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Diving Medicine ArticlesPseudoephedrine & Enriched-Air Diving?

By Dr. E.D. Thalmann, DAN Assistant Medical Director

Note: The decongestant pseudoephedrine is a commonly used drug by scuba divers, with mixed - though generally positive - reviews from sport divers, technical divers and diving professionals alike

DAN has received many inquiries for recreational divers who would like to know whether it is safe to take pseudoephedrine during enriched-air nitrox (EAN) diving. This inquiry is usually tied specifically to divers having read or heard the recommendation by diving organizations that pseudoephedrine be avoided with EAN.

It has been reported in dive publications and in EAN manuals that some drugs are CNS [central nervous system] exciters that predispose divers to CNS toxicity. The October 1995 American Academy of Underwater Scientists (AAUS) workshop on enriched air has been cited as the source for some of this information, including naming the decongestant pseudoephedrine HCL (found in Sudafed $^{\text{TM}}$ and other decongestant products) as a CNS exciter.

Before answering the question of whether pseudoephedrine may predispose a diver to oxygen toxicity during enriched-air diving and whether it is safe for air diving, it is useful to look at the line of reasoning on which I based it.

The first question is: How was it determined that there is an association between pseudoephedrine and CNS oxygen toxicity? (For a discussion of CNS oxygen toxicity, see If You Should Know About OXTOX). First, I needed to look at the American Association of Underwater Sciences (AAUS) workshop proceedings referenced in the statement by the cerification organizations. So I went to work.

After a few phone calls and emails, I discovered that no proceedings for that workshop were ever published. The statement regarding pseudoephedrine was based on an article in a technical diving training association's journal. In this article, the author cites several incidents involving decongestants and diving listed below. After each incident from the journal I have put my own comments in italics.

- A cave diver breathing a PO2 [oxygen partial pressure; see PO2 Definition] within limits (actual PO2 and depth not specified) died during a dive, the diver had a "high level" (concentration not specified) of pseudoephedrine in his blood. (This incident could have been an overdose; taking more that the recommended dose of any drug is always dangerous. It could have also been an oxygen convulsion or any one of a number of other conditions unrelated to diving, but which causes sudden death. There is not enough information to decide.)
- A cave diver "bolted" from his dive buddies during an air dive and was later found dead. He had exhibited this behavior before. On both occasions he had taken pseudoephedrine before the dive. (This incident seems to have features of excitability, a known side effect of pseudoephedrine and a symptom of oxygen toxicity.)
- A diver accustomed to diving to 160 fsw went almost comatose during an dive (breathing
 gas mixture not specified). On that particular dive he had taken pseudoephedrine (the
 article implied this was not usual). (This incident describes severe CNS depression, which is
 not a side effect of pseudoephedrine or oxygen toxicity.)
- A TRIMIX diver (breathing gas mixture and depth not specified) felt he was "losing it" and aborted the dive. He had taken a pseudoephedrine before the dive (the article implied this was not usual). (This incident may be due to excitability, a known side effect of pseudoephedrine and a symptom of oxygen toxicity.)
- A diver experienced feelings of apprehension and was fighting to maintain consciousness after taking a 12-hour Sudafed capsule. A similar incident occurred on another dive after





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she took Benedryl (an antihistamine) for a jellyfish sting. (The incidents described here are CNS depression, which is not a side effect of pseudoephedrine or oxygen toxicity. Benedryl, does cause drowsiness, so the diver's reaction to that drug is consistent with known antihistamine side effects. It is always recommended to avoid drugs that may cause drowsiness when diving.)

- On a Hydrolab dive in the ?s, one of Mount's dive partners was given Actifed (pseudoephedrine plus an antihistamine) for a cold. He went into a coma for two days before recovering. (This incident is not likely due to oxygen toxicity or the pseudoephedrine in Actifed. However, the antihistamine can cause extreme drowsiness if taken in large doses. Another possibility is that the dive's somnolence was due to whatever was causing his "cold.")
- On a shallow dive, a diver experienced symptoms of severe narcosis while using a
 breathing gas he considered unlikely to cause that severe a narcosis. He had taken
 pseudoephedrine prior to diving. (This incident describes CNS depression, not a side effect
 of pseudoephedrine or oxygen toxicity.)
- A diver reported through a contact in Australia that Oceaneering International, a commercial diving company, banned pseudoephedrine more than 10 years ago because of "adverse effects." (There is not enough information here to make any judgements about oxygen toxicity.)
- A contact in Australia reported incidents in recreational divers similar to those noted above to the author of the article in the technical diving journal. (There is not enough information here to make any judgements about oxygen toxicity.)

What can be made of these incidents? Starting with pharmacology, pseudoephedrine is a sympathomimetic (has effects similar to substances found in the sympathetic nervous system) whose major effect is to cause vasoconstriction in the lining of the nose and sinuses, thus reducing stuffiness and congestion. It is considered a mild central nervous stimulant, and its usual side effects are excitability, restlessness, dizziness, weakness and insomnia. Large doses (greater than those recommended) may induce several undesirable side effects including cardiovascular collapse and convulsions.

Sounds like pretty ominous stuff could occur from simply taking a drug to relieve a stuffy nose, doesn't it? Well, first of all, drug manufacturers are required to report any and all side effects that may be associated with a drug, no matter how rare. Even aspirin in high doses can cause cardiovascular collapse and convulsions.

The reality is that adverse reactions to pseudoephedrine are rare in healthy people when it is used as directed. That is not to say that certain individuals may have an idiosyncratic reaction to the drug and experience undesirable reactions to a drug while most others do not. For this reason, one should never use a drug for the first time just before diving and should make sure to use it long enough to determine that no hypersensitivity to the drug exists.

What the author has presented in his article constitutes anecdotal evidence that pseudoephedrine may be associated with some undesirable side effects when taken before a dive. The issue, however, is this: Does this anecdotal evidence point to a predisposition to oxygen toxicity from taking pseudoephedrine?

While we have some evidence of an association between pseudoephedrine and these side effects, we really need to establish a cause-and-effect relationship. The following five criteria are used to make this connection:

- statistical association;
- strength of association;
- timing of association;
- consistency of response; and
- biological plausibility.

"Statistical association" means that there is statistical evidence that symptoms that occur when pseudoephedrine is taken in association with certain types of dives are not a random occurrence. Mount did not provide enough information to establish a statistical association.

"Strength of association" means that very frequently, when the drug is taken before a dive, some sort of untoward effect usually occurs during or after the dive: that is, the incidence of effects when pseudoephedrine is take in association with a dive is very high.

Conversely, if no pseudoephedrine is taken, similar types of dives almost never produce side effects. Since we don't know how many individuals take pseudoephedrine before diving with no effects, like those reported above, we can't measure the incidence.

"Timing of association" means that the reported side effects usually occur if the drug is taken

before a dive, and not if it is taken afterward. Since only incidents in which the drug was taken before the dive were reported, we can't invoke this criteria.

"Consistency of response" means that the same effect is seen when the drug is taken, although the incidence may be rare. There does not seem to be any consistency in the symptoms reported above.

"Biological plausibility" means that there is some identified mechanism by which the drug could cause an undesirable side effect. In particular, we are interested in whether it may enhance susceptibility to oxygen toxicity. Here, we do have some evidence. In 1962, none other than DAN's Chief Executive Officer, Dr. Peter Bennett, while working as a research physiologist at the Royal Navy Physiological Laboratory in England, published a paper (Life Sciences; 12:721-727, 1962) testing the hypothesis that oxygen toxicity and nitrogen narcosis were caused by similar mechanisms.

He found that in rats, sympathomimetics seemed to enhance oxygen toxicity. Pseudoephedrine was not tested specifically, but it is a sympathomimetic, so we might infer that it has a similar effect. In addition, our current understanding of the mechanisms which produce oxygen convulsions would predict that sympathomimetic drugs might enhance susceptibility to oxygen convulsions. It has been shown that drugs which inhibit sympathetic stimulation seem to reduce the likelihood of oxygen convulsions in animals. No human studies have ever been done. Thus, at least a theoretical reason exists why pseudoephedrine should be avoided while diving on high PO2 dives.

What's the bottom line? In normal, healthy divers breathing air, occasional use of pseudoephedrine at the recommended dose is probably safe. This presumes that the drug has been taken during periods when no diving has occurred and that no undesirable reactions have occurred. However, one should avoid chronic (daily) use when diving, and it seems reasonable to avoid the drug entirely if diving while using oxygen-nitrogen mixes where the PO2 during a dive might exceed 1.4 ata, the current recommended "safe" open-circuit scuba limit.

Why the "long way around the barn" in reaching this conclusion? It is simply to present some tools and a logical process by which one can decide if anecdotal associations are due to an actual cause-and-effect relationship.

Next time you hear that someone has suffered an undesirable effect from taking a drug or trying out some new dive gear, apply the five criteria given above to decide for yourself whether a cause-and-effect relationship exists.

PO2 Definition

*The partial pressure of a gas is the measure of the number of molecules in a given volume. If a gas has only one component - 100 percent oxygen, for example - the partial pressure and the pressure are the same. With a gas mix, the partial pressure is the gas fraction times the total pressure. The physiological effects of a gas are due mainly to its partial pressure, no matter what the total pressure is.

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