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Quetiapine indication shift in the elderly: diagnosis and dosage in 208 psychogeriatric patients from 2000 to 2006

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SUMMARY

Rationale Quetiapine was approved in Germany as an atypical antipsychotic for treatment of schizophrenia in 2000, followed by the approval as an antipsychotic for treatment of bipolar mania in 2003. The approval of quetiapine for treatment of bipolar depression is expected. We hypothesized that the psychogeriatric prescription pattern for quetiapine shifts from the psychotic to the affective spectrum.

Methods Retrospectively we screened discharge reports of all geriatric inpatients of the psychiatric department of the Ruhr-University of Bochum in the period from January 2001 until March 2006 and identified 208 individual patients aged over 60 years, who had received quetiapine as final medication. Age, gender, daily drug dose, year of treatment and diagnosis (according to ICD-10) were recorded and analyzed.

Results Over the six-year time span, the proportion of affective disorders (F3) as indication for quetiapine in the elderly increased, whereas the proportion of dementia (F0) as indication for quetiapine decreased significantly. The proportion of schizophrenic disorders (F2) treated with quetiapine did not change significantly.

Discussion Since the decision of the German Federal Court in 2002 'off label' use goes to the expenses of the prescriber. So the decrease of quetiapine in dementia is probably due to its 'off label' status in dementia. The psychogeriatric indication shift for quetiapine towards affective disorders could be the consequence of good clinical experiences with the drug and growing evidence for its antidepressant effect.

Conclusion In addition to controlled pharmacological trials prospective clinical research is needed to evaluate the prescription attitudes of clinicians. Copyright © 2006 John Wiley & Sons, Ltd.

KEY WORDS — quetiapine; elderly; indication; shift; trend; bipolar; dementia; agitation; off label

INTRODUCTION

Quetiapine, an atypical antipsychotic belonging to the class of the dibenzothiazepines, was approved in Germany in 2000 for the treatment of schizophrenia and in 2003 for the treatment of mania (Perlis *et al*., 2006; Pini *et al*., 2006). Its approval as antidepressant is expected for 2006 due to promising study results (Calabrese *et al*., 2005; Gao *et al*., 2005). Especially in geriatrics, quetiapine is used 'off-label' for the treatment of agitation (Ballard and Waite, 2006; Volavka *et al*., 2006). Agitation refers to a range of behavioral disturbances including aggression, shouting, etc., occurring in approximately every second demented patient (Daiello *et al*., 2003; Tariot *et al*., 2004). Dopaminergic induced psychosis in Parkinson's disease (Wijnen *et al*., 2003; Ondo *et al*., 2005) and delirium (Pae *et al*., 2004; Boettger and Breitbart, 2005) are further clinically established psychogeriatric indications for quetiapine (Kim *et al*., 2003) mostly because of favorable side effect profile (Garver, 2000; Masand, 2000) with only very rare and non dose-dependent extrapyramidal motor disturbances (Jeste, 2004; Mintzer *et al*., 2004). Apparently quetiapine appears not to affect the endocrinologic system (Arvanitis and Miller, 1997; Emsley *et al*., 2000), as serumprolactine levels remain unchanged over the entire therapeutic dose range (De Borja Goncalves *et al*., 2005). Quetiapine is not

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associated with an increased risk for diabetes mellitus type II (Ostbye *et al*., 2005; Sacchetti *et al*., 2005), although single cases of possibly quetiapine induced diabetes are published (Koller *et al*., 2004; Lambert *et al*., 2006). Moderate weight increase can occur (Gurevitz *et al*., 2004; Brixner *et al*., 2006). Alterations in ECG or EEG are quite uncommon (Amann *et al*., 2003; Stollberger *et al*., 2005) and there is no sufficient evidence for an increased cardiovascular risk compared to other antipsychotics (Finkel *et al*., 2005). Rare side effects, observed in single cases, e.g. restless legs, pancytopenia and priapism (Iraqi, 2003; Pinninti *et al*., 2005; Andres and Vidal, 2006) are of no major clinical importance. Not so the case for the five most frequent adverse events registrated in the course of quetiapine treatment: headache (19%), sedation (18%), dizziness (10%), obstipation (9%) and orthostatic dysregulation (7%). From a clinical point of view, three out of these five problems—sedation, dizziness and orthostatic dysregulation—can become threatening for fragile psychogeriatric patients, especially in vicious combination, as falls resulting in fractures can occur.

The main focus of this study is the following: is the indication for quetiapine shifting towards affective disorders in psychogeriatrics?

METHODS

A total of 8.750 discharge reports on inpatient treatments were screened for quetiapine as final (recommended) medication in the time span from 1 January 2001 to 31 March 2006. Daily drug dose (DDD), age, gender and main diagnosis according to ICD-10 were recorded. Patients aged 60 or younger were excluded, as well as rehospitalizations. Thus 208 individual psychogeriatric patients were identified, all of them having been discharged on quetiapine. For the longitudinal evalution we formed year groups: five years (2001–2005) and one quarter (2006). With the data we performed consistency checks, trend analyses and correlation analyses.

RESULTS

From the 208 patients 125 were female, 83 male (60.1 *vs* 39.9%). The average age was 76.2 years, ranging from 61–96 years (SD = 7.93). In half of the patients the main diagnosis was one of the F0-category, a F2- or F3-diagnosis was registered in 26.9 and 23.1% respectively (see Table 1 for an explanation of F-categories).

Table 1. Daily drug dose for quetiapine in the three different indications (dementia, psychosis and depression) and for the whole sample. In addition the number of patients and their mean age is shown for each group and for the whole sample

Quetiapine in the elderly							
Indication (as ICD-10-diagnosis), DDD & age							
ICD10	DDD	SD	Min	Max	***n***	%	Age
F0	292.8	158.7	12.5	800	104	50.0	79.6
F2	408.3	272.1	100	1200	56	26.9	73.0
F3	235.1	142.0	50	600	48	23.1	72.5
Total	*264.4*	*220.2*	*12.5*	*1200*	*208*	*100*	*76.2*

age = mean age of the patients' sample; DDD = daily drug dose (mean, in mg); F0 = organic disorders; F2 = schizophrenia spectrum disorders; F3 = affective disorders; max = maximum dose of DDD; min = minimum dose of DDD; *n* = number of patients; SD = stan-standard deviation of DDD; % = percentage of patients.

The trend analysis revealed a significant decrease for F0- ($r^2 = 0.3911$), a significant increase for F3- ($r^2 = 0.7348$) and a steady state for F2-diagnoses ($r^2 = 0.0074$). To illustrate this finding, the proportion of each of the three diagnoses in each year group as well as the trend lines derived from a regression model are represented in Figure 1.

DISCUSSION

In Old Age Psychiatry quetiapine is indicated more often in affective and less often in dementing disorders. As an university department our patients' sample may probably not be representative, nor may our clinical strategies be generalized easily. Overmore, the small sample sizes for the year groups result in a loss of statistical power due to the longitudinal evaluation.

Dementing disorders

Although there is some evidence showing a good clinical effect of quetiapine in dementia (e.g. Fujikawa *et al*., 2004), there is slight, but in our study significant, tendency for the use of quetiapine moving away from dementia. This tendency could be due to a more defensive and conservative prescription strategy, as the legal and economic situation in Germany has made things more difficult these last years. 'Off-label use' goes to the expenses of the prescriber since the decision of the German Federal Social Court in 2002 concerning this matter. Thus it may be true that the decrease of quetiapine use in dementia is due to its 'off label' status in this diagnosis. Another possible

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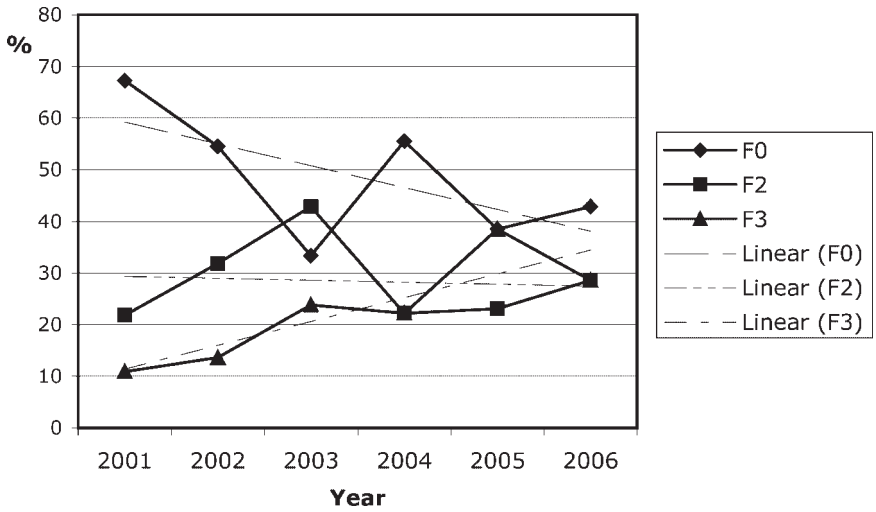

Figure 1. Quetiapine indication shift away from dementia and towards depression over the years 2001 to 2006. The indication (F0, F2 or F3) is shown proportionally for each year, the trend line deriving from a linear regression model. F0 = organic disorders; F2 = schizophrenia spectrum disorders; F3 = affective disorders.

explanation for the declining prescription figures in dementia is the side effect profile, as especially orthostatic problems and sedation sometimes limit the use of the drug in this multimorbide age group (Schneider *et al*., 2006). Unfortunately, official quetiapine dose recommendations for elderly patients are still not given, although some work has already been performed (e.g. Jaskiw *et al*., 2004; Kohnlein *et al*., 2004).

Affective disorders

The psychogeriatric indication for quetiapine is shifting towards affective disorders. This could be the consequence of good clinical experiences with the drug and the growing evidence for its antidepressant (Pae *et al*., 2005; Dando and Keating, 2006) and mood stabilizing (Vieta *et al*., 2005) effect which in some cases maybe superior to an antidepressant (Galynker *et al*., 2005). As the indication 'depression' is also 'off-label', we re-analyzed the diagnostic categories in more detail and found that only six out of 48 patients of the depressive subgroup showed psychotic features (coded by the figure '3' in the fourth place of the five places given by the ICD-10). So for just 12.5% of our depressive sample the indication could well have been the accessory psychotic experiences, instead of the affective disorder as diagnostic entity. Indication and diagnosis are not necessarily identical. Therefore prospective studies in clinical routine setting would be of great value.

CONCLUSIONS

An indication shift for the psychogeriatric use of the atypical antipsychotic agent quetiapine is described for the years from 2001 to 2006. It can briefly be described as moving away from dementia and towards depression. Interestingly enough, the trend towards affective disorders in clinical practice parallels a scientific debate triggered by promising findings concerning antimanic, antidepressant and mood-stabilizing effects of quetiapine and other atypical antipsychotics. Prospective clinical research is needed to evaluate the prescription attitudes of clinicians.

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