

Letters to the Editor

Intrathecal Clonidine Administration and Erectile Dysfunction: What Is the link?

TO THE EDITOR:

We read with great interest the work by Koman et al (1) dealing with the possible association between intrathecal clonidine and erectile dysfunction (ED). Indeed, the authors reported on the case of a 52-year-old man who presented with a history of chronic neuropathic pain treated with an intrathecal application of morphine for many years, but without considerable relief. When clonidine was applied in combination with morphine, the patient experienced a significant pain relief, but showed hypotension and ED, which disappeared after clonidine withdrawal, clearly demonstrating a cause-and-effect relationship.

Erectile dysfunction is a highly prevalent problem increasing with age, as well as the major men's sexual concern. ED shares common risk factors with cardiovascular diseases, i.e. diabetes mellitus, dyslipidemia, smoking, hypertension, absence of physical exercise and obesity, and may be secondary to endocrine-metabolic and neurological disorders or due to psychogenic factors.

Moreover, many different drugs can cause ED by affecting sexual hormone levels, neurotransmission, or blood circulation. Among them, antidepressants (especially those acting on the serotonergic pathways), neuroleptics, and antihypertensives are the drugs most often associated to sexual dysfunction (SD), including ED.

In particular, centrally acting antihypertensive agents such as methyldopa and clonidine, nonselective beta-adrenergic blockers, and potassium-sparing diuretics are those most often associated with SD; thiazide diuretics cause ED but may otherwise play a minimal role in other SD; alpha-adrenergic blockers, angiotensin converting enzyme inhibitors, and calcium channel blockers have little adverse effect on sexuality (2). Drug-related sexual side effects are strictly dose-dependent and disappear after the drug has been withdrawn. However, drugs dosages used for spinal intrathecal administration are usually low as to minimize

side effects, including SD.

Nevertheless, it has been reported that intrathecal baclofen may reversibly compromise erection and ejaculation particularly at higher doses (3).

To the best of our knowledge, intrathecal clonidine-induced ED has never been described before Koman et al's report (1).

Clonidine functions as a sympatholytic by stimulating presynaptic α_2 -receptors leading to decreased release of norepinephrine at both central and peripheral adrenergic terminals. It has also been proposed that the antihypertensive effect of clonidine is partly due to agonism on the 11-receptor or imidazoline receptor, which mediates the sympatho-inhibitory actions of imidazolines to lower blood pressure (4).

In addition to its influence on the autonomic nervous system, it is well established that clonidine is an effective analgesic, and this is also attributable to its α_2 -agonist activity.

Interestingly, Clark and Smith (5) demonstrated a dose-dependent inhibition of erectile reflexes, with inhibition occurring at doses lower than those required to induce copulatory dysfunction.

Thus, it is possible that clonidine may induce ED by decreasing sympathetic outflow (with a consequent inhibition of reflexive erection) as well as diminishing libido and ejaculation, even when intrathecally administered.

In conclusion, since ED-related clonidine intrathecal administration may be an overlooked and underreported problem, further prospective studies should be fostered to support this causal link.

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In response:

We really appreciate the comments regarding our work. We totally agree that the course of the patient reported on strongly suggests a cause-and-effect relationship. One may indeed assume a causal link based on the described physiological mechanisms.

The 2012 polyanalgesic consensus conference on intrathecal drug delivery (1) in the treatment of chronic pain recommended clonidine in combination with morphine as second line of 5. We were not able to find any numbers regarding the frequency of treatment with intrathecally administered clonidine. Yet based on the consensus recommendations a substantial number of patients seems plausible. Given the tremendous implication of sexual dysfunction on life quality which interfered with the therapeutic strategy, the described effect surely is one of relevance.

As stated, 2 male patients are given a therapy

which includes the intrathecal application of clonidine at our institution, none of them complained of erectile dysfunction. Therefore, apart from specific history-taking and course evaluation we gladly support the call for prospective studies by researchers treating a modest number of patients with intrathecally administered clonidine to support a causal link between the intrathecal application of clonidine and the development of erectile dysfunction.

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