Incidence of oxygen toxicity during the treatment of dysbarism. (NB)

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Smerz R.Incidence of oxygen toxicity events during the treatment of dysbarism Undersea Hyperb Med 2004; 31(2):199-202. Oxygen (O_2) toxicity may result from exposure to partial pressures of O_2 above 0.6ATA. Potential toxic exposure for divers occurs during the treatment of dysbarism. In the recompression chamber, PO_2 may range from 0.9ATA to 3.3ATA depending upon the treatment table employed. This retrospective study examines the nature and incidence of O_2 toxicity in 998 patients who underwent recompression treatment at our facility from 1983 through 2001. Only patients evaluated for diving related injury were considered for this study. Of 1189 charts reviewed, 998 patients received recompression and were entered into this study. The total number of treatment exposures was determined as was the total number of O_2 toxicity events characterized as either pulmonary or CNS, and patients were divided into male/female analysis. Overall incidence as well as the incidence for both toxicity types was determined, and their occurrence in both male and female patients was ascertained. 2166 recompressions were undertaken, 449 female and 1717 male. The peak PO_2 for these treatments ranged from 2.6ATA to 2.9ATA. 155 O_2 toxicity events occurred in 152 patients, 49 females and 103 males. Three patients, 2 females and 1 male, had mixed events. Incidence of an O_2 toxic event = 7.0 per 100 recompressions. Incidence of pulmonary toxicity overall = 5.0 per 100 recompressions, while CNS events = 2.0 per 100 recompressions with overall seizure rate = 0.6 per 100 recompressions. In females, pulmonary toxicity rate = 6.9 per 100 recompressions, CNS toxicity rate = 4.4 per 100 recompressions with seizures occurring at 1.3 per 100 recompressions. In males, pulmonary toxicity rate = 4.6 per 100 recompressions, CNS toxicity rate = 1.4 per 100 recompressions, and seizures at 0.4 per 100 recompressions.

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INTRODUCTION

Oxygen toxicity may result from exposure to partial pressures of O_2 above 0.6ATA. For divers this level of exposure may be encountered with the use of closed and semi-closed rebreathers, during saturation diving, with the use of O_2 for decompression, and during treatment for dysbarism (1). In the recompression chamber, partial pressures of O_2 may range from 0.9ATA to 2.9ATA depending upon the treatment table employed. Most facilities in the United States employ US Navy Treatment Table 6 where the peak PO_2 is 2.8ATA with an average treatment time of 4 hours and 30 minutes (2). The Hyperbaric Treatment Center at the University of Hawaii, John A. Burns School of Medicine, routinely employs deep treatment tables utilizing mixed gas combinations for divers with dysbarism. These tables result in PO_2 exposures ranging from 2.4ATA to 2.9ATA with an average treatment time of 6 hours and 26 minutes (3). Although several studies have studied the incidence of O_2 toxicity in the clinical hyperbaric setting, no published accounts specifically report the incidence of O_2 toxicity during the treatment of dysbarism. This study examined the nature and incidence of O_2 toxicity in patients who received recompression for dysbarism at our facility from 1983 through 2001.

METHODS

Only patients who had been evaluated for suspected diving related injury were considered for this study. 1189 eligible patient records were reviewed. Since any recompression exposure represented a potential risk for development of O_2 toxicity, any patient who had been subjected to recompression, regardless of whether their final diagnosis was dysbaric in nature, was entered into the study. 998 patients (731 men, 267 women) met this criterion. The total number of recompression exposures for these patients, including multiple exposures for some, was determined (2166), and subdivided by gender (male, 1717; female 449 exposures). The total number of O_2 toxicity events was then determined. Any symptom suggestive of O_2 toxicity, regardless of severity and not otherwise explainable was considered a toxic event, and therefore would represent the most robust estimate of incidence. These events were then characterized as either pulmonary or CNS. Overall incidence, pulmonary and CNS incidence, and gender specific incidence for both types was then ascertained. Relative risk comparing genders was determined and Fisher's Exact Test was used to assess statistical significance.

RESULTS

155 O_2 toxicity events (110 pulmonary, 45 CNS [14 seizures]) occurred in 152 patients (103 men, 49 women). Three patients, 2 women and 1 man, had mixed events. The overall incidence of O_2 toxicity was 7.1 per 100 recompressions (pulmonary = 5.0/100, CNS = 2.0/100 [seizures = 0.6/100]). In women, the overall incidence was 10.9 per 100 recompressions (pulmonary = 6.9/100, CNS = 4.4/100 [seizures = 1.3/100]). In men, the overall incidence was 6.0 per 100 recompressions (pulmonary = 4.6/100, CNS = 1.4/100 [seizures = 0.4/100]). The relative risk (RR) of an O_2 toxic event for women was 1.8 times that of men overall, 95% CI(1.316 to 2.515) $p< .0001$; 1.5 times that of men with pulmonary toxicity, 95% CI(1.004 to 2.243) $p< .0001$; 3 times that of men with CNS toxicity, 95% CI(1.715 to 5.457) $p= .0005$; and 2.8 times that of men with seizures, 95%CI(1.000 to 8.224) $p= .1015$.

DISCUSSION

Paul Bert first described O_2-induced seizures in animals in 1878, and Damant and Phillips observed the first O_2 seizures in humans in 1933. Lorain Smith noted the development of pulmonary damage to the lungs from O_2 in 1899 (4). Since these early observations, a significant amount of research has been done on O_2 toxicity in attempts to both define and understand the circumstances and mechanisms of injury, as well as to predict and mitigate its occurrence. It has been shown that the development of O_2 toxicity depends upon the oxygen partial pressure, the duration of exposure, and inter- and intra-individual variability in susceptibility. For the diver, the most serious expression of CNS toxicity would be a seizure occurring while underwater, leading potentially to drowning. Behnke reported that hyperbaric oxygen at 3ATA was tolerated for periods up to three hours, and that the incidence of CNS toxicity in US Navy divers was 2% (5). Yarbrough reported that the incidence in dry chambers for CNS symptoms was 0% at 2.8 ATA for durations up to two hours and 77% at 3.4ATA for the same duration (6). Young reported an incidence of 0.3% seizures in clinical HBO_2 treatment exposures at ppO_2s between 2.5 and 3.0ATA (7). Rettenmaier *et al*, reported CNS toxicity incidence in the clinical HBO_2 setting as 1.1% for a ppO_2 range of 2.0 to 3.0ATA (8). Donald showed significant variations in

O_2 tolerance among individuals and in the same individual from day to day as well as that immersion and exercise independently and concomitantly enhanced the risk of CNS toxicity (9). Butler and Thalmann demonstrated that in working US Navy divers, there was a significantly increased risk of seizure at partial pressures of 1.8ATA or greater (10). These studies were influential in the development of guidelines recommending a peak O_2 partial pressure of 1.6ATA for divers using mixed gases or pure oxygen. However, under hyperbaric conditions with the patient at rest, Lambertsen showed that higher O_2 partial pressures can be tolerated with a low risk for seizures and other CNS symptoms (11). Clark and Lambertsen noted that at O_2 partial pressures of 0.5 to 2.0ATA, exposure durations were more limited by the pulmonary effects which can develop after 3-6 hours of exposure to a ppO_2 at 2.0ATA or greater (12). These effects result in a decrement of a number of pulmonary function parameters. Lambertsen introduced a time-dose relationship known as the Unit Pulmonary Toxic Dose (UPTD) concept and correlated it with vital capacity measurements. The UPTD can be used to predict the average decrement in vital capacity for a specific time-dose exposure (13). To mitigate pulmonary effects, a number of researchers investigated intermittent exposure to extend O_2 tolerance by alternating hyperoxic and normoxic exposure periods (14). This practice resulted in doubling the exposure duration prior to development of a 4% decrement in vital capacity and consequently, has been widely adopted as standard procedure at facilities where capabilities permit. While there have been several studies investigating the incidence of O_2 toxicity in the clinical hyperbaric setting, there have been no studies of its occurrence during the treatment of dysbarism exclusively where O_2 exposure and treatment duration are more severe. With the exception of treatments for clostridial myonecrosis and carbon monoxide poisoning where maximum treatment pressure is 3.0ATA, and the treatment of dysbarism where the peak partial pressure of oxygen is 2.8ATA, most other conditions are treated at 2.4ATA or less. Because O_2 partial pressures are typically lower and the exposure time is less during these treatments, one would expect a lower overall incidence of O_2 toxicity to be reported even when diving accidents are included. The US Navy Table 6 has a peak O_2 pressure of 2.8ATA, lasts 4 hours and 30 minutes and has a UPTD of 645 (2). The patients in this study were exposed to peak O_2 of 2.4 to 2.9ATA (average 2.8). The average treatment time was 6 hours and 26 minutes and the average UPTD was 875. The average number of treatments per patient was 2.1. In addition to determining what the actual incidence of O_2 toxicity was, there was also interest in knowing if these patients were at increased risk for toxicity. Based upon the work of Lambertsen (11), one would have expected to see an incidence rate of greater than 10% for CNS O_2 toxic symptoms in this patient population. Likewise, at a UPTD of 875, there is an estimated average decrement in the vital capacity of 4%-5% with clinical symptoms expected in 50% of the cases. The actual incidence of CNS O_2 toxicity was 2% (seizures 0.6%) and symptomatic pulmonary O_2 toxicity was seen in 5% of the cases. These results compare favorably with predicted outcomes and those of other studies of O_2 recompression of divers, and therefore suggest that these patients are not at increased risk as a result of the use of deep tables. Though the overall incidence of O_2 toxicity was relatively low, this study found that women were more likely to be susceptible to O_2 toxicity. Past studies have either involved only males or made no distinction by gender. The relative risk overall for women for CNS and pulmonary toxicity was significantly greater than that of men, and although the relative risk for seizure was not statistically significant, it still was 2.8 times that of men. These findings may have implications for women who are exposed to increased partial pressures of O_2 while diving with mixed gas such as Nitrox as well as in routine hyperbaric therapy.

CONCLUSIONS

The overall incidence of O_2 toxicity in this group of patients treated using the HTC deep tables was low and the risk of O_2 toxicity similar to other recompression treatment tables. O_2 toxic seizures occurred in less than 1% of exposures to increased partial pressures of O_2 ranging from 2.4ATA to 2.9ATA. Women were at significantly greater risk (1.5 to 3.0) than men for a toxic event.

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