

Exacerbation of Extrapyraxidal Symptoms Associated with Drug-induced Akathisia after Intramuscular Administration of Biperiden in a Patient with End-stage Gastric Cancer: A Case Report

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Abstract

Introduction: The Anti-cholinergic drug Biperiden is used to treat Parkinsonism, an adverse effect of Psychotropic drugs, Dyskinesia, and Akathisia. In the palliative care field, Biperiden is used to treat Akathisia that has developed as an adverse effect of antipsychotics for managing delirium. There are tablets, granules, and injectable preparations of this drug; thus, it can be used for patients with various conditions.

Discussion: In addition to changing and withdrawing the causative drug, Propranolol, Mirtazapine, and Biperiden, an anticholinergic drug, may be administered to manage drug-induced Akathisia. However, Biperiden used to treat drug-induced Akathisia may exacerbate the Akathisia.

Conclusion: Here, we describe administering intramuscular Biperiden to a patient with gastric cancer at the end of life. When Biperiden is administered to treat drug-induced Akathisia and exacerbation of the Akathisia occurs, it is important to consider whether the deterioration in Akathisia is caused by the Biperiden, rather than simply continuing to administer it.

Keywords: Exacerbation of extrapyramidal symptoms; Drug-induced Akathisia; Biperiden; Cancer

Introduction

Delirium reportedly occurs in 90% of patients with end-stage cancer patients just before death [1]. Antipsychotic drugs are often administered in an attempt to control such delirium when it is difficult to control with non-drug therapy [2,3]. Akathisia may occur as an adverse effect of antipsychotic drugs [4]. Several groups have studied the prevalence and characteristics of anti-psychotic drug-induced Akathisia in patients with delirium in palliative care settings. An Australian study found an 11% incidence of akathisia in hospice and palliative care settings [5] and a Japanese study found a 4.8% incidence of Akathisia in a cancer center [6]. Akathisia, a neuropsychiatric syndrome, is characterized by an uncomfortable and subjective inner sensation and an urge to exercise with repetitive leg movements that may involve the trunk and arms [7]. Akathisia is so stressful that it is reportedly a risk factor for suicide; thus, relief of Akathisia-related distress is important [8]. The anticholinergic Biperiden is used to treat Parkinsonism, parkinsonism as an adverse effect of psychotropic drugs, dyskinesia, and Akathisia. In the palliative care field, Biperiden is used to manage Akathisia as an adverse effect of antipsychotics administered to control delirium. There are tablets, granules, and injectable preparations of this drug; thus, it can be used for patients with various conditions. Biperiden can cause extrapyramidal symptoms, such as asthenia, difficulty concentrating, and tension associated with anxiety. Here, we describe a patient with cancer at the end of life whose Akathisia was exacerbated by intramuscular Biperiden.

Case Description

The present patient was a 72-year-old man with a history of gastric cancer that was first diagnosed at age 69, at which time he underwent surgical resection. There was no evidence of metastatic disease at the time of diagnosis. A little over two years later, he presented with jaundice and loss of appetite and was diagnosed as having obstructive jaundice associated with recurrent disease. He underwent palliative

percutaneous transhepatic gallbladder drainage with the aim of relieving his obstructive symptoms. Because of his inability to tolerate oral intake because of ileus caused by cancerous peritonitis, he was started on total parenteral nutrition (TPN). He was also referred to our palliative care team (PCT) for management of abdominal pain and nausea and the increasing insomnia associated with these sources of significant discomfort.

Oxycodone 12 mg/day was started by continuous subcutaneous injection for the pain caused by cancerous peritonitis. Oral Zolpidem 10 mg/day and brotizolam 0.5 mg/day were prescribed for his insomnia. However, because they were difficult to take orally, he was started on chlorpromazine injections 12.5 mg/day in anticipation of antiemetic effects. His pain, nausea, and insomnia stabilized. However, on the 41st day, he manifested drug-induced Akathisia. On the Barnes Akathisia Rating Scale (BARS) [9], he scored one point on the objective subscale, one point on the subjective subscale (awareness), one point on the subjective subscale (distress), and two points on the global subscale. Olanzapine 2.5 mg/day was therefore substituted for chlorpromazine; however, there was no improvement.

On the 43rd day after initiating oxycodone, zolpidem, and brotizolam, a gastroenterologist was consulted regarding management of his drug-induced akathisia and he was started on intramuscular

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Symptoms	day 43 11:00	day 43 15:00 (used Biperiden)	day 44 11:00	day 45 11:00
Gait	-	-	-	1
Bradykinesia	2	2	2	2
Sialorrhea	0	3	2	2
Muscle rigidity	0	2	0	0
Tremor	0	2	2	0
Akathisia	2	1	0	1
Dystonia	0	0	0	0
Dyskinesia	1	1	1	1
Overall severity	2	3	2	2

Table 1: Drug Induced Extra-Pyramidal Symptoms Scale (DIEPSS) score.

biperiden, after which he manifested fluency, hyperactivity, and increasing frustration. However, he did not meet the Caroff and Mann criteria for diagnosis of neuroleptic malignant syndrome [10]. Because of temporary worsening of his extrapyramidal symptoms, the patient did not receive any other additional drugs on that day. He showed some improvement the following day. The course of his symptoms was evaluated using the Drug-induced Extrapyramidal Symptoms Scale (DIEPSS) [11], as shown in the Table 1. (Table 1)

On the 50th day, he was transferred to a hospice and ended the intervention.

Discussion

To the best of our knowledge, this is the first reported case of intramuscular Biperiden exacerbating drug-induced Akathisia in a patient with gastric cancer at the end of life. Delirium related to malignancy is common in patients with cancer and can cause them discomfort. Overall, 30%-40% of patients with end-stage cancer develop delirium [12], and 90% of them reportedly develop delirium just before death. Antipsychotic drugs are often used to attempt to control delirium that is difficult to control with non-drug therapy [2,3]; however, antipsychotics can cause drug-induced Akathisia [13]. Akathisia, which comprises extrapyramidal symptoms, occurs in nearly 20% of patients receiving antipsychotic drugs and antidepressants [14]. In addition to changing and withdrawing the causative drug, Propranolol, Mirtazapine, and Biperiden, an anticholinergic drug, may be administered for drug-induced Akathisia [15]. Biperiden is reportedly effective against Akathisia, even when administered intramuscularly [16]. The most important point of this case discussion is that Biperiden used to treat drug-induced Akathisia may exacerbate the Akathisia. Chlorpromazine, an antipsychotic drug used for nausea in the palliative care field [17], was used to alleviate nausea in our patient. However, this drug should be given with caution because antipsychotics, especially Phenothiazines and Butyrophenones, can cause drug-induced Akathisia. Biperiden may be used in patients who have difficulty with oral medication as a result of drug-induced Akathisia, but may cause extrapyramidal symptoms, such as asthenia, difficulty concentrating, and anxiety [18]. Therefore, in the unlikely event that this adverse effect of biperiden is observed, it is important to consider whether the deterioration in Akathisia is attributable to the Biperiden rather than blithely continuing to administer it.

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