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## Viagra - curse or blessing for a diver?

Drugs & Diving // Medication & Diving

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### Viagra - curse or blessing for a diver?

*It's relatively likely that some males in their 40s, 50s, and 60s take viagra and may also be SCUBA divers. Therefore, they should be warned about the fact that viagra taken before diving is very likely to increase the risk of DCS whereas taken afterwards it may be a remedy.*

When researchers decide to treat small rodents with drugs and send them diving in a hyperbaric chamber, SCUBA divers know these researchers are hoping to find a remedy for decompression sickness. Even more, a study like this surely attracts attention when the drug in question is viagra, probably the most well-known drug ever.

However, less well-known may be viagra's active substance, sildenafil, which was originally tested as a drug for lowering hypertension. Its beneficial effect for the male part of humanity was more or less a side effect which was then extensively marketed by Pfizer – as we all know only too well.

Nowadays, sildenafil is licensed to treat pulmonary hypertension and other vascular diseases. In an off-label use it has successfully been used to treat swimming induced pulmonary edema (SIPE) in triathletes. The main difference to viagra is that it is administered in lower doses than its famous relative.

### PDE5-inhibitors, exogenous and endogenous NO, and vasodilation

In general, sildenafil acts on the endothelium - the inner layer of blood vessels and dilates them by simply potentiating the vasodilator effect on smooth muscle relaxation. It does this by inhibiting an enzyme, phosphodiesterase type 5 (PDE5). In short, it is a PDE5-inhibitor. It lowers blood pressure by dilating vessels. These effects are similar to the effect NO (nitric oxide) has on vessels – it also dilates them. Therefore, scientists thought a vasodilator like sildenafil (viagra) could be protective against decompression sickness (DCS) in SCUBA divers. DCS develops from bubbles that form from micronuclei in blood vessels after decompression and NO-releasing agents are believed to have the ability to reduce this bubble formation and prevent serious decompression sickness.

### Sildenafil pre-treatment study

However, all hopes for a new remedy for DCS were destroyed when the scientists – Blatteau, Brubakk, Gempp, Castagna, Rizzo, and Vallée – investigated the effect of pre-treatment with sildenafil in an animal model and found that sildenafil doesn't protect against DCS at all but instead would even cause harm and divers should better be warned about it.



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To evaluate the clinical effects of sildenafil, the researchers pre-treated small rodents with 10mg/kg of sildenafil one hour prior to exposure. Then the rodents underwent a simulated dive to 90 msw for 45 minutes in a hyperbaric chamber before staged decompression. Half an hour after the dive, neurological DCS symptoms, blood cell count and quantification of the level of circulating bubbles in the right cavities were clinically assessed. The control group was not pre-treated with sildenafil but received the same volume of water prior to the dive of equal conditions.

#### **Negative outcome of the study**

As mentioned above, the scientists' hopes were refuted: there were more cases of DCS in the sildenafil group than in the untreated control group. Further findings were: reduced platelet counts in the sildenafil group - a biomarker for decompression stress. This is owed to the fact that in DCS gas bubbles damage the vascular endothelium and provoke an inflammatory response resulting in the activation of leukocytes which transmigrate through the vascular endothelium after DCS, explaining the reduction in counts.

#### **Beneficial effects on swimmers**

However, as disappointing as these findings were in regard to decompression sickness, they should not be mixed up with the beneficial effects sildenafil has on SIPE (swimming induced pulmonary edema) in triathletes in which it has effectively mitigated the symptoms of swimming induced pulmonary edema when taken before starting the activity. Swimming, although a water sport activity as well, is a totally different kind of sport compared to SCUBA diving. Greater depths and higher pressures in SCUBA diving make the main difference. What is good for one can be bad for the other.

#### **How to explain...**

The researchers' explanation for the increased risk of DCS when taking sildenafil prior to diving is that the increased cerebral blood flow due to sildenafil's vasodilator effect in the central nervous system is causing a higher blood flow in the brain with a higher load of considerably more inert gas during hyperbaric exposure which may then generate bubbling and severe DCS in neurological tissue.

#### **So, what do we know now?**

Sildenafil as well as NO (i.e. endogenous or exogenous) are both powerful vasodilators. In preconditioning studies, NO has shown to be an effective agent in reducing the risk of DCS. But it's not that simple that the use of a vasodilator alone lowers the risk of DCS. There is obviously a difference between endogenous/exogenous NO donors and a drug like the PDE5 inhibitor sildenafil. An endogenous NO donor is released as consequence of exercise, an exogenous NO donor can be taken in as food. In the above mentioned study, sildenafil was not able to reduce bubble formation in an animal model, but NO (nitric oxide) is known to reduce bubble formation in rodents as well as in man as was demonstrated in preconditioning studies (see Balestra et al.). Thus, NO donors must involve properties and mechanisms different from those encountered with sildenafil. This suggests that the presence of gas nuclei attached to the vessel wall is not directly influenced by the vasodilator effect related to the relaxation of the smooth muscle. NO seems to have specific effects that are involved in the reduction of the number of gas nuclei adhering to the surface of the endothelium. It can also diffuse to the luminal surface of the endothelium and trigger important physiological effects such as scavenging superoxide radicals, inhibiting platelet aggregation, modulating endothelial layer permeability and attenuating leukocyte function.

Sildenafil, however, does not seem to have these specific effects.

#### **Possible remedy after decompression**

However, what may not be beneficial in one situation can be beneficial in other circumstances: the elevation of cerebral blood flow and the improvement of functional recovery of ischemic tissue have been shown to be beneficial in the treatment of stroke with sildenafil 24 hours after onset of ischemic stroke. This gives new hope that sildenafil could be useful as an adjuvant (i.e. supportive) treatment of ischemic neurological DCS in divers who have not recovered after initial treatment with hyperbaric oxygen.

#### **What do we learn from this?**

##### **SCUBA DIVERS:**

Preconditioning methods (like sauna and light exercise) are beneficial when done prior to diving. They trigger the release of endogenous NO which scavenges micronuclei from the inner layer of blood vessels and are therefore likely to reduce the risk of DCS.

Heavy exercise or sauna within 24-48 hours after diving increases the risk of DCS because it increases the blood flow in most tissues and leads to increased bubble formation from off-gassing nitrogen.

In the animal model, sildenafil increases the risk of DCS when taken prior to diving. (We have no

knowledge of cases in human divers.)

If already hit by DCS and already treated in a hyperbaric chamber, sildenafil may be beneficial after diving and HBO treatment because it might help alleviate the symptoms of neurological DCS by increasing cerebral blood flow. This is an assumption based on stroke studies in rodents and requires more research.

SWIMMERS, TRIATHLETES and other EXTREME ATHLETES:

Successful off-label use of the drug has shown that sildenafil taken in low doses can successfully treat the symptoms of SIPE and/or altitude sickness.

#### A warning

The researchers of this study conclude that pre-treatment with sildenafil (viagra) – or other drugs with a similar effect mechanism (i.e. PDE5-inhibitors) – promotes the onset and severity of neurological decompression sickness (DCS). This is an important finding and should be spread among the community of divers.

As always with taking any drugs in SCUBA diving, divers should first consult with their (diving) physician. This is especially true for viagra. Possible interactions with other drugs and interferences with underlying diseases in the ambience of diving should always be discussed and clarified upfront.

#### To shed more light on it...

Research has shown that further studies on oxidative stress markers in the central nervous system (CNS) are needed to better understand the underlying mechanisms of sildenafil in DCS.

#### Sources:

Link to this paper: <http://www.ncbi.nlm.nih.gov/pubmed/23580342>

Paper on preconditioning: Blatteau JE, Gempp E, Balestra C, Mets T, Germonpre P (2008) Pre-dive sauna and venous gas bubbles upon decompression from 400 kPa. *Aviat Space Environ Med* 79(12): 1100–1105 [PubMed]

Paper on Sildenafil and SIPE: <http://www.medicalnewstoday.com/articles/306754.php>

*AlertDiver.eu*, 2016; 65

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