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CASE REPORT

Intraoperative Nasal Bleeding Complication of Treatment With the Selective Serotonin Uptake Inhibitor Sertraline

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Abstract

Selective serotonin reuptake inhibitors (SSRIs) are affecting the blood clotting system through peripheral serotonin. This may lead to an impaired blood clotting and bleeding complications. The present article describes a case of a 31 year old male patient on treatment with the SSRI sertraline, who developed postoperative bleeding complications following nasal surgery. A routine assessment of the blood clotting system yielded all parameters within standard ranges. An additional platelet function test showed decreases for platelet aggregatin and decreases for platelet disaggregation. Preceeding surgery in SSRI treated patients, testing for platelet function therefore is highly advisable to prevent severe bleeding complications. (German J Psychiatry 2005:8 (1):16-18).

Keywords: Selective serotonin reuptake inhibitors, sertraline, nasal bleeding, blood clotting system

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Introduction

Selective serotonin reuptake inhibitors (SSRIs) are frequently administered to patients suffering from depressive, compulsive and anxiety disorders. SSRIs are considered a first choice medication of these disorders for their outstanding effectiveness and the speed of onset as well as for their safety in overdose and their favourable side-effect profile. SSRIs are now among the most frequently prescribed psychotropic drugs. Prescription of SSRIs in Germany was at 150.9 million defined daily dosages in 2002. This is 25% of the prescribed antidepressive drugs in Germany (Schwabe et al., 2004).

Bleeding complications of SSRI treatment have been observed in numerous cases (Alderman et al. 1992; Calhoun et al., 1996; Cooper et al., 1998; Humphries et al, 1990; Lake et al., 2000; Ottervanger et al., 1994; Wilmshurst et al., 1996; Yaryura-Tobias et al., 1991). Several recent studies propose a beneficial effect of SSRIs for the survival of depressed patients after ischemic events (Schlienger et al., 2003). These side-effects both originate from the SSRIs influence on the blood clotting system through peripheral serotonin.

Less than 5% of the body's serotonin resides in the central nervous system. About 95% of the serotonin is peripherally stored by platelets or metabolised by the monoamine oxidase A of the liver or the by the pulmonary vascular endothelium. SSRIs block the serotonin uptake by platelets and reduce the serotonin metabolism by the pulmonary vasculature. Additionally SSRIs reduce serotonin platelet and whole blood serotonin levels, presumably by clearing the exceeding serotonin from the pulmonary and hepatic metabolisms (Skop et al., 1996).

Platelet activation is accompanied by the secretion of several chemotactic and mitogenic factors, such as platelet factor 4 (PF4), β-thromboglobuline (β-TG) and serotonin. These factors activate and recruit other platelets and cause the

irreversible platelet-to-platelet aggregation (Schlienger et al., 2003).

Celada et al. showed a decrease of platelet serotonin levels by 89% and plasma serotonin levels by 60% after a 12 weeks administration of 100-150 mg fluvoxamine per day in depressed patients (n=11) (Celada et al., 1992). Pollock et al. additionally investigated the effect of paroxetine on the platelet release products PF4 and β-TG in depressed patients during a 6 week treatment (n=10). In these patients, mean PF4 and β-TG decreased after 1 week and remained low after 3 and 6 weeks of treatment with paroxetine (Pollock et al., 2000).

However, clinically significant bleeding time prolongations may mainly develop in patients with preexisting platelet abnormalities, since reports of bleeding complications in SSRI treatment remain rare (Skop et al., 1996).

Previously published single cases of bleeding complications in SSRI treatment report varying laboratory data. Cooper et al. observed normal platelet count, prothrombin time, international normalized ratio (INR), partial thromboplastin time (PTT) and bleeding time in a case of ekchymoses after 15 days of treatment with 20 mg fluoxetine per day (Cooper et al., 1998). Wilmshurst et al., who report a case of eye haemorrhage after 1 week of treatment with 20 mg fluoxetine per day, found a normal blood count (including platelet count) (Wilmshurst et al., 1996). In another case of peripheral ecchymoses reported by Calhoun et al., a repeatedly verified prolonged bleeding time of 12.5 minutes (normal 2,5-9,5 minutes) after a 4 month treatment with 50 mg sertraline per day (Calhoun et al., 1996). In another case of ecchymoses of the legs after a 2 week treatment with 20 fluoxetine per day, Ottervanger et al. found bleeding time, platelet count, PTT, and thromboplastin time to be within the normal range. Platelet aggregation with ristocetin was normal, but platelet aggregation with addition of epinephrin was elevated (Ottervanger et al., 1994).

Case Report

The patient, a 31 year old male with a combined personality disorder and a recent depressive episode, has been admitted to our otorhinolaryngology department. The patient, showing a chronically impaired nasal respiration, was to be surgically treated by an ethmoid ectomy and a septoplasty. Before admission, the depressive episode has been successfully treated for several weeks before admission with sertraline 150 mg per day. The patient also received 1 mg finasteride per day (a 5-α-reductase inhibitor for the treatment of androgenetic allopecia) as a long term treatment.

Preceding surgery, all relevant standard laboratory parameters were determined. All collected parameters were within the reference range. Hemoglobine was at 5.2 g/dl, INR was at 0.93, PTT was at 34.1 seconds and thrombine time was at 20.4 seconds.

Following surgery the patient developed an unexpected haemorrhage within the treated nasal area. The mild but steady haemorrhage persisted for about 24 hours and was partially contained by tamponades. At about 36 hours after surgery a heavy haemorrhage redeveloped in the treated area, accompanied by hypertensive blood pressures. These heavy haemorrhages persisted for several hours and returned for at least once a day on the following days. It was attempted to stop the bleeding with the administration of antifibrinolytic tranexamic acid (4 x 500 mg on day 1 after surgery and 500 mg on day 2 after surgery). These attempts paused the bleeding for a maximum of 1-2 hours respectively. The blood pressure was at mildly elevated levels post surgery, but they never exceeded 150/100 mmHg. A treatment with 10 mg amlodipine per day was started on day 4 after surgery. Under treatment with amlodipine, blood pressure levels were normalized.

On day 2 after surgery, a complete status of the blood clotting system was determined. Again, all standard clotting parameters were within the reference range. Hemoglobine was at 12.8 g/dl, INR was at 0.93, PTT was at 34.6 and thrombine time was at 16.2 seconds. However, in this more detailed examination we found clear indicators for an impaired thrombocyte aggregation. Thrombocyte aggregation (TA) with collagen 1.0 µg/ml was at 70% (reference 70-95%), TA with arachidonic acid 1 mM was at 3% (reference 70-95%) and TA with epinephrin 8.0 µM was at 25% (reference 60-95%). Thrombocyte desaggregation (TD) with ADP 1.0 µM/l was at 85% (reference 0-50%), TD with ADP 2.0 µM/l was at 91% (reference 0-50%) and TD with ADP 5.0 µM/l was at 50% (reference 0-30%).

The haemorrhages terminated on day 5 after the surgery, partly attributed to the successful treatment of the mild hypertension with amlodipine. Hemoglobine measured the lowest at day 7 after the surgery (9.5 g/dl). On day 6 after the surgery treatment with sertraline was stopped.

Discussion

Surgical interventions in patients treated with SSRIs can result in serious hemorrhagic conditions. Even smaller routine operations can sporadicly lead to significant intra- and postoperative bleeding.

SSRIs only impair the thrombocyte aggregation, other constituents of the blood clotting are not affected. As our case demonstrates, common laboratory testing may not elicit all cases of prolonged bleeding time in patients on SSRI treatment. ITT and PTT, frequently used for screening tests, may well be within their standard ranges.

The findings for platelet function may have been influenced by the ongoing treatment with the antifibrinolytic tranexamic acid. Tranexamic acid is known to preserve platelet function, this has been explicitely shown for collagen induced platelet aggregation (Miyashita et al., 2000). Therefore, without the influence of tranexamic acid, even more severe deviations from standard platelet function might have been detected.

Patients treated with SSRIs should be tested for their thrombocyte aggregation preceding all invasive clinical procedures. For best feasibility, we recommend to test for the respective laboratories standard range of platelet function tests. It is

highly advisable to include testing for TA with epinephrin, collagen and arachidonic acid, since we found these to be impaired. Special attention should be given to patients on a co-medication of glucocorticoids, anticoagulants and acetylsalicylic acids, as these impose additional hazards for bleeding complications.

SSRIs enhance the risk of upper intestinal bleeding. Also in these cases, an impaired thrombocyte aggregation should be taken into consideration for patients on SSRI treatment. Expecially in patients with a history of upper intestinal bleedings, this risk should be accounted for before the onset of a SSRI medication (Van Walraven et al., 2001).

Preceding scheduled surgery, SSRI treatment most advisably should be ceased at least several days in advance in all psychiatrically justifiable cases. To our knowledge, there is no clear indication of how long the inhibitory effect on the thrombocyte aggregation continues after the cessation of SSRI treatment. In all other cases laboratory testing for thrombocyte aggregation may well be sufficient in the prevention of hazardous bleeding complications in patients treated with SSRIs.

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