some companies do permit 0.9 bar as an upper limit. Decompression is generally carried out at a PO_2 of 0.5 bar. (Personal communications, Jean Pierre Imbert, Divetech, France and Lyubisa Matity, Hyperbaric Unit, Mater Dei Hospital, Malta.)

3. POT in saturation diving

In 8 different saturation dives made to depths of between 300 and 450 m sea water (msw) for 14–30 days, with a PO_2 of between 0.4 and 0.6 bar (n = 46), chest symptoms and reduced diffusion capacity were ascribed to POT (Thorsen et al., 1990). This change in lung function was seen to be related to POT because with intermittent reduction of the PO_2 during decompression (alternating between 0.5 and 0.3 bar), no reduction in lung function was observed (Thorsen et al., 2006).

One report of an experimental chamber saturation dive at 450 msw for 210 h, followed by 51 h at 360 msw (a total of 261 h), and with a PO_2 of 0.5–0.6 bar, demonstrated deterioration of lung function which was ascribed to POT (Lehnigk et al., 1997). In 2 of the 8 subjects (25%), there was a large decrease in pulmonary diffusion capacity. Our calculated *POT index* for 261 h amounts to 4433, which is indicative of very serious POT. Inserting 25% into Eq. 3 yields K = 136. We have suggested that recovery may take place simultaneously with prolonged exposure to a low PO_2 (Arieli, 2019). In comparison with short hyperoxic exposures, the prolonged hyperoxic exposure in saturation dives induces acclimatisation to hyperoxia, with considerable changes in gene expression (Kiboub et al., 2018).

To adjust these two opposing effects of cumulative toxicity and the recovery process, the following equation may be used:

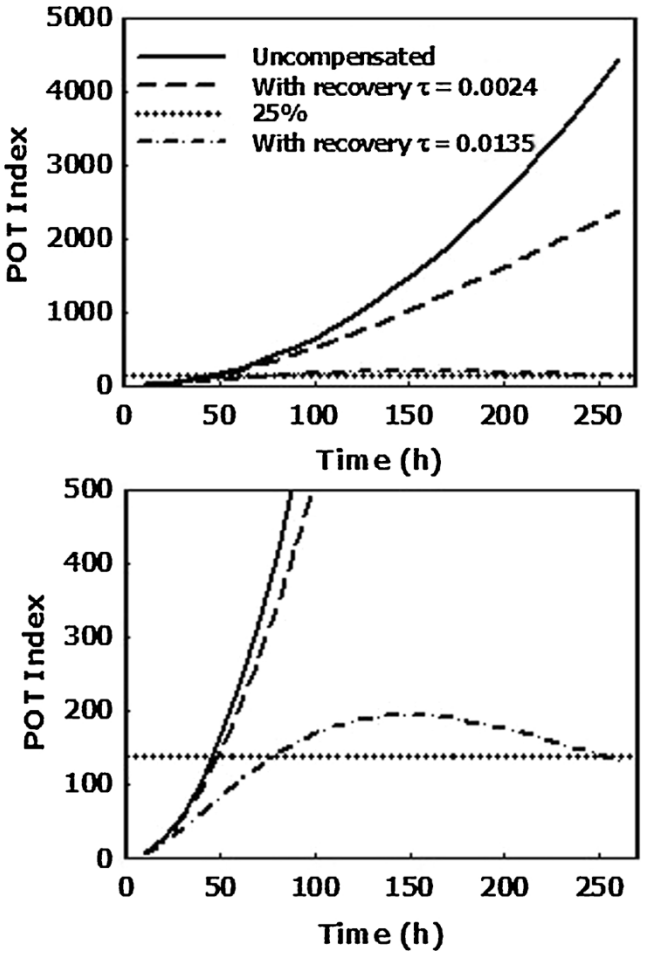

Fig. 2. *POT index* calculated for the 261 h exposure to a PO_2 of 0.55 bar, for cumulative toxicity only (Eq. 1), or for both cumulative toxicity and recovery which take place throughout the exposure (Eq. 4). The recovery time constant is either the lowest value 0.0024 h^{-1}, or the value which yields K = 136 at the end of exposure, namely 0.0135 h^{-1}. The complete range is shown in the upper panel, with the expanded lower section shown in the lower panel. The line for 25% (K = 136) is also shown.

$$POT\ index = t^2 \times {PO_2}^{4.57} \times e^{-\tau \times t} \quad (4)$$

where t is the toxic hyperoxic time in h (with a PO_2 > 0.48 bar, U.S. Department of the Navy, 2018), PO_2 is in bar, and τ is the time constant in h^{-1}. An even lower hyperoxic limit is possible, because a reduction in pulmonary diffusion capacity was demonstrated with a PO_2 of 0.42 bar in an exposure which lasted 15 days (Suzuki et al., 1991).

Initially, we selected the low time constant of 0.0024 h^{-1}, which is appropriate for a PO_2 of 1.1 bar. The calculated values of the *POT index* without recovery and with concomitant recovery are presented in Fig. 2. Both values of K are too high (Fig. 2, upper panel), and a recovery time constant of 0.0135 h^{-1} was therefore solved to yield K = 136 at the end of the exposure. We suggest that with a very mild toxic drive, the accompanying recovery responses will be above the minimal value. In that case, Eq. 4 will take the form:

$$POT\ index = t^2 \times {PO_2}^{4.57} \times e^{-0.0135 \times t} \quad (5)$$

The line for the recovery time constant 0.0135 h^{-1} has a maxima. Injury could be related either to the maxima or to the end value of the *POT index*.

It was suggested by Caldwell et al. (1966) that pulmonary diffusion capacity may be a more sensitive measure of POT than the reduction in vital capacity (VC). A reduction of 15% in pulmonary diffusion capacity was found for a saturation dive in which 5 days and 5 h spent at a PO_2

of 0.42 bar was followed by decompression over a period of 11 days and 12 h with a PO_2 of 0.495 bar (Suzuki et al., 1991). For the decompression phase of this dive, our *POT index* calculated using Eq. 5 yielded the values 125 at peak and 74 at the end of the exposure. In the same report, exposure to 300 msw for 15 days with a PO_2 of 0.42 bar resulted in a much milder reduction of 4.6% in pulmonary diffusion capacity, our calculated *POT index* being 19. In a further study (Suzuki, 1994), recovery with a PO_2 of 0.5 bar over a period of 2 or 19 days gave a peak *POT index* of 50 and 125, respectively. A reduction in pulmonary diffusion capacity seems therefore to occur only during extended decompression.

Thorsen et al. (1993) found reductions in pulmonary diffusion capacity, mid-expiratory flow and peak oxygen uptake after 12 days of decompression from a saturation dive with a PO_2 of 0.5 bar. The calculated values for our *POT index* were 125 at peak and 72 at the end. In a further study (Thorsen et al., 1994), a significant reduction in pulmonary diffusion capacity and a decrease in $FEF_{25-75\%}$ were reported after deep saturation dives. Our *POT index* calculated using Eq. 5 for the decompression phase (over a period of 12 days and with a PO_2 of 0.55 bar) was 193 at peak and 110 at the end. In a simulated saturation dive to 450 msw (Hyacinthe et al., 1981), there was a mean reduction of 12.3% in pulmonary diffusion capacity, where the end *POT index* we calculated using Eq. 5 was 170. We have proposed a *POT index* of 250, which corresponds to a 2% reduction in VC, as the exposure limit for POT (Arieli, 2019). A lower *POT index* may be more appropriate for saturation diving.

4. Conclusions

Both the cumulative pulmonary toxic effect and concomitant recovery are suggested to operate at the lower toxic range of PO_2 used in saturation diving. Our proposed calculation tool may be used for testing different saturation exposure profiles. Additional experimental data may serve further to refine the recovery time constant and timing of the initiation of recovery, which will improve the prediction power. It may well be that recovery is initiated at some time after the start of the hyperoxic exposure, and not at the beginning as we have suggested here as a first approximation.

Conflict of interest

The authors declare that they have no conflict of interest.

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