

Quetiapine and micturation disorders

Introduction

Quetiapine (Seroquel[®]) was granted a marketing authorisation in 1998 and is indicated for *treatment of schizophrenia and treatment of moderate to severe manic episodes*.

Quetiapine is an atypical antipsychotic agent structurally related to olanzapine and clozapine with high affinity for serotonergic type 2 (5-HT₂) receptors and moderate affinity for dopamine type 2 (D₂) receptors, whereas antagonism of D₁ and 5-HT_{1A} receptors is relatively weak. Appreciable affinity for alpha-₁ adrenergic, alpha-₂ adrenergic, and histamine H₁ receptors has also been observed [1,2] Dizziness, headache, constipation, dry mouth, somnolence, orthostatic hypotension and tachycardia are the most common ADRs.

The Netherlands Pharmacovigilance Centre Lareb has received reports of both urinary incontinence and urinary retention, ADRs that are not mentioned in the SPC.

Reports

Untill June 16th 2005 Lareb received 130 reports concerning quetiapine. In three reports (table 1, patients A-C) urinary incontinence was reported. Four patients (D-G) perceived urinary retention.

Table 1. reports of urinary incontinence and urinary retention associated with the use of quetiapine.

Patient, Sex, age	Suspect Drug, dose, Indication for use	Concomitant medication	ADR	Time to onset, outcome
A F, 39	quetiapine 2 dd. 200mg, -	lormetazepam	Urinary incontinence	4 months, recovered
B F, 40	quetiapine 3 dd. 200mg schizophrenia	omeprazole, clomipramine, lorazepam	Urinary incontinence	recovered after cessation
C M, 19	quetiapine 2 dd. 200mg psychosis	-	Urinary incontinence	4 weeks, unknown
D M, 22	quetiapine 5 dd. 100mg schizophrenia	oxazepam	Urinary retention	6 months, unknown
E M, 35	quetiapine 1dd. 300mg psychosis	temazepam	Urinary retention	3 days, recovered after cessation
F M, 39	quetiapine 1 dd. 300mg, venlafaxine major depression	-	Urinary retention	3 / 13 days, recovered after cessation of venlafaxine
G F, 29	quetiapine 2 dd. 300mg, paroxetin psychosis	-	Urinary retention	7 weeks, recovered after cessation of paroxetin

Other sources of information

Literature

A large number of papers exist describing urinary incontinence while using other atypical antipsychotics like olanzapin and clozapin [3-5]. However, no literature on urinary incontinence in quetiapine users was found in Medline.

Urinary retention while using quetiapin was described by Sokolski *et al.* [6]. This case study describes repetitive urinary retention in a 48-year old woman after dose increasements. Each time the retention resolved upon after catheterisation and dose decreasement. Also other atypical antipsychotics like risperidon and haloperidol are associated with urinary retention [7].

Databases

In the Lareb database quetiapine is disproportionally associated with both urinary incontinence (ROR: 13.3, 95% CI: 4.8-36.5) and urinary retention (ROR: 12.7, 95% CI: 4.6-34.8). Also to the database of the Uppsala Monitoring Centre of the WHO quetiapine and urinary incontinence (ROR: 2.5, 95% CI: 1.6-3.9) as well as urinary retention (ROR: 4.2, 95% CI: 2.9-6.1) are disproportionally reported.

Prescription data

Total number of prescriptions of quetiapine are shown in table 2.

Table 2. Total number of prescriptions of quetiapine per year since 2000 (Source: GIP College voor Zorgverzekeringen, Diemen).

	2000	2001	2002	2003	2004
Quetiapine	15.849	32.731	53.891	87.636	139.693

Mechanism

Quetiapine has a high affinity for adrenergic α_1 receptors. This alpha-adrenergic blockade of the sfincter of the bladder is assumed to cause urinary incontinence [8,9] while agonists result in continence and retention [5,8].

Urinary retention could be an effect of antagonism on muscarine (M_3) receptors on the Detrusor muscle. However low affinity of quetiapine for cholinergic receptors makes this a less plausible explanation.

It is postulated that the affinity for $5HT_2$ receptors in the Onuf nucleus inhibit micturation by facilitating sphincter function [8]. However, serotonergic stimulation of $5HT_4$ receptors located the m. Detrusor would facilitate micturation [10].

Discussion

Several mechanisms affecting micturation, involving different neurotransmitters, sites of action and receptor subtypes, may lead to both incontinence or retention and may play a role when using quetiapine. From the available data we have no clue to predict if retention or incontinence will prevail. In theory a case of incontinence could be caused by overfilling of the bladder.

Conclusion

Lareb received 3 cases of urinary incontinence and 4 cases of urinary retention. Both ADRs are disproportionally associated with quetiapine in both the Lareb and the WHO database, which is indicative, but not conclusive of a causal relationship. Both ADRs could potentially be explained from its pharmacological action. Urinary incontinence and urinary retention are lacking in the SPC of quetiapin.

References

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