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LETTER TO THE EDITOR

Severe anticholinergic drug-induced delirium in a young adult after renal transplantation

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Anticholinergics are commonly used for detrusor hyperreflexia. Their modes of action are considered to be dependent on anticholinergic activity, central nervous system-mediated relaxation, and local anaesthetic properties [1]. Oxybutynin is a widely used substance among these drugs. Because of its biochemical properties that allow the passage through the blood–brain–barrier, oxybutynin can cause neuropsychiatric adverse effects [2,3]. Changes in mental state secondary to treatment with oxybutynin have been reported for the elderly with cognitive impairment or high comorbidity [4–7]. With regard to the frequent use of oxybutynin during the early post-transplantation phase, especially in patients without remaining diuresis during chronic haemodialysis therapy, we consider it of high interest to report our recent observations.

A 38-year-old patient who had been on haemodialysis because of glomerulonephritis received a renal allograft at our hospital. The donor's cause of death was cerebral trauma after myocardial infarction. Number of human leucocyte antigen mismatches was 1-1-2, cold ischaemia time was 15 h, warm ischaemia time was 51 min and donor and recipient both were cytomegalovirus negative. The first 9 days after transplantation passed without any complication. The patient's calculated creatinine clearance (according to the MDRD formula) was stable at about 50 ml/min/m^2. Trough values of cyclosporine A remained within the target range (200–250 μg/l).

Oxybutynin was started for severe bladder spasms directly after transplantation at a dose of 15 mg/day. The patient remained polyuric with 6–10 l urine volume per day and the medication with oxybutynin was continued.

On the 10th day post-transplantation, the patient rapidly developed auditory, visual and even tactile hallucinations and delusions of persecution. These symptoms were accompanied by fluctuating disorientation and agitation alternating with somnolence. His movements became apraxic, within 1 day he lost the ability to walk by himself. He remained in bed with his eyes shut completely; meanwhile he became agitated and needed to be physically immobilized for his own protection. When asked, he could describe himself in fantasized surroundings and involved in multiple and mostly frightening activities. Any dispensable medication like gastric ulcer prophylaxis, fungal prophylaxis and antispasmodics was stopped, except the immunosuppressive treatment with mycophenolic acid (1440 mg/day), prednisolone (20 mg/day), cyclosporine A and the antihypertensive medication (nitrendipine, furosemide). Any systemic disease, infection, cerebral bleeding and ischaemia were excluded by clinical examination, blood chemistry and a brain computed tomography. He had neither seizures nor substance abuse disorders in his medical history. Furthermore, there were no known psychiatric disorders in his family history.

According to our psychiatrist, the patient was treated with haloperidol, followed by an aggravation of the symptoms. In respect of the different forms of delirium (postoperative, drug-induced and alcohol withdrawal) haloperidol improves delirious symptoms irrespective of their cause except for anticholinergic forms of delirium, which typically stay unchanged or even worsen. Therefore, we assumed an anticholinergic delirium. Oxybutynin was the only anticholinergic drug administered. We started antagonistic treatment with fractionated i.v.-application of the anticholinesterase inhibitor physostigmine (0.5–2 mg every 30 min.). After the first application of physostigmine, the patient showed prompt decrease in muscle tonus and hyperactivity and after two nights of insomnia, he promptly fell asleep. He presented himself completely reorientated with only few short phases of hallucinations after continuous application of physostigmine for 2 days. In our patient, the symptoms continued for 3 days after discontinuation of oxybutynin – possibly because of renal insufficiency. Several days later, the patient could be discharged from hospital with stable renal function. Neither mental nor vegetative abnormalities were noticed during the following months in the outpatient clinic.

Even in young asymptomatic individuals, electroencephalographic abnormalities have been observed in a randomized, single-blind parallel-group study after application of oxybutynin [2]. The Netherlands pharmacovigilance Foundation Lareb reported on 17 cases of psychiatric disorders after oxybutynin since 1988, and the UK Committee on Safety of Medicines received 73 reports

about adverse psychiatric reactions to oxybutynin including 27 reports on confusion, hallucinations or paranoia [6]. Although the association between the use of oxybutynin and neuropsychiatric adverse effects has not been confirmed in a recent study in daily practice, this trial may not have covered patients treated as in-patients [8].

Our clinical observation provides further evidence that oxybutynin may induce severe acute psychotic disorders. If use of anticholinergics cannot be avoided, trospium chloride might be preferred as it does not pass the intact blood–brain–barrier.

Angela K. Götz,[1] Stephan W. Reinhold,[1] Alexander Szecsey,[2] Bernhard Banas[1] and Bernhard K. Krämer[3]
1 Klinik und Poliklinik für Innere Medizin II, University of Regensburg, Regensburg, Germany
2 Klinik und Poliklinik für Psychiatrie und Psychotherapie der Universität am Bezirksklinikum, Regensburg, Germany
3 Medizinische Klinik I, Marienhospital Herne, Klinikum der Ruhr-Universität Bochum, Herne, Germany

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