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Shift from first generation antipsychotics to olanzapine may improve health-related quality of life of stable but residually symptomatic schizophrenic outpatients: A prospective, randomized study

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Objectives: The aim of this study was to elucidate, whether shift from first generation antipsychotics (FGA) to olanzapine can affect health-related quality of life (HRQoL) of residually symptomatic schizophrenic outpatients.
Methods: Patients were randomized to either olanzapine or to continuation on their FGA. The 15D-measured HRQoL at baseline and end-point (after 12 weeks) was compared.
Results: Patients ($n = 21$) randomized to olanzapine achieved better HRQoL than those ($n = 21$) who continued on their FGA. This difference on the 15D (0.048 on a 0–1 scale; $p = .037$) was clinically important and comparable to that resulting from common surgical interventions, for example, hip or knee replacement.
Conclusions: HRQoL of stable outpatients with residual symptoms or adverse effects may improve substantially after shift from FGAs to olanzapine.

Keywords: Schizophrenia, Olanzapine, Atypical antipsychotics, Conventional antipsychotics, 15D

Second generation antipsychotics (SGAs) have become a standard of care in severe psychotic disorders despite inconsistent evidence on their advantages over first generation antipsychotics (FGAs). It has been maintained that SGAs are at least as efficacious as FGAs in alleviating positive and negative symptoms of illness, but offer improved neurocognitive functioning and adverse effect profile and tolerability. This would suggest better health-related quality of life (HRQoL)—the most important outcome from the patient's point of view. However, while in some studies SGAs have resulted in improved HRQoL as compared to FGAs, in some other studies they failed to do so.

Despite reported ability of stable patients with severe psychiatric conditions to reliably self-rate their HRQoL, these patients' subjective perspective, probably the key

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aspect of the HRQoL, has been neglected until recently. Furthermore, only few studies (with inconclusive results) have reported the use of subjective, generic measures of HRQoL like Short Form 36 Health Survey (SF-36), Sickness Impact Profile (SIP), or 15D. These instruments, in contrast to the disease-specific ones, permit also comparisons of different medical interventions across different mental and somatic disorders.

On SF-36, outpatients on olanzapine achieved greater change on Mental Component Summary Scores than those on haloperidol (3), but in first-episode patients these two drugs were equal (9). Also regarding other SGAs versus FGAs, the results have been conflicting. On SIP, higher scores on SGAs versus FGAs were reported by some authors (10). So far, no SGAs versus FGAs studies with 15D have been published. The positioning of the SGAs-related benefits against those for different medical or surgical interventions has usually not been discussed.

This secondary report from our 12 week randomized, controlled, open parallel group study (1) set out to test, whether olanzapine will improve the HRQoL of clinically stable but symptomatic outpatients treated previously with FGAs. We also compared the HRQoL of the patients at baseline with that of age-standardized general population.

SUBJECTS AND METHODS

The inclusion and exclusion criteria, as well as descriptive data of the patients and study design have been reported earlier (1). In brief, FGA-treated stable outpatients with schizophrenia or schizo-affective disorder suffering from residual symptoms or adverse effects, after a complete description of the study gave written informed consent and were randomized to either continue their previous medications or to shift to olanzapine. HRQoL was measured at baseline and at follow-up (12 weeks) by the 15D, a generic, 15-dimensional, standardized, self-administered instrument that can be used both as profile and single index (utility) measure (8). HRQoL data were analyzed for all participants whose baseline and follow-up 15D data were available.

Independent samples *t*-test was used to compare the study subjects' HRQoL with that of age-standardized general population as well as the patient groups at baseline and follow-up. To account for possible differences between the groups in relevant variables at baseline, be the differences statistically significant or not when analyzed individually, the effect of medication on HRQoL at week 12 was estimated with linear regression analysis. The dependent variable was the 15D score at 12 weeks and the explanatory variables were age, gender, body mass index (BMI), time since diagnosis, Positive and Negative Symptom Scale (PANSS), Barnes (akathisia), Clinical Global Impression, severity (CGIs), and the 15D score, all at baseline values, and finally the medication (FGA or olanzapine) used. Pearson correlation was calculated between longitudinal changes in HRQoL and those in relevant clinical parameters. A $p \leq .05$ was considered statistically significant.

Table 1. Regression Analysis for Explaining the Variance in the 15D Score at Week 12 in Patients with Schizophrenia or Schizo-affective Disorder after Continuation of Their FGA Medication ($n = 21$) or Shift to Olanzapine ($n = 21$)

Variable	Coefficient (SE)	*t*	Significance (*p*)
Constant	.17952 (.168)	1,067	.295
1. Sex (0 = female, 1 = male)	.04139 (.022)	1.873	.071
2. Age, years	−.00324 (.002)	−1.528	.137
3. Time from diagnosis (months)	.00024 (.000)	1.886	.069
4. CGIs	.01698 (.014)	1.232	.228
5. PANSS positive	−.00262 (.002)	−1.175	.250
6. PANSS negative	−.00141 (.002)	−.570	.573
7. PANSS general	.00079 (.002)	.441	.663
8. Barnes (akathisia)	.00370 (.003)	1.112	.275
9. BMI	.00207 (.002)	1.037	.308
10. 15D score	.73450 (.092)	7.970	.000
11. Study medication (FGA = 0, olanzapine = 1)	.04807 (.022)	2.184	.037

Note. Variables 2–10 at baseline.

RESULTS

15D data were available for twenty-one patients in olanzapine and twenty-one patients in FGA groups. The number of dropouts did not differ (four in each group, none due to side effects).

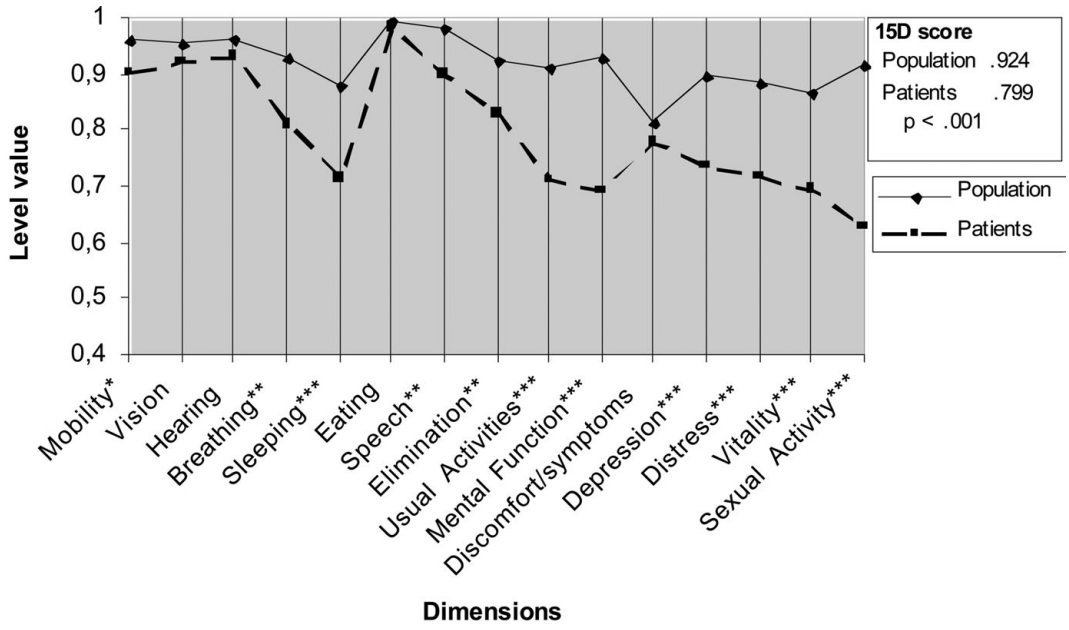
The patients scored at baseline lower than age-controlled general population on a majority of the 15D dimensions and the 15D utility score (see Figure 1).

Despite the randomization, there was a statistically significant difference at baseline between the groups in the 15D utility score (but not in other parameters, data not shown). After standardizing for the baseline 15D score and other covariates, the 15D score in the olanzapine group at 12 weeks was 0.048 units higher (on a 0–1 scale) than that in the FGA group ($p = .037$) (see Table 1).

Prospective changes in the 15D score did not correlate with those in the PANSS, Barnes or CGIs (data not shown).

DISCUSSION

In our FGA-treated outpatients with suboptimal treatment outcome and HRQoL lower than that of general population, shift to olanzapine improved HRQoL, while continuation on the pre-existing FGAs did not. The achieved mean utility score difference of 0.048 (on a 0–1 scale) on olanzapine versus FGA was also clinically important, because the



- p < 0.05; ** p < 0.01; ***p < 0.001
- Patients at baseline, n=42, vs. age-standardised general population, n=2622

Figure 1. The 15D profiles and scores of general population and residually symptomatic FGA-treated outpatients with schizophrenia or schizo-affective disorder.

minimum clinically important difference in the 15D score is ±0.03 (7).

The olanzapine-related improvement in HRQoL was smaller than that reported for coronary artery bypass or balloon angioplasty (score change 0.11 and 0.10, respectively), but comparable to primary hip replacement (0.05) or cervical or lumbar neurosurgery (0.04 and 0.06), and larger than knee replacement (0.03) or secondary hip replacement or cataract surgery (0.01 each) (2;4–6).

Of interest, the changes in the 15D score in the olanzapine group did not correlate with changes in psychopathology or neurological adverse effects measures. This might point to an independent beneficial effect of olanzapine on the HRQoL, with mediators still to be established. It is also possible that these variables measure different concepts.

CONCLUSION

HRQoL of stable outpatients with residual symptoms or adverse effects may improve substantially after shift from FGAs to olanzapine.

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