

Autopsic Examination Case of Levomepromazine Toxicity

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Abstract

Levomepromazine is an antipsychotic drug that is used clinically for a variety of distressing symptoms. A 39 year old female was found dead in the living room. A full autopsy was performed approximately 30 h after death. Analysis of available biological fluids was carried out. The concentration for levomepromazine was 3.0 g/ml in blood and 380 g/ml in stomach contents. We clearly showed the cause of death was ascribed to levomepromazine overdose.

Keywords: Levomepromazine; Overdose; Autopsy

Introduction

Analgesics, antiemetics, sedatives and anxiolytics titrated to the individual patient's level of need should be prescribed and any medication, which is not essential for symptom control, discontinued. Drugs administration is preferably via subcutaneous routes, and the amount of patient manipulation related to medication delivery, reduced to a minimum. In severe cases, where patients experience an unbearable and/or refractory symptom burden, palliative sedation therapy may be considered as an important and necessary therapeutic intervention [1,2]. The aliphatic phenothiazine is a neuroleptic with low antipsychotic potency first used in psychiatry for the treatment of schizophrenia [3]. Levomepromazine acts as an antagonist at histamine type 1, muscarinic-cholinergic, dopaminergic 2, alpha-1 adrenoceptor and 5HT-2 receptors [4,5], and due to a half-life 15-30 hours makes once daily administration practicable. It can be administered subcutaneously, intravenously or orally. Known adverse drug effects include postural hypotension, skin irritation, drowsiness, dry mouth, dystonia, neuroleptic malignant syndrome, Parkinsonism and epilepsy by lowering the seizure threshold [6-8]. Adverse effects appear associated with higher doses and rapid introduction of the drug [9-11]. We present the documented case of a fatality caused by an overdose of levomepromazine.

Case Report

The deceased was a 39 year old female found dead in the living room. A full autopsy was performed approximately 30 h after death. Autopsy findings showed the congestion at the organ level and pulmonary edema. Cardiac blood and stomach contents were collected for toxicological analysis. All specimens were initially subjected to a thorough qualitative analysis. Screening was performed for basic, acidic, and neutral drugs and volatiles by standard chromatographic methods. The levomepromazine concentration was 3.0 g/ml in blood and 380 g/ml in stomach contents. It was above its therapeutic limit. The flunitrazepam concentration was 0.1 g/ml and 3.3 g/ml, the brotizolam was 0.2 g/ml and 0.6 g/ml, and sodium valproate was 12 g/ml and 30 g/ml respectively. They were within their therapeutic limit (Table 1).

| | Blood | Stomach content (µg/ml) |
|------------------|-------|-------------------------|
| Levomepromazine | 3 | 380 |
| Flunitrazepam | 0.1 | 3.3 |
| Brotizolam | 0.2 | 0.6 |
| Sodium valproate | 12 | 30 |

Table 1: The drug concentration of blood and stomach contents.

Discussion

Levomepromazine is a drug with broad-range applicability and effectiveness in the treatment of symptoms had already been demonstrated in a study by Oliver et al. in 1985 [12]. The use of levomepromazine for symptom control has been considered in several published systematic reviews concerning individual symptoms, such as the treatment of nausea and vomiting, breathlessness or sedation [13-15]. Table 1 presents the essential pharmacokinetic data of the drug. Levomepromazine is predominantly used for the treatment of nausea and vomiting, and for severe delirium or agitation. Actually, sedation was reported as a noted side effect of levomepromazine, whereas subsequent studies in the 1990 turned that side effect into a benefit and started to realize the value of the drug as a part of treatment where sedation was indicated and/or intended [16,17]. Effectiveness of sedation was measured in only some of the papers, mostly subjectively rather than with standardized tools [12,16,18]. There are a large number of papers dealing with the use of levomepromazine in palliative sedation, most of them recommend its use in combination with midazolam or as a second line drug for continuous sedation if midazolam is ineffective [15,16,18-20]. In this case, flunitrazepam, brotizolam and sodium valproate were combined. Although they were within their therapeutic limit, they might strengthen the effect of levomepromazine by drug-drug interactions.

Conclusion

Levomepromazine is widely used as antipsychotic, anxiolytic, antiemetic and sedative drug. The findings suggest acute toxicity, and the cause of death was ascribed to levomepromazine overdose.

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