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CASE REPORT

Adding metoclopramide to paroxetine induced extrapyramidal symptoms and hyperprolactinemia in a depressed woman: a case report

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Abstract: A 54-year-old Japanese woman was diagnosed with major depressive disorder and prescribed paroxetine 20 mg/day. In around May 2013, the patient experienced gastric discomfort, so metoclopramide was prescribed. Beginning on June 4, 2013, the patient was given metoclopramide, 10 mg intravenously, twice per week. On the seventh day after beginning metoclopramide, facial hot flushes, increased sweating, muscle rigidity, and galactorrhea were noted. Extrapyramidal symptoms (EPS) rapidly subsided in response to an intramuscular injection of biperiden. Blood biochemical tests revealed an elevated serum prolactin level of 44 ng/mL. After stopping metoclopramide, EPS disappeared. Serum prolactin level decreased to 15 ng/mL after 4 weeks. In our case, although no adverse reactions had previously occurred following the administration of metoclopramide, the patient developed EPS and hyperprolactinemia following the administration of this antiemetic in combination with paroxetine. Paroxetine and metoclopramide are mainly metabolized by CYP2D6, and they are inhibitors for CYP2D6. We report a case with EPS and hyperprolactinemia whose plasma paroxetine and metoclopramide level rapidly increased after the addition of metoclopramide. Our experience warrants the issuing of a precaution that adverse reactions may arise following the coadministration of metoclopramide and paroxetine even at their respective standard dose levels.

Keywords: metoclopramide, paroxetine, extrapyramidal symptoms, SSRI, hyperprolactinemia, depression

Introduction

Selective serotonin reuptake inhibitors (SSRIs) are the first-line antidepressants used in primary care and psychiatric practices. Paroxetine, one of the most potent SSRIs, is widely used in the treatment of depression and is a strong selective CYP2D6 inhibitor. Metoclopramide is a drug with a highly potent antiemetic effect and is considered to cause relatively few adverse reactions. In this report, the extrapyramidal symptoms and hyperprolactinemia occurred in a patient receiving a standard dose of metoclopramide concomitantly with an SSRI for the relief of gastrointestinal symptoms, which were due to the exacerbation of depression.

Case report

Written informed consent was obtained from the patient to publish this paper. A 54-year-old Japanese woman presented with depressed mood, psychomotor retardation, and loss of interest. She was diagnosed with major depressive disorder according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition (DSM-IV-TR) in 2006 and was subsequently prescribed paroxetine 20 mg/day. In around May 2013,

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the patient experienced gastric discomfort and visited the Department of Internal Medicine. Metoclopramide, a drug previously taken by the patient that had caused no adverse reactions, was prescribed, but the symptoms persisted. The depressed mood and psychomotor retardation subsequently worsened to a degree such that they interfered with daily activities. The gastric discomfort also gradually worsened; thus, beginning on June 4, 2013, the patient was given metoclopramide, 10 mg intravenously, twice per week in the outpatient emergency care unit. On the seventh day after beginning metoclopramide, facial hot flushes, increased sweating, muscle rigidity, and galactorrhea were observed. The patient's extrapyramidal symptoms were rated on the Drug-Induced Extra-Pyramidal Symptoms Scale[1] with a score of 16. The extrapyramidal symptoms rapidly subsided in response to an intramuscular injection of biperiden. Blood biochemical tests revealed an elevated serum prolactin level of 44 ng/mL. The extrapyramidal symptoms were considered to be because of the coadministration of metoclopramide and paroxetine prescribed for the relief of somatic symptoms, such as gastric discomfort arising from recurrent depression. The patient's depressive symptoms were rated on the Hamilton Rating Scale for Depression[2] with a score of 19. Metoclopramide was thus discontinued, and the dose of paroxetine was increased to 40 mg/d. Seven days later after stopping metoclopramide, the Drug-Induced Extra-Pyramidal Symptoms Scale score improved to 0. The Hamilton Rating Scale for Depression score also improved to 5, and the serum prolactin level decreased to 15 ng/mL after 4 weeks.

Discussion

Metoclopramide is a drug with a highly potent antiemetic effect and is considered to cause relatively few adverse reactions. Several reports described that metoclopramide caused extrapyramidal symptoms via its inhibitory effect on dopaminergic neurons.[3–5] In most of these papers, it was speculated that the extrapyramidal symptoms were evoked when the drug was administered in high doses. In our case, however, although no adverse reactions had previously occurred following the administration of metoclopramide, the patient developed extrapyramidal symptoms and hyperprolactinemia following the administration of this antiemetic in combination with paroxetine. Paroxetine is an SSRI that is often prescribed for the management of depression, panic disorder, and obsessive–compulsive disorder. There have been several reports indicating the occurrence of extrapyramidal symptoms due to SSRI administration.[6–8] The underlying mechanism of these symptoms is thought to be due to excessive serotonin, which exerts an inhibitory effect on nigrostriatal dopaminergic neurons.

Moreover, paroxetine and metoclopramide are mainly metabolized by cytochrome P450 (CYP) 2D6.[9] Paroxetine is a potent inhibitor for CYP2D6, and metoclopramide is a moderate inhibitor for CYP2D6. We report a case with extrapyramidal symptoms and hyperprolactinemia whose plasma paroxetine and metoclopramide level rapidly increased after the addition of metoclopramide.

In our case, the extrapyramidal symptoms and hyperprolactinemia occurred in a patient receiving a standard dose of metoclopramide concomitantly with an SSRI for the relief of gastrointestinal symptoms, which were due to the exacerbation of depression. Our experience with this patient warrants the issuing of a precaution that adverse reactions may arise following the coadministration of metoclopramide and paroxetine even at their respective standard dose levels.

Disclosure

The authors report no conflicts of interest in this work.

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