Eur J Clin Pharmacol (2005) 61: 543–544
DOI 10.1007/s00228-005-0956-z

CASE REPORT

**Ansgar Buecking · Caroline Louise Vandeleur
Yasser Khazaal · Daniele Fabio Zullino**

Mirtazapine in drug-induced excessive sweating

Received: 11 February 2005 / Accepted: 3 May 2005 / Published online: 9 July 2005
© Springer-Verlag 2005

Abstract Excessive sweating is a well-known side effect of a selective serotonin reuptake inhibitor treatment, but little is known about the impact of sweating on treatment discontinuation or the general quality of life of patients. In this case report, we present a patient suffering from excessive sweating induced by escitalopram. When mirtazapine was administered as an additional treatment, a dose-dependent reduction of drug-induced excessive sweating was observed. Taking into account the particular serotonin antagonistic properties of mirtazapine, its eventual influence on the regulation of body temperature and diaphoresis in the central nervous system is discussed.

Keywords Escitalopram · Mirtazapine · SSRI · Antidepressant · Sweating · Diaphoresis · Temperature regulation · 5-HT receptor · Serotonin

Introduction

Over the past two decades, selective serotonin reuptake inhibitors (SSRIs) have become the gold standard for the treatment of the majority of mood and anxiety disorders. Although their overall tolerability is generally satisfactory, SSRIs are also known to cause a large number of side effects, with gastro-intestinal and sexual disturbances being particularly emphasized in recent publications. Excessive sweating is another well-known side effect, which occurs in about 10% of patients receiving SSRIs [1], but little is known about the impact of sweating on treatment discontinuation or the general quality of life of patients. There are several reports from clinicians describing management of drug-induced excessive sweating in patients with the use of drugs such as benztropine [2, 3], clonidine [4], and cyproheptadine [5]. In this report, we present an observation made in the treatment of sweating with mirtazapine, which is known to have particular serotonin (5-HT) antagonistic properties.

A. Buecking (✉) · C. L. Vandeleur · Y. Khazaal · D. F. Zullino
University Department for Adult Psychiatrie, Lausanne, Switzerland
E-mail: Ansgar.Buecking@chur.ch
Tel.: +41-21-3161637
Fax: +41-21-3161626

Case report

Mr A, a 63-year-old man, has been known for an affective bipolar disorder type I since the age of 45 years. He has mainly been suffering from recurrent and persistent depressive episodes. Over the last 10 years, many different pharmacological treatments were tried by both his psychiatrist and his general practitioner, none of which was efficacious in durably stabilizing his mood. Finally, the patient was referred to our specialized outpatient clinic in order to re-evaluate his treatment. The patient reported having received the following antidepressant drugs over the past 10 years: trazodone (200 mg/day), fluoxetine (40 mg/day), moclobemide (600 mg/day), trimipramine (50 mg/day), mianserin (30 mg/day), venlafaxine (37.5 mg/day), and escitalopram (5 mg/day). He had subsequently been treated with mood stabilizers, including lithium sulfate (1,320 mg/day) and carbamazepine (400 mg/day), and he was taking valproic acid (2,000 mg/day) at the moment of his transfer to our clinic. Because of suffering from permanent and distressing anxious tension as well as chronic insomnia, he also received benzodiazepines (lorazepam 7.5 mg/day).

In addition, as he was suffering from arterial hypotension, hyperuricemia, chronic gastritis, hypercholesterolemia, coronary heart disease, and essential tremor, he was concomitantly treated with simvastatine (20 mg/day), aspirin (100 mg/day), pantoprazol (40 mg/day), allopurinol (150 mg/day), propanolol (160 mg/day), and nitroglycerine (0.8 mg occasionally).

On this medication, the patient experienced multiple drug-related side effects, including persistent gastro-

intestinal disturbances, cognitive impairment, aggravation of his tremor, and excessive sweating. These side effects, as well as the recurrent depressive episodes, resulted in a considerable reduction of his quality of life. On arrival at our clinic, the antidepressant treatment consisted of escitalopram 5 mg/day. The dose was progressively increased to 30 mg/day. After 1 month, the patient experienced a satisfactory improvement of his mood as well as of his general anxiety level and therefore wished to continue this antidepressant agent for a longer period. However, on this dose increase the pre-existing sweating worsened considerably. In both winter and summer time, he carried a towel around his neck to dry his face and reported changing his clothes two or three times per day.

Considering the serotonergic profile of escitalopram, and the 5-HT_2 and 5-HT_3 receptor blocking properties of mirtazapine [6], the latter drug was introduced at 15 mg/day, as an additional treatment, to possibly modulate 5-HT-dependent thermoregulation and sweating. About 2 weeks later, the excessive sweating was considerably reduced and the patient reported a noticeable improvement of his quality of life. The patient tolerated his new treatment combination well and, progressively, the dose of mirtazapine was increased to 60 mg/day. This dose increase resulted in a complete remission of the excessive sweating, and 10 months later the improvement persisted.

Discussion

To our knowledge, this is the first observation of mirtazapine as an effective ''antidote'' treatment for SSRI-induced sweating. A dose-dependent effect on excessive sweating was observed in the range between 15 mg/day and 60 mg/day. The mirtazapine prescription was also well tolerated in conjunction with a large number of other drugs administered simultaneously.

Little is known about the regulation of body temperature and diaphoresis in the central nervous system. However, there is evidence that activation of central 5-HT_{2A} receptors plays an important role in the elevation of body temperature [7]. As mirtazapine possesses 5-HT_2 blocking properties, the observed therapeutic effect on sweating may possibly be associated with a modulation of serotonergic thermoregulation.

We are fully aware of the many potential drug interactions that may have influenced the observed effects. For this reason, the extrapolation of a general ''antidote'' effect of mirtazapine for SSRI-induced sweating is limited and there is clearly a need for further investigation involving controlled clinical trials. However, we hope that the present case report may contribute to understanding the mechanisms underlying SSRI-induced sweating, suggesting a critical role of the 5-HT_2 receptor.

References

1. Nelson JC (1997) Safety and tolerability of the new antidepressants. J Clin Psychiatry 58(Suppl 6):26–31
2. Pierre JM, Guze BH (2000) Benztropine for venlafaxine-induced night sweats. J Clin Psychopharmacol 20(2):269
3. Garber A, Gregory RJ (1997) Benztropine in the treatment of venlafaxine-induced sweating. J Clin Psychiatry 58(4):176–177
4. Feder R (1995) Clonidine treatment of excessive sweating. J Clin Psychiatry 56(1):35
5. Ashton AK, Weinstein WL (2002) Cyproheptadine for drug-induced sweating. Am J Psychiatry 159(5):874–875
6. Stahl SM (1997) Psychopharmacology of antidepressants. Martin Dunitz Ltd., London
7. Sugimoto Y, Ohkura M, Inoue K, Yamada J (2001) Involvement of serotonergic and dopaminergic mechanisms in hyperthermia induced by a serotonin-releasing drug, p-chloroamphetamine in mice. Eur J Pharmacol 430(2–3):265–268