Case Report

Non-Fatal Intoxication with a High Dose of Citalopram in a Suicidal 14-Year-Old Girl

Johannes Weigl[1], Timo Vloet[1], Karin Egberts[1], Wolfgang Briegel[2], Julia Kratz[2], Marcel Romanos[1], and Manfred Gerlach[1]

[1] University Hospital of Würzburg, Center of Mental Health, Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Würzburg, Germany
[2] Leopoldina Hospital Schweinfurt, Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Schweinfurt, Germany

Abstract: The use of selective serotonin reuptake inhibitors (SSRIs) like citalopram in the clinical treatment of depressive symptoms in children and adolescents has become increasingly common, although application is mostly off-label. The increasing number of prescriptions is not only due to their good efficacy, but also due to their good tolerability and the comparatively low risk in cases of intoxication. However, there is discussion about the cardiac safety of overdose ingestion of citalopram. Here, we report in detail on an adolescent with depressive symptoms who used 800 mg of citalopram in order to attempt suicide. In contrast to other case reports in adults, our patient showed only mild neurological symptoms and no cardiac toxicity or symptoms of a serotonin syndrome, despite a high citalopram blood concentration measured about two hours following ingestion of citalopram (633 ng/ml; therapeutic reference range for adults 50–110 ng/ml).

Keywords: Citalopram, SSRIs, antidepressants, intoxication, adverse drug reactions, suicide attempt

Nicht-tödliche Citalopram-Intoxikation bei einem 14-jährigen suizidalen Mädchen

Zusammenfassung: Die klinische Anwendung von selektiven Serotonin-Wiederaufnahme-Hemmern wie Citalopram zur antidepressiven Behandlung von Kindern und Jugendlichen ist trotz häufig fehlender Zulassung weit verbreitet. Steigende Verschreibungszahlen sind nicht nur auf die Wirksamkeit, sondern auch auf die gute Verträglichkeit und das verhältnismäßig niedrige Risiko bei Intoxikation zurückzuführen. Dennoch bestehen Bedenken bzgl. des kardialen Risikos bei Überdosierung. In diesem Fallbericht wird detailliert der klinische Verlauf einer depressiven Jugendlichen, die 800 mg Citalopram in suizidaler Absicht einnahm, beschrieben. Im Gegensatz zu einigen Fallberichten bei Erwachsenen zeigte die Patientin trotz erhöhter Blutspiegelwerte zwei Stunden nach Einnahme von Citalopram (633 ng/ml; therapeutischer Referenzbereich: 50–110 ng/ml) nur milde neurologische Symptome und keine Anzeichen einer kardiologischen Toxizität oder eines Serotonin-Syndroms.

Schlüsselwörter: Citalopram, SSRIs, Antidepressiva, Intoxikation, unerwünschte Arzneimittelwirkung, Suizidversuch

Introduction

Citalopram is an antidepressant within the group of the selective serotonin reuptake inhibitors (SSRIs). The use of SSRIs in the clinical treatment of depressive symptoms in children and adolescents has become increasingly common, although application is mostly off-label (Taurines et al., 2014). The increasing number of prescriptions is not only due to their good efficacy, but also due to their good tolerability and the comparatively low risk in cases of intoxication. However, there is a discussion about the cardiac safety of overdose ingestion of citalopram (Tarabar et al., 2008; Uchida et al., 2015). The American Food and Drug Administration (FDA) released a safety announcement about the potential risk of abnormal heart rhythm under high doses of citalopram, recommending that citalopram should no longer be used at doses higher than 40 mg per day, and should be discontinued in patients with a persistent QTc interval longer than 500 ms (FDA Drug Safety Communication, 2012). Clinical effects resulting from over-dosage can provide some important information on potential risks of a medication, which are unusual in the therapeutic range. So

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far, there is only a limited number of reports of pure citalopram intoxications in adults. To the best of our knowledge this is the first detailed report on an adolescent with depressive symptoms who used 800 mg of citalopram in order to attempt suicide.

Case Report

The 14-year-old Caucasian girl had been included in an on-going prospective, naturalistic, multicentre pharmacovigilance study ("TDM-VIGIL"), which aims at collecting epidemiological prescription data, to evaluate therapeutic effects and to monitor adverse drug reactions (ADRs) of off-label antidepressants and antipsychotics in children and adolescents. The study, in which altogether 1,000 patients shall be enrolled, is registered with *ClinicalTrials.gov* (EudraCT: 2013-004881-33). Furthermore, the study is in accordance with the Declaration of Helsinki. All citalopram serum concentration measurements were performed in the TDM laboratory of the Center of Mental Health of the University Hospital Würzburg. Informed consent was obtained from the patient and her parents to publish this case report.

No somatic diseases, developmental disorders or severe life events were reported in the medical history. The patient was treated in a child and adolescent psychiatric outpatient unit; the treatment included psychoeducation and cognitive-behavioural psychotherapy for major depression and non-suicidal self-injury, which was diagnosed by an experienced child and adolescent psychiatrist according to ICD-10. After developing suicidal ideation, inpatient treatment was initiated and continued for 18 weeks. Psychopharmacotherapy with 20 mg citalopram started eight weeks after admission to the hospital and was increased to 60 mg after 11 weeks because of insufficient benefits and low serum trough levels (body weight: 76.6 kg, body length: 173 cm; citalopram 20 mg/day: 36 ng/ml; 40 mg/day: 41 ng/ml; therapeutic reference range for adults 50–110 ng/ml, Hiemke et al., 2011). During outpatient treatment after discharge with 60 mg of citalopram, depressive symptoms were still fluctuating, but no suicidal ideation was observed. Overall, a benefit from medication was documented by the clinicians. Apart from a slight increase of QTc interval (see below), adverse drug reactions were not observed under high-dose therapy; therefore, no further serum level was measured during the application of 60 mg citalopram. The following suicidal event was thus unexpected for both therapist and mother.

One month after discharge and under continued therapy in the outpatient unit, the girl ingested a total of 800 mg citalopram (approximately thirteen times her daily dose). According to the patient, she took the drug at home with suicidal intent but did not associate this act with a specific situation or triggering event. The girl was admitted to paediatric intensive care two hours after ingestion by the emergency medical service, which had been alarmed by the girl's mother. She showed mild clinical symptoms, which included dizziness and drowsiness and received a single dose of activated charcoal for gastrointestinal decontamination. Further therapeutic interventions were not required. Vital parameters (blood pressure and heart rate) were monitored and values were in the normal range. Additional diagnostic measures included blood sampling, taken about two hours after ingestion of citalopram. The measured citalopram concentration was 633 ng/ml (corresponds to 1.95 mmol/ml), almost triple the toxic alert level of 220 ng/ml (Hiemke et al., 2011). Other blood values showed no significant changes, with the exception of a non-specific mild elevation of haemoglobin and blood glucose.

The day after intoxication, the Bazett-corrected QT interval (QTc) was 438 ms, which decreased to 405 ms the following day. Other ECG-parameters were in the standard range. Remarkably, previous ECG recordings revealed a dose-dependent increase of QTc intervals (QTc without medication: 409 ms, with 20 mg citalopram/day: 426 ms, with 40 mg/day: 443 ms, with 60 mg/day: 460 ms).

After three days of paediatric treatment, the patient was transferred to a child and adolescent psychiatry inpatient unit and was discharged three weeks later. Neither somatic symptoms nor further psychiatric emergencies occurred in this period. In addition, blood sampling and an ECG at discharge from the psychiatric unit showed no pathological findings. In particular, the QTc interval was normal (418 ms) as medication was discontinued after over-dosage. Since discharge from inpatient treatment the girl has continuously received outpatient psychiatric treatment once to twice a week. No further suicide attempt has occurred since then. The treatment with citalopram was stopped and no other psychopharmacotherapy was initiated. The girl is currently successfully attending an internship.

Discussion

Clinical data concerning the toxicity of high-dose ingestion of citalopram especially in adolescents are poor, which is why we decided to publish this well-documented case report of a 14-year-old girl who ingested a total of 800 mg citalopram to attempt suicide. The report of Jimmink and colleagues (2008) included four (out of 26) subjects aged 13 to 19 years, but no clinical details on these patients have been reported by the authors. Moreover, 87.5 % of poisoning incidents also involved ingestion of

other drugs. Citalopram overdoses often have only mild to moderate symptoms, particularly with ingestions under 600 mg in adults (Jimmink et al., 2008; Kraai and Seifert, 2015). However, with higher doses, severe manifestations have been reported, including QTc prolongation, Torsades de Pointes, seizures, and serotonin syndrome.

Although most patients recover from citalopram overdose, high-dose ingestions can produce severe effects and fatalities may occur. A mortality index of 4.2 per 10,000 exposures is stated by the U.S. National Poison Data System for citalopram in depressive patients 12 years and older (Nelson and Spyker, 2017), which is quite high compared to other SSRIs like escitalopram (0.9) or fluoxetine (0.8) but lower than in tricyclic antidepressants like amitriptyline (37.5).

In contrast to other case reports in adults, our patient showed only mild clinical symptoms, no cardiac toxicity or symptoms of a serotonin syndrome, despite a high citalopram blood concentration measured about two hours following ingestion of citalopram (633 ng/ml; therapeutic reference range for adults 50–110 ng/ml; Hiemke et al., 2011). It is likely that the patient's early admission to paediatric intensive care and the administration of activated charcoal for gastrointestinal decontamination contributed significantly to this good clinical outcome. However, the clinician must be aware of potential large ingestions of citalopram to produce life-threatening effects and monitor closely for neurologic and cardiovascular ADRs.

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Dr. Johannes Weigl
Universitätsklinikum Würzburg
Klinik für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie
Margarete-Höppel-Platz 1
97080 Würzburg
Germany

johannes.weigl@hotmail.com

