

Diving and antidepressants

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Abstract

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Psychoactive drugs pose a risk to both the diver and his or her buddy. Little is known about the safety of diving with antidepressants. Amongst the potential interactions with the diving environment are: somnolence; convulsions; a bleeding tendency (potentially worsening decompression illness, DCI), alterations to glucose metabolism and psychiatric side effects. Fluoxetine may potentially reduce the inflammatory process associated with DCI. This article presents guidelines for recreational diving in combination with antidepressants. These guidelines were endorsed at a meeting of the Dutch Association for Diving Medicine in 2015 and are solely based on 'expert' opinion.

Introduction

Scuba diving is a relatively safe sport, as long as the rules of recreational diving are adhered to. A preventative diving medical examination is aimed at detecting any medical risks and then issue an appropriate recommendation accordingly. Psychiatric issues and psychopharmacologia pose a risk to both the diver and his or her buddy. Not much is known about what exactly happens with medicines in hyperbaric conditions. Rat studies show that the blood-brain barrier becomes more permeable for medications.¹ Also, there are indications that antidepressants increase susceptibility to nitrogen narcosis; however, there is no scientific evidence for this claim.

The Divers Alert Network Europe in discussing what little is known about the interaction between psychiatric disease and pharmacological agents used in its treatment, make the general comment that *"in terms of danger to divers, [antipsychotic] medications usually play a secondary role to the condition for which the medication is prescribed. Plainly a powerful drug, a mood-altering medication, should be used with care by divers. Drugs that carry warnings indicating they are dangerous for use while driving or when operating hazardous equipment should also be considered risky for divers; if they're dangerous for drivers, they're risky for divers. It is important to consider the possibility of additive effect of nitrogen narcosis on the actual effects of the medication."*²

The following guidelines, endorsed by the Dutch Association for Diving Medicine in 2015, formulate conditions for recreational diving in combination with antidepressants. Depression itself will not be considered here but will be discussed in future guidelines. No research is available about the effect of hyperbaric situations on psychotropic

medication or psychiatric disorders. This means that these guidelines cannot be substantiated beyond the level of 'expert opinion' and are not rigid. If justified, individual cases may warrant a deviation from these guidelines which are intended to support rational clinical practice.

Method

PubMed was searched for articles using the following terms: *"antidepressants and diving"*. Twenty-one articles were identified of which only two research articles were used, Nineteen articles did not fully match the subject. Furthermore, there are many posts to be found on scuba message boards, only one recent guideline and one recent article on the Divers Alert Network (DAN) Europe website. PubMed was also searched for literature reviews using the following terms: *"antidepressants and seizures"*, *"antidepressants and bleeding"* and *"antidepressants and hypoglycemia/hyperglycemia"*. The combined search resulted in identification of five literature reviews, one cohort and one follow-up study to be reviewed.

Applying these guidelines

- This document relates to recreational sports diving. The recommendations given are not aimed at professional divers, including dive masters and instructors.
- Under Dutch law (ARBO-besluit, H6, Afd 5, Art 6.14) an instructor must be *"physically and mentally capable of recognizing and, if possible, preventing hazards"*. Divemasters and recreational diving instructors with psychiatric issues are in principle unsuited to carrying out diving instruction, but may be deemed suitable for personal recreational sports diving activities based on the current guidelines.
- These guidelines are not set in stone. The scientific

rationale has its limitations and deviation from the recommendations may be justifiable in individual cases.

- The key principle is that the individual diver is primarily responsible for his/her health and safety, as well as the health and safety of his/her buddy.
- The existence of other medical contraindications should be checked for each diver, including the indication for the use of the relevant substances.

Classification of antidepressants

- Traditional:
amitriptyline, clomipramine, dosulepin, doxepin, imipramine, maprotiline, nortriptyline.
- Modern:
selective serotonin reuptake inhibitors (SSRIs) (also known as serotonin-specific reuptake inhibitors); citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline;
serotonin and norepinephrine reuptake inhibitors (SNRIs); duloxetine, venlafaxine.
- Other:
trazodone, bupropion, mianserin, mirtazapine, moclobemide, agomelatine;
monoamine oxidase inhibitors (MAOIs) (non-selective); phenelzine, tranylcypromine.

Side effects of antidepressants

Antidepressants have several side effects that may pose risks when diving with compressed air. These include: drowsiness and sleepiness; convulsions; increased bleeding tendency; hypoglycaemia; mania, dry mouth and blurred vision.

DROWSINESS AND SLEEPINESS

Hypnosedation often occurs with antidepressants that have a strong antihistaminic or noradrenergic action (the traditional medicines; of the modern medicines, trazodone, mianserin and mirtazapine).³ SSRIs and SNRIs can also cause hypnosedation, especially in higher doses.

SEIZURES

An antidepressant overdose may induce seizures. At a normal dose of clomipramine, and more so with bupropion, there is an increased risk of the occurrence of convulsions.⁴ One review of the newer antidepressants considered the risk generally to not be very different from the incidence of first seizure in the general population, whereas the risk with tricyclic antidepressants at effective therapeutic doses is relatively high.⁵ Ten years later a follow-up study of 151,005 depressed patients showed that the current use of SSRIs or SNRIs is associated with a twofold increased risk of first-time seizure compared with non-use, while current use of tricyclic antidepressants (mostly low dose) is not associated with seizures.⁶ Treatment initiation in SSRI and SNRI users is associated with a higher risk of seizures than longer-

term treatment.⁶ However an analysis of 238,963 British patients diagnosed with depression led to the conclusion that risk of seizures is significantly increased for all classes of antidepressants.⁷ There are no data on whether these agents increase risks of or sensitivity to central nervous system oxygen toxicity.

INCREASED BLEEDING TENDENCY

Case reports and observational studies show that the SSRIs may cause bleeding complications.^{8,9} An increased bleeding tendency has a theoretical risk of making any neurological decompression sickness (DCS) worse than it might otherwise have been without antidepressants and also making bleeding associated with barotrauma worse. The mechanism behind this increased risk is probably the inhibition of serotonin reuptake in the thrombocyte, which affects primary haemostasis. Serotonin is a potent vasoconstrictor and increases blood platelet aggregation. The use of antidepressants with high serotonin affinity (such as fluoxetine, sertraline, clomipramine and paroxetine) slightly increases the risk of high gastrointestinal bleeds.¹⁰ This increased risk may well be only clinically relevant for risk patients: those using warfarin¹¹ and non-steroidal anti-inflammatories (NSAIDs),¹² users with a history of bleeding with surgical procedures, and in the elderly. Concurrent use of NSAIDs or antiplatelet drugs increases the risk for upper gastrointestinal bleeding, but this risk might be reduced significantly by concomitant use of acid-suppressing drugs.¹³ Antidepressants appear not to increase the risk of a haemorrhagic cerebrovascular accident.¹⁰ However, clinical studies show that antidepressant use may be associated with an increased risk of new subclinical cerebral microbleeds.¹⁴ Data are very limited on other types of bleeding. There are risks attached to the combination of an antidepressant with a NSAID or warfarin. In such circumstances, the NSAID could be replaced with a selective COX-2 inhibitor.

HYPERGLYCAEMIA AND HYPOGLYCAEMIA

Between April 1995 and February 2010, the Dutch Pharmacovigilance Centre Lareb received ten reports of hypoglycaemia with the use of a SSRI by patients with known type 1 diabetes mellitus.¹⁵ Evidence about the effects of antidepressants on glucose metabolism comes mainly from case reports, animal studies and studies involving relatively small groups of patients.¹⁶ In short, the result is that the various types of antidepressants may have paradoxical effects on the glucose system, as they can increase the risk of both hyperglycaemia and hypoglycaemia depending on the specific medication used.¹⁷ Moreover, antidepressants may have either a positive or a negative effect on other glycaemic and metabolic parameters, such as glycated haemoglobin (HbA1C), serum insulin, insulin sensitivity and body weight. Diabetes patients who are treated with antidepressants must remain watchful as their diabetes may become unbalanced. Symptoms of hypoglycaemia or hyperglycaemia occurred from four days to five months

after starting the antidepressant treatment, with more than two-thirds occurring within a month.¹⁷

DRY MOUTH AND BLURRED VISION

Dry mouth, blurred vision, perspiring and difficulty urinating often occur with the older (traditional) medicines and are due to unwanted blocking of cholinergic receptors. A dry mouth can be particularly annoying, as the air in the diving cylinder is dry and must be moistened. A considerable amount of fluid loss may occur during a dive; immersion and a lower water temperature cause peripheral vasoconstriction and a central shift of blood volume which leads to a diuresis.

PSYCHIATRIC SIDE EFFECTS

The chances of developing mania when taking antidepressants for bipolar depression approaches 14% and for unipolar depression 6%.¹⁸ Antidepressants do not very likely lead to an increase of suicidal thoughts or suicide in adults over 25 years of age.¹⁹ A meta-analysis of 4,582 patients in 24 placebo-controlled trials showed that the use of antidepressant drugs in paediatric patients is associated with a modest increased risk of suicidality.²⁰

Reduction and discontinuation of antidepressants

Antidepressants are not addictive and do not lead to dependency. However, non-specific withdrawal symptoms may occur during reduction and after discontinuation. The symptoms are usually mild, start two to five days after discontinuation and last between one to three weeks. Fluoxetine has such a long half-life, that there are few complaints following its withdrawal. The most commonly reported complaints are flu-like and gastrointestinal symptoms, problems sleeping and psychotic symptoms, but cognitive dysfunction, neurological symptoms and movement disorders may also occur. It is important to distinguish between a relapse of the depression and withdrawal symptoms. There is a clinically significant relapse rate of mood disorders and anxiety disorders after stopping antidepressants.^{21,22}

Fluoxetine

Increased levels of proinflammatory circulating cytokines have been detected in animal models of DCS, which supports the theory that severe DCS is a systemic process characterized by an inflammatory response syndrome.²³ Fluoxetine has anti-inflammatory properties and suppresses pro-inflammatory cytokine production, e.g., circulating interleukin-6, resulting in improvement of depressive symptoms.^{24,25} An interesting finding is that fluoxetine dramatically reduces the incidence of DCS and promotes motor recovery in mice, possibly by reducing inflammatory processes resulting from DCS.^{26,27} Further studies are needed to better elucidate these mechanisms and their relevance to clinical DCS.

Recommendations for diving whilst on antidepressants

- Only modern antidepressants: SSRIs, SNRIs and others, such as bupropion and agomelatine, are tolerated better than the traditional medicines that, above all, cause more sleepiness and drowsiness.
- Only a single psychotropic medicine: more than one psychotropic medicine will increase the risk for potentially dangerous side effects whilst diving and susceptibility to nitrogen narcosis.
- Well-adjusted medicine for a minimum of three months: this will allow for resolution of side effects, e.g., heightened arousal and anxiety.²⁸
- No significant side effects;
- Compliant with medication and other therapy;
- No diving during reduction of medication: there is a chance of (non-specific) withdrawal symptoms during reduction and after discontinuation and there is a clinically significant relapse rate of mood and anxiety disorders after stopping antidepressants.
- The condition for which drugs were prescribed should have resolved and treatment should be in the maintenance phase. This means that the diver should have returned to work and normal daily life.²⁸
- Maximum diving depth of 18–20 metres (60–65 feet) is advised to minimise the risk of DCI and the slight theoretical risk of worsening inert gas narcosis.
- No combination with NSAIDs: because of an increased bleeding tendency with modern antidepressants, their combination with NSAIDs should be avoided in diving.
- No combination with anticoagulants: because of an increased bleeding tendency with modern antidepressants, their combination with anticoagulants should be avoided in diving.
- No combination with epilepsy: the combination of diving with antidepressants and epilepsy is absolutely contraindicated because the incidence of convulsions is slightly higher with all antidepressants.
- In diabetes mellitus: diabetes may become unbalanced in patients treated with antidepressants; the advice is for an evaluation by an internist/sports diving physician.

Who should carry out the examination?

The recommendation to the Dutch Association for Diving Medicine is that with the use of the guidelines, certified sports diving physicians should be able to arrive at a well-considered opinion on whether a diver should be deemed suitable or unsuitable for diving with compressed air. In case of doubt or a complicated underlying condition, a psychiatrist/sports diving physician may be asked to carry out a specialist examination.

Conclusions

There are indications that antidepressants increase nitrogen narcosis. Modern antidepressants, especially SSRIs, SNRIs as well as bupropion and agomelatine are tolerated better

than the traditional medicines which, above all, cause more sleepiness and drowsiness. There is a slight chance of the development of convulsions with antidepressants, especially with bupropion and clomipramine. SSRIs may cause bleeding complications, which may only be clinically relevant for users of warfarin and NSAIDs. SSRIs seem not to cause orthostatic hypotension, but there are indications that their use by patients with type 1 diabetes mellitus could unbalance glucose metabolism. The possible shift to mania during reduction or after discontinuation of the medication could pose a danger to the diver and his/her buddy.

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