

## ■ Sildenafil increases cerebrovascular reactivity

Diomedi et al. found a significant improvement of cerebrovascular reactivity 1 hour after 50 mg of sildenafil (Viagra). Effects on cerebral endothelial function could contribute to sildenafil-induced migraine.

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## ■ Effect of sildenafil (Viagra) on cerebral blood vessels

Commentary by Karen C. Johnston, MD, MSc

Sildenafil is a selective inhibitor of phosphodiesterase type 5 and is used for the treatment of male erectile dysfunction. It causes relaxation of vascular smooth muscle via a cyclic guanosine monophosphate (cGMP) second messenger that results in a vasodilatory effect in the corpus cavernosum. A dilatory effect on peripheral blood vessels has also been identified and vascular side effects primarily include facial flushing, nasal congestion, headache, and other minor symptoms. Blood pressure reduction, especially when sildenafil is used in conjunction with nitrates, has been recognized and therefore its use in association with nitrates is not recommended. Due to concerns regarding the risk of sildenafil in patients with cardiovascular disease, a consensus panel recommended a risk stratification and patient management pro-

cess prior to initiation of therapy in patients with cardiovascular disease.<sup>1</sup> Transient ischemia,<sup>2</sup> stroke,<sup>2</sup> and intracerebral hemorrhage<sup>3</sup> have also been reported in association with use of sildenafil but causality remains unclear.

Early exploration of the relationship between sildenafil and cerebral blood flow has not demonstrated any substantial effect on flow. In a randomized, double-blind, placebo controlled trial of 28 men, Diomedi et al. again suggest that sildenafil does not affect cerebral blood flow velocity. However, using a breath holding index and transcranial Doppler to assess the endothelial response to hypercapnia, they demonstrated that a single 50 mg dose of sildenafil produces an improvement in cerebrovascular reserve. Though this may reduce the concern for the use of sildenafil in patients

at risk for cerebrovascular disease, it may increase the concern in migraineurs as migraine is a recognized side effect. Further studies are necessary to evaluate subjects with known cardiovascular and cerebrovascular disease and with higher dosing regimens and repeated dosing. Such studies may help to inform decisions on the risk benefit ratio of using this therapy in specific patient populations.

### References

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