Correspondence

Clinical Practice Guideline: The Palliative Care of Patients With Incurable Cancers

by PD Dr. med. Steffen T. Simon, Dr. med. Anne Pralong, Prof. Dr. med. Lukas Radbruch, Prof. Dr. med. Claudia Bausewein, and Prof. Dr. med. Raymond Voltz in issue 7/2020

Adverse Effects of Antipsychotics Are Relevant in Palliative Care Too

The presented update of the S3 guideline on palliative care of patients with incurable cancers recommends for first line treatment of nausea and vomiting (not induced by tumor therapy) antidopaminergic substances, among others (1). Haloperidol is named as an example. Antipsychotic drugs "with a broad spectrum of action" are recommended as second line therapy, a term that is not used in psychopharmacotherapy and which does not allow any conclusions about substances other than levomepromazine, which is the example used in the article. Independently of this terminological question, the article does not give enough space to the discussion of several crucial aspects.

Firstly, the evidence in support of the effectiveness of haloperidol in treating nausea and vomiting in palliative care is not consistently regarded as sufficient, as can be concluded from a Cochrane review (2). Furthermore, the use of haloperidol (and all other antipsychotic drugs) in this indication is off-label use, with all consequences for information-education, documentation, and liability. Primarily, however the use of haloperidol (or other antipsychotic drugs) is associated with numerous adverse effects, some of which are clearly relevant in the palliative care setting. In addition to an increased risk for cardiac repolarization disorders, disturbances in the extrapyramidal motor system (EPMS), acute dystonias, choreiform and parkinsonian syndromes, as well as akathisia/tasikinesia can develop (3), which can severely impair a patient's remaining quality of life. Disorders of the EPMS are possible for all antipsychotic drugs, but are particularly common for first generation antipsychotics (such as haloperidol and levomepromazine) as well as for other antipsychotic drugs with a high affinity to the dopamine D2 receptor (3). In addition to disorders of the EPMS, sedation, impaired mental functions—such as cognition, affect, and impetus (3)—and raised mortality as a result of treatment with antipsychotic drugs (especially haloperidol) need to be borne in mind (4). DOI: 10.3238/arztebl.2020.0462a

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Prof. Dr. Maximilian Gahr, MA
Prof. Dr. Bernhard J. Connemann
Klinik für Psychiatrie und Psychotherapie III, Universitätsklinikum Ulm
maximilian.gahr@uni-ulm.de

In Reply:

Gahr and Connemann rightly note that the evidence for haloperidol is limited. Overall, the treatment of nausea and vomiting in the palliative setting is supported by little evidence. Furthermore, the choice of drug classes and of pharmacological mechanisms of action is also limited. These issues are discussed in more detail in the long version of the guideline. We also refer to the long version of the guideline regarding the question of off-label use.

We agree that the discussion about the risk of cardiac repolarization disorders and of extrapyramidal side effects, due in particular to haloperidol, is essential. Important adverse drugs reactions are described in the guideline. However, when balancing risks and benefits, it should be borne in mind that the doses mentioned in the guideline for haloperidol and levomepromazine are low compared to those recommended in psychiatric treatment (2). For haloperidol, the guideline states a single oral dose of 0.5–1 mg, and a usual maximum subcutaneous dose of 5 mg/24 h. In the psychiatric setting, the recommended dosages depend on the indication and are, for example, 2–10 mg/d (up to 20 mg/d) for the treatment of schizophrenia and schizoaffective disorders and 5–20 mg/d intramuscularly for states of acute agitation (2). The study cited by Gahr and Connemann that showed increased mortality as a result of antipsychotic treatment, especially haloperidol, relates to long-term use. Patients with a life-limiting disease were excluded from the analysis (3). Due to the limited treatment duration and the low doses used in treating nausea and vomiting, the risk for extrapyramidal side effects is clearly lower than when administered as an antipsychotic drug. Furthermore, intravenous administration of low doses of haloperidol does not seem to affect the QT interval (4). DOI: 10.3238/arztebl.2020.0462b

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On behalf of the authors
Dr. med. Anne Pralong
Zentrum für Palliativmedizin, Uniklinik Köln
anne.pralong@uk-koeln.de

Conflict of interest statement
The authors of all contributions declare that no conflict of interest exists.