

MODERN INDICATIONS FOR THE USE OF OPIPRAMOL

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SUMMARY

Opipramol is considered as a pharmacological agent that does not fit the classification taking into account the division of antidepressants, antipsychotics and anxiolytics. It has a structure related to tricyclic antidepressants but it has a different mechanism of action, i.e. binding to sigma1 and to sigma2 sites. It has been regarded as an effective drug in general anxiety disorders together with other agents like SSRI's, SNRI's, buspirone and pregabalin for many years. It can however also be indicated in other conditions, e.g. it may be used as a premedication in the evening prior to surgery, positive results are also observed in psychopharmacological treatment with opipramol in somatoform disorders, symptoms of depression can be significantly reduced in the climacteric syndrome. The latest data from literature present also certain dangers and side effects, which may result due to opipramol administration. Mania may be induced not only in bipolar patients treated with opipramol, but it can be an adverse drug reaction in generalized anxiety disorder. This analysis shows however that opipramol is an important drug still very useful in different clinical conditions.

Key words: opipramol – depression - anxiety disorders - somatoform disorders

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INTRODUCTION

Depressive and anxiety disorders are nowadays treated in different ways. The most important methods in this field remain pharmacology, psychotherapy or a combination of those two methods (Krysta 2014, Klasik 2012). Antidepressants are the most frequently prescribed drugs in general anxiety disorder (GAD) (Reinhold 2015), or in panic disorder (PD). In that condition sometimes, for a limited period of time, benzodiazepines are used as an additional drug (Locke 2015). Agents like mirtazapine and SSRI's are effective in the treatment of PTSD (Schneier 2015). Antidepressants in combination with other medication are also beneficial in somatoform disorders (Kleinstaub 2014). A thymoleptic drug which has an anti-anxiety and weak antidepressive action, used mainly in the pharmacological treatment of general anxiety and somatoform disorders is opipramol (Krupka-Matuszczyk 2012).

INDICATIONS FOR THE USE OF OPIPRAMOL

Opipramol was introduced to the treatment in the 60s. It was synthesised as one of the tricyclics similar to previously entered imipramine, however, clinical trials have not allowed to qualify opipramol in the group of antidepressants. Nevertheless, in view of these data, opipramol had been extensively used, especially in ambulatory practice (Jaracz 2003). It does not inhibit

the neuronal uptake of norepinephrine and/or serotonin (Müller 2004). It has a different mechanism of action. It binds to sites sigma1 and sigma2, and no reuptake-inhibiting properties are observed. This drug is widely prescribed in many European countries, like Germany and it has a strong anxiolytic efficacy in the treatment of GAD (Möller 2001). It is suggested that effects at sigma2 sites are involved in the anxiolytic properties of opipramol (Volz 2004). According to Murawiec (2012) opipramol does not fit the classification taking into account the division of antidepressants, antipsychotics and anxiolytics. Therefore it requires a separate discussion as it is relatively poorly explored. It has been considered as a potent drug in general anxiety disorders for many years along with SSRI's, SNRI's, buspirone and pregabalin, as it has anxiolytic efficacy superior to placebo (Boerner 2007a, Boerner 2007b, Gale 2007). The duration of treatment depends on the indication and the clinical condition of the patient. The dose Proposed by Prusiński (2003a) is 150 mg for several months (of course if there are no major side effects). According to Indian authors (Mohapatra 2013) the recommended dose for adults is 50 mg in the morning, 50mg in the afternoon, and 100 mg in the evening. It is proposed that after achieving an improvement, the dose is reduced to reach the maintenance dose of 50 mg 2 times/day. But if necessary, the dose can be also raised to 100 mg 3 times daily. It should not be discontinued quickly, because its sudden withdrawal, especially if higher doses, it can cause nausea, vomiting, anorexia, headache and insom-

nia. In the elderly it is advisable to use lower doses—about 1/3 or even 1/2. The most common mistake made during pharmacotherapy in the outpatient is that opipramol is used in very small doses and the drug is taken over too short a period (Prusiński 2003b). Except from the traditional form of the drug introduced in the 60s, a search for new pharmacological options has been made. The appearance of sustained release opipramol dihydrochloride matrix tablets turned out to be a new attitude in the treatment of depression and anxiety (Gönüllü 2006). Opipramol can also be indicated in other conditions, e.g. it may be used as a premedication in the evening prior to surgery (Hueppe 2011, Gerlach 2002). On the other hand in case of surgical interventions, a modification of opipramol therapy can be necessary in a perioperative period in order to avoid interactions (Redel 2013). Positive results are also observed in the treatment with opipramol in somatoform disorders (Freyberger 1998, Volz 2004) and the specific anxiolytic effect of opipramol include in particular somatic symptoms of anxiety (Krupka-Matuszczyk 2013, Święcicki 2013). Symptoms of depression can be significantly reduced in the climacteric syndrome (van Lith & Motke 1983). Opipramol, is not a hypnotic drug, but it promotes sleep, so it can be used widely in the treatment of some forms of insomnia (Müller 1998). Attempts are also made to use opipramol in post-traumatic stress syndrome (PTSD) and gastrointestinal dyskinesias (Vademecumleków 1997). It can have a positive effect in a so called "drug rebound headache", which refers to headaches occurring every day in patients with migraine and tension headaches as a consequence of taking analgesics or ergotamine every day. Opipramol turned out to be effective, when taken by increments from half tablet up to three in 6 days, and the treatment was then continued for 4–6 weeks (Prusinski 1999). Some possible indications for opipramol are still the matter of research. Animal studies suggest that there could be a possible clinical application in peptic ulcer patients with a comorbid depression (Dursun 2009). Opipramol, as potent sigma ligand, could theoretically be an anti-ischemic agent helpful in neurological conditions (Rao 1990).

TOLERANCE AND SIDE EFFECTS

As already mentioned above, opipramol has found wide applications, which resulted not only from its effectiveness, but also from the tolerance by patients and relatively few side effects (Prusiński 2003b). Fatal poisonings with this agent are very rare (Skopp 1996). Anyway the data from literature draw the attention to few, but possible side effects. Mania may be induced in some cases not only in bipolar patients treated with opipramol (Firoz 2015), but it can be an adverse drug reaction in generalized anxiety disorder (Kar 2015). Although opipramol is a drug prescribed orally, some rare attempts to its parenteral use have been described.

Barańska-Rybak et al. (2014) published a case report of recurrent abscesses with a coexisting fever following the injection of a mixture of tramadol, opipramol, and clonazepam. Another interesting case report describes a patient with unipolar depressive treated with maprotiline and opipramol with biologically proven severe acute hepatitis caused by those two antidepressants (Braun 1998). In spite of those rare adverse events reported in the literature, opipramol is generally regarded as a safe pharmacological agent useful in different clinical conditions.

CONCLUSIONS

Opipramol is an efficient drug in general anxiety disorders along with SSRI's, SNRI's, buspirone and pregabalin having an efficacy better than placebo. It can also be indicated in other conditions, e.g. it may be used as a premedication in the evening prior to surgery, positive results are also observed in psychopharmacological treatment with opipramol in somatoform disorders, symptoms of depression can be significantly reduced in the climacteric syndrome. It is a safe drug and has few side effects. A few reports show that e.g. mania may be induced not only in bipolar patients treated with opipramol, but it can have an adverse drug reaction in generalized anxiety disorder. The above analysis shows that opipramol is an important drug with a wide range of indications.

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