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Antidepressants and Diving....

A Summary

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Lately we've had quite a lot of calls regarding antidepressants and diving, so we thought we'd put some information together.

As we are all aware, the WRSTC diving medical requirements questionnaire asks if the diver is taking any prescribed medications, and a positive response means that a physician **MUST** assess the diver. However, even when approval is received from a physician, it is the dive professionals choice whether or not they are willing to take the student. Bearing this in mind, we felt it was important to highlight some of the issues to consider when faced with a potential student who is taking antidepressants.

In terms of danger to divers, medications usually play a secondary role, with the primary concern being the underlying condition for which the medication has been prescribed. There is a paucity of research investigating the relationship between various mental conditions and diving. However, some assumptions can be made. For example, if the individual is severely depressed, suicidal, out of touch with reality or paranoid with delusions or hallucinations, they obviously shouldn't dive. However, it is more common that we are faced with someone who has been diagnosed with a depressive disorder, anxiety or phobia, and many of whom may be considered fit to dive. So what do these disorders mean, and what considerations should we give to each individual?

Depressive disorders, which include depression (unipolar disorder) and manic depression (bipolar disorder) are incredibly common affecting 10-19 million US adults per year, with the highest percentage of cases being diagnosed in 25-44 year olds. Commonly known as clinical depression, these disorders are differentiated by short-term states of depressed mood or unhappiness by an imbalance in the chemicals within the brain, known as neurotransmitters. Clinical signs can include feeling down or empty; having reduced interest in activities that were once pleasurable; disturbed sleep and fatigue; changes in appetite; loss of libido; difficulty in paying attention, concentrating or making decisions; feelings of

worthlessness and guilt and in some cases contemplation of suicide. In addition, people suffering with bipolar disorder may alternate depressive episodes with manic ones, which may be demonstrated as periods of elation, racing thoughts, poor judgment, recklessness and a tendency to be easily distracted. Treatment of such disorders typically involves psychotherapy, antidepressants or both, and in the majority of cases (particularly unipolar depression) improvement is seen within a few weeks. Fitness to dive will depend on the mental state of the individual, how long they have been on medication, which medication(s) they are receiving and whether or not they are in remission. In fact the UK Sports Diving Medical Committee Guidelines state that divers who are taking antidepressants must satisfy the following criteria:

- Patients should only dive on the newer antidepressants. The older tricyclics reduce the fit threshold, can cause dysrhythmias and are sedative. At standard dosages, modern antidepressants such as the SSRIs citalopram, fluoxetine and paroxetine have a low seizure rate of <0.1% compared with the general population. They are also non-sedating and do not appear to impair cognitive function.
- They should only be on one psychotropic medication.
- They should have been used for a minimum of three months before diving to allow for resolution of side effects e.g. heightened arousal and anxiety.
- The condition for which they were prescribed should have resolved and treatment should be in the maintenance phase. This means that they should have returned to work and normal daily life.
- There must be no history of upward mood swings associated with loss of judgement. For upward mood swings to be significant they have to be persistent for at least four days with an unequivocal change in functional mood observed by others. The symptoms include decreased need for sleep, racing thoughts and excessive involvement in pleasurable activities that have a high potential for painful consequences. Thus a history indicating loss of judgement with unrestrained buying sprees, sexual indiscretions etc are incompatible with diving. Antidepressants are known to worsen this condition.
- There is a significant relapse rate when stopping antidepressants. Following withdrawal, further information regarding the patient's mental health will need to be obtained from the GP. The patient should also not dive during the withdrawal phase. For short acting antidepressants such as Paroxetine, the suggested period is six weeks.

In addition, there can be issues related to the specific medication. Drugs frequently used to treat depression include three major classes: the selective serotonin reuptake inhibitors (SSRIs), tricyclic/tetracyclic medications

(TCAs/TeCAs) and the monoamine oxidase inhibitors (MAOIs), along with a few uniquely acting compounds. There are few studies examining alterations in drug metabolism or side effects with immersion, however, the general side effects are known and these in themselves may present some issues in the aquatic environment.

Commonly prescribed SSRIs include:

- Citalopram (Celexa®, Cipramil®, Paxoran®)
- Fluvoxamine (Luvox®, Faverin, Fevarin®, Floxyfral®)
- Paroxetine (Paxil®, Pexeva®, Seroxat®, Brisdelle®, Rexetin®)
- Fluoxetine (Prozac®, Sarafem®, Unprozy®, Prozep®, Oxsac®, Fluzac-20®, Magrilan®, Fluxetil®, Flusac®, Flumed®, amongst others)
- Sertraline (Zoloft®, Lustral®, Deprax®, Altruline®, amongst others)

This group of drugs act to increase the extracellular level of serotonin by inhibiting the reuptake into the presynaptic cell, and thereby increase the amount available to bind to the postsynaptic receptor within the neuron. Common side effects include anxiety and restlessness (especially in the initial stages of therapy), drowsiness and dizziness, dry mouth, tremor and increased bruising or bleeding (this is a mild increase and typically not significant unless therapy is combined with aspirin or non-steroidal anti-inflammatory drugs such as ibuprofen, diclofenac, sulfasalazine or piroxicam. However, barotrauma to sinuses, ears or lungs may cause significant haemorrhage, and could exacerbate the bleeding phase of DCI. It is therefore recommended by some that the maximum depth should be an EAD of 30m to minimise the risk of DCI and slight theoretical risk that they might increase narcosis. In contrast, a recent study of hyperbaric induced DCS demonstrated fewer manifestations of DCS in mice pre-treated with fluoxetine when compared with placebo and a decrease in the pro-inflammatory cytokine IL-6, which served as a marker of systemic inflammation in DCS.

In general, provided divers are receiving only a single medication, are fully functional (ie: able to drive, work etc) and their underlying disease is in remission, most individuals would be considered fit to dive. However, other considerations should involve any other medications (even over the counter preparations such as aspirin) and the planned dive depth. It is not advisable to suddenly discontinue these medications as this can lead to a plethora of side effects.

Commonly prescribed MAOIs include:

- Phenelzine (Nardil®, Nardelzine®)
- Tranlycypromine (Parnate®, Jatrosom®)
- Isocarboxazid (Marplan®)

By inhibiting MAO, these drugs prevent the breakdown of multiple neurotransmitters such as serotonin, melatonin, noradrenaline (norepinephrine), adrenaline (epinephrine) and dopamine, thereby altering neurotransmission and neurochemistry.

Common side effects include dizziness, drowsiness and less commonly tremor, however, these are usually transient and resolve within the first few months of therapy, and therefore in the stable patient unlikely to influence their ability to dive. However, perhaps of more concern is the interaction with not only other medications, but also foods containing tyramine, which can lead to a hypertensive crisis and be fatal. Foods particularly high in tyramine include (but is not limited to) aged cheeses, cured meats, tofu, shrimp paste, soy sauce, coconut, peanuts, avocado, certain red wines, some yeast extracts and spoiled foods. Clinical signs of hypertensive crisis include retinal haemorrhage, headache, vomiting, bloody urine, nosebleed, chest pain and arrhythmia. In addition, combination with other drugs/foods which increase serotonin levels (such as SSRIs, Tramadol, St Johns Wort, certain migraine medications (triptans) or stimulants such as cocaine, methamphetamine, MDMA) can result in Serotonin Syndrome, which is characterized by headache, confusion, agitation, hypomania, shivering, sweating, high heart rate, muscle twitches, vomiting and diarrhoea and even coma/death. Therefore, if an individual wishes to dive on these medications they should be questioned of any lifestyle changes/choices and monitored for signs of interactions (which manifest quickly after occurring).

In addition, it is not advisable to suddenly discontinue these medications as this can lead to a number of side effects.

Commonly prescribed TCAs and TeCAs

TCAs:

Doxepin (Adapin®, Sinequan®, Deptran®)

Nortriptyline (Aventyl®, Pamelor®, Sensoval®, Norpress®, Allegron®, Noritren®, Nortrilen®)

Amitriptyline (Elavil®, Endep®, Levate®, amongst others)

TeCAs:

Desipramine (Norpramin®, Pertofrane®)

Amoxapine (Asendin®)

Loxapine (Loxapac®, Loxitane®, Adasuve®) (typically used for Schizophrenia rather than depression)

Maprotiline (Deprilept®, Ludiomil®, Psymion®)

Mazindol (Mazanor®, Sanorex®)

Mianserin (Bolvidon®, Norval®, Tolvon®) also classified as a Noradrenergic and specific serotonergic antidepressant (NaSSA)

Setiptiline (Tecipul®) also classified as a NaSSA

Mirtazepine (Remeron®, Avanza®, Axit®, Mirtaz®, Zispin®) also classified as a NaSSA

Trazodone (Depyrel®, Desyrel®, Mesyrel®, Molipaxin®, Oleptro®, Trazodil®, Trazorel®, Trialodine®, Trittico®) also a serotonin antagonist and reuptake inhibitor (SARI)

TCAs can be used to treat depression, anxiety or chronic pain (ie: IBS). The dose for chronic pain is typically much lower than the anti-depressant dose and with time side effects may be minimal. Therefore, it is important to establish which condition is being treated, the drug dose and the length of time that the individual has been medicated. As antidepressants TCAs and TeCAs are often used in combination with other agents or when other medications have proven ineffective. They are associated with a greater frequency of side effects than the second-generation (SSRIs, MAOI) medications. Side effects can include (but are not limited to) marked drowsiness (especially in the initial phase of treatment), dizziness, dry mouth and occasionally blurred vision. In some instances TCAs and TeCAs can lead to an increased heart rate and lower the threshold for seizures; it is for these reasons that it is often advised not to dive whilst receiving these medications. In addition, it is not advisable to suddenly discontinue these medications as this can result in numerous withdrawal effects.

Other medications (many of these have serious side effects that could lead to a fatality during diving):

Venlafaxine (Effexor®, Efexor®, Trevilor®): This is a serotonin-noradrenaline reuptake inhibitor (SNRI) typically reserved for use when other treatments have failed due to the greater frequency of side effects. Common side effects include headache, nausea, insomnia, drowsiness, dry mouth, constipation, sexual dysfunction, sweating and nervousness. However, less common but potentially worrisome side effects include, an increased bleeding tendency, a decreased seizure threshold, cardiac arrhythmias, delirium, pulmonary infiltration with eosinophils (a white blood cell) and an increase in suicidal tendencies. In addition, there is a high incidence of withdrawal syndrome associated with cessation of this medication. This is thought to be due to its short half-life. Whilst the effect of immersion on this drug's half-life remains unknown, it is not uncommon for drug metabolism to be increased, potentially putting the diver at risk of withdrawal syndrome.

Bupropion (Wellbutrin®, Zyban®) can be used as an antidepressant, or an aide to stop smoking. It is unique in it's mode of action, and demonstrates fewer side effects than most antidepressants. Unfortunately, one of the recognised side effects is an increased incidence of seizures. It is for this reason it was temporarily withdrawn from the market before being reintroduced with a lower recommended dosage. Other worrisome side effects include anxiety, dry mouth, vomiting, dizziness, chest pain, elevated heart rate, increase blood pressure, fainting and hallucinations.

Topiramate (Topamax®) is an anticonvulsant that may be prescribed for bipolar disorder, post-traumatic stress disorder, borderline personality, migraine and addiction. Side effects can be widespread, and include seizure, hallucinations, somnolence, nausea, disturbance in attention, impairment of motor skills, bleeding tendencies, slowing of the heart and fainting.

Valproic Acid (Depakote®) is an anticonvulsant that can be prescribed for migraine, bipolar mania or epilepsy. Side effects are common and can include (but are not limited to) bleeding tendencies, drowsiness, dizziness, nausea, infection, seeing double, hallucinations, confusion, vertigo and pleural effusion (fluid within the chest cavity).

Methylphenidate (Ritalin®) is a psychostimulant, which is typically prescribed for attention deficit disorder, but may also be given for depression, postural orthostatic tachycardia disorder (markedly elevated heart rate when rising) and narcolepsy. Side effects include anxiety/nervousness (especially when initially prescribed), depression, headaches, mania, rapid heart rate, hypertension and suicidal ideation.

Buspirone (Buspar®) is a psychotropic drug typically prescribed to decrease anxiety. In some countries it is only licenced as a short-term medication as it is associated with a plethora of side effects which can include elevated heart rate, chest pain, nervousness, dizziness, muscular pain, disturbance in attention, confusion, anger, abnormal co-ordination, fainting, altered blood pressure (high and low), muscle cramps, bruising, stroke, heart attack and hallucinations.

Lithium (Lithonate®, Eskalith®, Lithobid®, Lithane®) is commonly prescribed for the treatment of bipolar disorder, although it may be used to treat other diseases. Many authors advise not diving when on Lithium as the half-life is altered during immersion, increasing the incidence of side effects, which can include seizure, muscular weakness, drowsiness, slurred speech and balance problems.

In summary, depression is common, and in many circumstances people who are diagnosed with depression or anxiety may be cleared for diving by either a physician or DMO. However, whether or not an instructor is happy to accept that individual, as a student is still at the discretion of the instructor. In order to minimise risks to the dive group the individual should be in remission (ie: free of signs of disease, mood swings or manic behaviour and back to a 'normal life-style' ie able to drive/work etc); they should be on monotherapy (one medication) and should have been receiving a standard maintenance dose, without notable side effects, for a prolonged period (at least 3 months). Lifestyle factors which could influence the drug metabolism/side effects should be discussed and older drugs such as Lithium or the TCAs for which there is an increased risk of seizures should be avoided. At no point should discontinuation/alteration of the treatment regime be recommended by anyone other than the physician.

References available upon request