PSYCHOPHARMACOTHERAPY

4.4. Quality of life in the long-term treatment and the role of second-generation antipsychotics

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Key words: schizophrenia; bipolar disorder; treatment outcome; quality of life; second-generation antipsychotics

Summary

Health-related quality of life (QoL) represents important measure of treatment outcome in mental disorders. Numerous studies indicate that QoL of people with schizophrenia and bipolar disorder is similar to that of patients with chronic physical conditions. It has been shown that schizophrenia patients can themselves reliably assess their QoL; in addition to the objective scales various self-reporting instruments are used. Patients with bipolar disorder have QoL consistently higher than patients with schizophrenia and similar to that found in people with unipolar depression. Quality of life can be negatively affected by drug-induced side-effects and subjective treatment response. The second-generation antipsychotics (SGA) have superior efficacy on QoL over classical antipsychotics in approximately half of the studies with schizophrenia; in the other half those groups are comparable. However, in none of the trials novel antipsychotics were inferior. All SGA (clozapine, olanzapine, risperidone, amisulpride, quetiapine, ziprasidone, or remoxipride) have been found to be beneficial for patients well-being. The

most investigated drugs that convincingly improve QoL in schizophrenia are olanzapine and risperidone (including depot form). Results of several studies indicate that individual antipsychotics may differ in their effects on QoL, with suggested superiority of olanzapine. In bipolar disorder, SGA consistently showed their superiority over placebo in effects on QoL. The most studied SGA in bipolar disorder is olanzapine. More long-term controlled double-blind trials are needed to definitively uphold superiority and different effects of individual SGA on QoL of patients with schizophrenia and bipolar disorder.

4.4.1. Quality of life in people mental disorders

Success or failure of treatment of mental illness can not be assessed just by the simple symptom reduction. With the progress of pharmacotherapy of severe mental disorders, increased attention has been paid to the various aspects of long-term treatment. Psychiatric rating scales measuring symptom severity do not reflect improvement or worsening of the patients functional status, subjective satisfaction or well-being. Thus, more valid measures of real-life outcome and treatment efficacy criteria are needed. Recent research and clinical evaluation is focused predominantly on quality of life of patients with mental disorders (Katschnig et al, 2005).

The term 'quality of life' itself is a rather complex concept comprising broad spectrum of health issues, including symptoms of illness, functional outcome (self-care, mobility, physical activity), capacity to play active roles at home and at work, social skills in interpersonal relationships, ability to have intimate relationships and integrate to the community, emotional state (anxiety, stress, depression, loss of self-control, spiritual well-being), cognition, sleep and rest, energy, vitality, perception of health condition and general sense of life satisfaction (Bergner 1989). Quality of Life has been defined by the World Health Organization as an individuals perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept incorporating in a complex way the persons physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of the environment (WHO, 1993). More specific concept 'health-related quality of life' refers to the aspects of quality of life that can be directly attributed to illness and its consequent therapy (Nam-

joshi and Buesching, 2001). Another narrower concept is more economically derived cost-utility model of quality of life.

Impact of illness on quality of life, was first investigated in people with various physical impairments and disorders and only recently, since 1980's, mental disorders have become the focus of research and clinical evaluation (Lehman et al, 1982; Lehman, 1983). When assessing the quality of life in people with mental disorders, several domains have to be considered: subjective well-being and satisfaction, objective functioning in social roles, environmental circumstances (Katschnig et al, 2005). Besides subjective well-being, no less important is an ability to adapt to routine demands of everyday life, take care of oneself, to play social roles and availability of material resources and social support. Moreover, other important factors associated with chronic severe mental disorders affect life of mentally ill, such as stigmatization, social isolation, lack of financial support, safety issues (Lehman et al, 1982).

For the measurements, various self-reporting instruments, questionnaires, or structured interviews and objective scales are used. The advantage of using generic instruments is a possible comparison across interventions in various conditions, the drawback may be their lack of sensitivity. On the other hand, illness-specific instruments are more sensitive but they are limited to the relevant dimensions of disorders they were developed for (Namjoshi and Buesching, 2001). Most frequently used tools in psychiatric research for evaluation of treatment efficacy and outcome are Quality of Life Scale (Heinrichs et al, 1984), Short Form 36 Health Survey (Ware et al, 1992), WHO Quality of Life Instrument – WHOQOL-100 and WHOQOL-BREF (WHOQOL Group, 1998), Manchester Short Assessment of Quality of Life (Priebe at al, 1999) and many others.

4.4.2. Quality of life in schizophrenia and bipolar disorder

Health-related quality of life is being investigated in almost every neuropsychiatric disorders, (Katschnig et al, 2005), but the special attention has been dedicated to schizophrenia and more recently bipolar disorder, as well.

Numerous studies have been published on quality of life in schizophrenia. It reflects burden of illness on life satisfaction, difficulties and events, social adjustments, standard of living and especially serves as a measure of outcome (Bobes and García-Portilla, 2005). From the perspective of quality of

life, schizophrenia both shares some of the clinical characteristics of physical chronic illnesses, e.g. chronicity, palliative rather than curative treatments, social stigma, subjective nature of illness and at the same time has some specific characteristics, such as distressing inner experience, side effects of antipsychotics (Gee et al, 2005). Although most of the authors agree that quality of life and psychotic symptoms are two independent domains, severity or persistence of positive, negative, affective, or cognitive symptoms may significantly contribute to the subjectively perceived well-being.

Perception of life satisfaction in schizophrenia patients is predominantly impaired by the restrictions in their social life and relationships, financial constraints, reduced control of behavior, loss of opportunity to meet professional role, labeling and attitudes from others, psychological responses to living with schizophrenia, side effects and attitudes to medication (Lehman, 1983; Gee et al, 2005). Somewhat surprisingly, satisfaction with other areas, e.g. leisure and occupational activities may not be different from general healthy population. Although this fact could suggest that patients with schizophrenia overestimate their real life situation, most of the studies evidence that stabilized schizophrenia patients themselves are able very reliably assess their quality of life. In the evaluation of their condition they can reach good agreement with caregivers (assessment by proxy).

Summarizing the results of the schizophrenia research, there is conclusive evidence that compared to the healthy population the quality of life of people suffering from schizophrenia is impaired from both objective and subjective prospective. Reduced quality of life is not associated only with the chronic course of illness, it can be detected already in first-episode patients with schizophrenia (Browne et al, 2000).

Until recently, much less data were available on quality of life in bipolar disorder. This was usually explained by the absence of illness-specific measures for bipolar patients and the reluctance of the patients to complete self-reported measures, particularly when in manic phase. Nevertheless, three recent reviews summarized published findings on health-related quality of life in bipolar patients (Namjoshi and Bueschnig, 2001; Dean et al, 2004; Michalak et al, 2005). The authors concluded that patients with bipolar disorder have a lower quality of life than general population to the degree that is comparable to that of people with other chronic non-mental medical conditions. Studies comparing quality of life across mental illnesses found that patients with bipolar disorder have quality of life consistently higher than patients with schizo-

phrenia and similar to that found in people with unipolar depression. Not surprisingly, euthymic bipolar patients had higher scores than patients with mania and mixed or depressed patients. It appears that depressive symptoms are the primary determinant of quality of life in bipolar disorder. Some studies suggested a gender difference, with females reporting lower scores in all dimensions of quality of life, except for mental health. Results of the research on the impact of psychotic symptoms in bipolar disorder are still equivocal. Overview of the studies in bipolar disorder concluded that quality of life in bipolar patients is markedly impaired (Namjoshi and Bueschnig, 2001; Dean et al, 2004; Michalak et al, 2005).

4.4.3. Impact of drug-induced side effects on quality of life

One of the factors that significantly influence quality of life in people with severe chronic mental disorders is long-term pharmacotherapy. Drugs can affect well-being both directly, through reduction of symptoms (positive, negative, affective, cognitive) and indirectly, due to the side effects that may pose more severe burden than illness itself.

Negative impact of side effects on quality of life was confirmed by a naturalistic study of 161 patients with schizophrenia stabilized on conventional or novel antipsychotics (Ritsner et al, 2002). Although quality of life between the two groups did not differ, patients with side effects reported less satisfaction in domains of subjective feelings and general activities. Similar findings, strong association between side effects and less overall satisfaction with patients lives, have been reported by other authors, as well (Hofer et al, 2004; Strejilevich et al, 2005). Since the introduction of antipsychotic drugs into treatment of schizophrenia patients complained feeling 'fuzzy or dull', of being 'unable to think straight', feeling 'like a zombie' (Awad and Vorungati, 2004). Vorungati and Awad labeled these feelings as a syndrome of 'neuroleptic dysphoria' (2004). A study investigating subjective perception of side effects of drug therapy found that patients do not distinguish side effects from symptoms of illness, they just classify drugs as 'good' or 'bad' (Carrick et al, 2004), or alternatively they believe that medication makes their condition worse (Awad and Vorungati, 2004). Interestingly, a recent investigation of a sample of stable schizophrenia patients during 52-week relapse prevention trial found that withdrawal from antipsychotic drug did not improve patients quality of life (Beasley et al, 2006). Patients who were taken off their medication and who were 'nonrelapsing', without exacerbation, did not expe-

rience greater improvement in their quality of life than patients continuing with olanzapine treatment.

Similarly to the quality of life assessment, subjective response to treatment and impact of drugs on patients well-being is measured by various instruments; e.g., Drug Attitude Inventory (Hogan et al, 1983), Subjective Well-being Under Neuroleptics (Naber, 1995). The subjective acceptance of medication is becoming increasingly important outcome measure of tolerability in trials of new drugs, naturalistic observational studies and switch studies.

4.4.4. Effect of second-generation antipsychotics on quality of life in schizophrenia

Since their introduction, long-term treatment with second-generation antipsychotics (SGA) has been associated with great expectations. SGA are characterized by a more favorable profile of side effects and, in general, are better tolerated. Thus, the assumption was that they would be also superior in effects on quality of life. Nevertheless, the results of studies investigating their impact in schizophrenia have been so far equivocal in supporting this presumption (Table 1). Their better efficacy was shown in approximately half of the published papers; in the rest SGA were comparable to the conventional antipsychotics (Corrigan et al, 2003). The variety of findings can be partially attributed to the differences in study design and methodology; the studies are frequently retrospective, cross-sectional, or open non-controlled trials, with short-term follow-up, using heterogeneous instruments (scales) to assess quality of life. For example, no difference was found between typical and atypical antipsychotics in improvement of quality of life in two large double-blind randomized controlled trials comparing olanzapine and haloperidol in 309 patients treated for 12 months (Rosenheck et al, 2003), risperidone and flupenthixol in 144 patients over period of 25 weeks (Hertling et al, 2003); or in a prospective comparison of 307 patients treated with conventional and novel antipsychotics for 2.5 years (Kilian et al, 2004). No statistically significant difference between olanzapine and haloperidol in improvement of quality of life was also observed among 195 first-episode schizophrenia patients in a 1-year follow-up (Strakowski et al, 2005). Similarly, interim analysis of the largest prospective observational study SOHO (The European Schizophrenia Outpatient Health Outcomes) at six months indicated that quality of life in patients in all treatment groups (olanzapine, risperidone, quetiapine, amisulpride, clozapine, oral conventional, and depot conventional antipsychot-

Table 4.4.1. Comparison of effects of conventional (CA) and second-generation (SGA) antipsychotics on quality of life in schizophrenia.

Study	N	Medication	Results
Naber 1995	66	Clozapine Coventional AP	CLO > CA
Essock et al, 1996	227	Clozapine Chlorpromazine	CLO = CLP
Rosenheck et al, 1997	178	Clozapine Haloperidol	CLO > HAL
Franz et al, 1997	64	Second-generation AP Conventional AP	SGA > CA
Hamilton et al, 1998	335	Olanzapine Haloperidol, placebo	OLZ > HAL, PL
Revicki et al, 1999	828	Olanzapine Haloperidol	OLZ > HAL
Tunis et al, 1999	1155	Olanzapine Haloperidol	OLZ > HAL
Colonna et al, 2000	488	Amisulpride Haloperidol	AMI > HAL
Carriére et al, 2000	199	Amisulpride Haloperidol	AMI > HAL
Hamilton et al, 2000	778	Olanzapine Haloperidol	OLZ > HAL
Voruganti et al, 2000	230	CLO, OLZ, RIS, QUE Conventional AP	CLO=OLZ=RIS=QUE>CA
Stallard a Joyce, 2001	40	Olanzapine Conventional AP	OLZ = CA
Ritsner et al, 2002	161	Second-generation AP Conventional AP	SGA = CA
Nasrallah et al, 2004	369	Risperidone Depot Placebo	RIS > PL
Kilian et al, 2004	307	Second-generation AP Conventional AP	SGA = CA
Ritsner et al, 2004	133	Olanzapine, risperidone Conventional AP	OLZ = RIS > CA
Rosenheck et al, 2003	309	Olanzapine Haloperidol	OLZ = HAL
Hertling et al, 2003	144	Risperidone Flupenthixol	RIS = FLU
Strakowski et al, 2005	195	Olanzapine Haloperidol	OLZ = HAL
De Lima et al, 2005	197	Olanzapine Conventional AP	OLZ > CA
Haro et al, 2005	9028	OLZ, RIS, QUE, AMI, CLO oral conventional depot conventional	OLZ=RIS=QUE=AMI=CLO=CA

AMI = amisulpride
CA = conventional antipsychotics
CLO = clozapine
CLP = chlorpromazine
FLU = flupenthixol
HAL = haloperidol
OLZ = olanzapine
PL = placebo
RIS = risperidone
SGA = second-generation antipsychotics
QUE = quetiapine

ics) improved into the same degree (Haro et al, 2005). This naturalistic trial used as an assessment tool a patient self-rated generic health-related instrument EuroQol-5 Dimensions; multivariate analysis showed some differences among the cohorts in Visual Analogue Scale of the EuroQol-5. Greater clinical improvement in symptom domains (CGI overall symptoms, positive, negative, cognitive, and depressive) in patients with olanzapine and clozapine was associated with quality of life improvement.

On the other hand, scrutinizing results of the long-term schizophrenia trials, it should be emphasized that in quality of life measurements none of the studies reported that SGA were less effective than classical neuroleptics. Essentially all tested drugs of this class (clozapine, olanzapine, risperidone, amisulpride, quetiapine, ziprasidone, or remoxipride) have been found to be beneficial for patients well-being. The most data available come from olanzapine and risperidone trials. Positive effects of olanzapine on quality of life in schizophrenia patients, superior to haloperidol, were initially reported in add-on analyses of the first double-blind studies (Hamilton et al, 1998; Revicki et al, 1999; Tunis et al, 1999). Advantage of olanzapine in improvement of quality of live over conventional antipsychotics was also observed in a recent naturalistic controlled study with 197 patients (de Lima et al, 2005). Risperidone improved quality of life in two open studies after 8-month treatment in 318 patients (Bobes et al, 1998) and after one year in a sample of 684 patients (Mahmoud et al, 2004). Also, a depot form of long-acting injectable risperidone showed positive effects on patient's quality of life, as evidenced by a double-blind, placebo-controlled 12-week study (Nasrallah et al, 2004) using the Short Form 36 Health Survey (SF-36), an open one-year follow-up of 615 patients (Fleishhacker et al, 2005), or a study of patients switched from previous olanzapine treatment (Gastpar et al, 2005). Cross-sectional comparison of impact of SGA on quality of life among 230 patients following 6 months of treatment confirmed superiority of clozapine, quetiapine, risperidone, and olanzapine over conventional antipsychotics in subjective self-evaluation of quality of life (measured by the inventory Sickness Impact Profile); no statistically significant difference among the drugs was found (Voruganti et al, 2000). In this study, olanzapine, risperidone a quetiapine were also better tolerated, had less side effects, positive subjective treatment responses, favorable attitudes towards therapy and lower prevalence of neuroleptic dysphoria.

In the direct head-to-head comparisons, olanzapine and risperidone were equally effective in quality of life enhancement after 6 months of treatment in a sample of 182 first-episode patients measured by the EuroQol scale (Montes

Table 4.4.2. Change in quality of life in schizophrenia after the switch to the second-generation antipsychotics (open trials)

Study	N	Medication	Duration	Results
Meltzer et al, 1990	38	Clozapine	6 months	+
Bobes et al, 1998	318	Risperidone	8 months	+
Cook et al, 2002	43	SGA	2 years	+
Vorungati et al, 2002	150	SGA (RIS, OLZ, QUE)	2-6 years	+
Mehnert et al, 2003	725	Risperidone Depot	1 year	+
Mahmoud et al, 2004	684	Risperidone	1 year	+
Zhang et al, 2004	25	SGA	3 years	+

+ ..... marks improvement

Table 4.4.3. Direct comparison of the second-generation antipsychotics in quality of life in schizophrenia.

Study	N	Medication	Results
Tran et al, 1997	339	Olanzapine Risperidone	OLZ = RIS *(OLZ > RIS in 1 subscale)*
Grainger et al, 1998	339	Olanzapine Risperidone	OLZ > RIS *(in 1 subscore QLS, n.s. total score)*
Ho et al, 1999	42	Olanzapine Risperidone	OLZ = RIS
Gureje et al, 2003	65	Olanzapine Risperidone	OLZ > RIS *(in several subscores and items)*
Namjoshi et al, 2003	548	Olanzapine Ziprasidone	OLZ > ZIP *(in 1 subscore QLS, n.s. total score)*
Montes et al, 2003	182	Olanzapine Risperidone	OLZ = RIS
Naber et al, 2005	114	Olanzapine Clozapine	OLZ = CLO

CLO = clozapine
OLZ = olanzapine
ZIP = ziprasidone

et al, 2003), in a cross-sectional study of 133 patients where both drugs were also superior to the conventional antipsychotics according to the self-report and observer-rated measures (Ritsner et al, 2004), or in a cross-sectional survey (McGrath and Tempier, 2005). Nonetheless, results of two double-blind prospective randomized trials comparing both drugs suggest that olanzapine may improve quality of life in some measures better than risperidone. In the first study (Gureje et al, 2003) of 65 patients olanzapine after 30 weeks of treat-

ment improved total score and 3 out of 4 subscores of the Quality of Life Scale (QLS) and 7 of 9 items of the SF-36, while the risperidone-treated patients did not improve in any of the QLS scores, just in one item of SF-36. Moreover, in a between group comparison, olanzapine was significantly superior to risperidone in one subscale of the QLS ('intra-psychic foundation') and one of the SF-36 ('emotional role-functioning limitation'). The second double-blind controlled study comprising study sample of 339 patients treated for 28 weeks (Grainger et al, 1998) showed superiority of olanzapine in one QLS subscore ('interpersonal relations') and nonsignificant trend favoring olanzapine in the total QLS score. Another direct comparison with a different SGA, ziprasidone, in a 28-week double-blind study of 548 patients, olanzapine was significantly more effective in improvement of 2 subscores of QLS and 3 items of SF-36 according to the last observation carried forward analysis (Namjoshi et al, 2003; Breier et al, 2005).

The longest studies that confirmed positive effects of new antipsychotics on quality of life were 3-year retrospective evaluation of a small sample of 25 patients switched to SGA (Zhang et al, 2004) and a long-term (2-6 years) follow-up of 150 patients who had been also switched from conventional antipsychotics to SGA – risperidone, olanzapine, or quetiapine (Vorungati et al, 2002). The investigation by Vorungati and collaborators showed beneficial effects of the switch in both self-reported quality of life inventories (FACES quality of life assessment and Saint Louis Symptom Scale). In the later study by Vorungati et al all three novel medications (olanzapine, quetiapine, risperidone) were better tolerated, improved drug adherence, psychosocial functioning and last but not least, quality of life measured by the QLS, Global Assessment of Functioning and Sickness Impact Profile.

4.4.5. Effect of second-generation antipsychotics on quality of life in bipolar disorder

The use of conventional antipsychotics in the treatment of bipolar disorder is associated with the same adverse events as in schizophrenia. In addition, people with mood disorders might be at increased risk for acute movement disorders and tardive dyskinesia (Mukherjee et al, 1986). In several studies the standard mood stabilizing and antimanic drugs approved for treatment of bipolar disorder, lithium and anticonvulsants (e.g., valproic acid, carbamazepine, lamotrigine, gabapentin), showed improvement in functioning, as

measured by the indirect index of Global Assessment of Functioning (GAF) (review Dean et al, 2004).

As in schizophrenia trials, more vigorous research of the impact on the health-related quality of life of bipolar patients was done with the second-generation antipsychotics (Table 4). The most studied drug of this class is olanzapine, most of the data are the secondary efficacy analysis derived from large efficacy trials. In a randomized, placebo-controlled study of 139 bipolar I patients with manic or mixed episodes, olanzapine significantly increased all dimensions of the SF-36 except for 'vitality" dimension over the acute three-week treatment period (Namjoshi et al, 2002). Olanzapine was superior to placebo in the 'physical functioning' dimension. In the subsequent 49-week open-label extension, olanzapine-treated patients demonstrated improvement in most of the SF-36 dimensions ('bodily pain', 'general health', 'role limitations due to emotional functioning', and 'social functioning'), but not in 'vitality'. Moreover, a positive relationship between clinical outcome measured by the decrease of the total score on the Young Mania Rating Scale and quality of life was observed. Shi and collaborators (2002) compared olanzapine and haloperidol in a double-blind study of 453 patients in acute mania. Olanzapine

Table 4.4.4. Second-generation antipsychotics in quality of life in bipolar disorder.

Study	N	Medication	Duration	Results
Namjoshi et al, 2002	139 (manic or mixed)	Olanzapine Placebo	3 weeks double-blind + 49 weeks open extension	OLZ > PL
Shi et al, 2002	453 (acute mania)	Olanzapine Haloperidol	12 weeks	OLZ > HAL
Namjoshi et al, 2004	336 (acute mania)	Li/Val + olanzapine Li/Val + placebo	6 weeks	OLZ > PL
Revicki et al, 2003	120 (acute mania)	Olanzapine Divalproex	12 weeks	OLZ = DIVAL
Shi et al, 2004	833 (bipolar depression)	Olanzapine Olanzapine/Fluoxetine Placebo	8 weeks	OLZ > PL OFC > PL OFC > OLZ
Calabrese et al, 2005	542 (bipolar depression)	Quetiapine Placebo	8 weeks	QUE > PL

DIVAL = divalproex
HAL = haloperidol
Li = lithium
OFC = olanzapine/fluoxetine combination
OLZ = olanzapine
PL = placebo
QUE = quetiapine
Val = valproic acid

showed better efficacy than haloperidol in numerous dimensions of the SF-36 during 6-week acute phase ('general health', 'physical functioning', 'role limitations due to physical problems', 'social functioning', and 'vitality'). The superiority of olanzapine on the SF-36 was maintained over the following 6-week continuation phase, together with significantly greater improvement in the measures of work and household activities. Also olanzapine adjunctive treatment to mood stabilizers (lithium or valproic acid) compared to placebo in a 6-week trial with 336 bipolar I patients resulted in improvement of quality of life according to the Lehman Brief Quality of Life Interview (Namjoshi et al, 2004). In a study comparing efficacy of olanzapine and divalproex sodium in acute mania no significant drug difference was found in the Quality of Life Enjoyment and Satisfaction Questionnaire (Revicki et al, 2003). Out of 120 randomized subjects, 65% were followed beyond 3 weeks (up to 12 weeks) and only 43% patients completed the quality of life questionnaire.

There are two double-blind randomized placebo-controlled studies investigating effect of antipsychotic treatment on quality of life in bipolar depression. The first 8-week trial with olanzapine and olanzapine/fluoxetine (OFC) combination in 833 patients showed a superiority of both active arms over placebo according to many dimensions of the SF-36; in addition OFC group outperformed placebo on the Quality of Life in Depression Scale total score (Shi et al, 2004). Moreover, OFC was significantly better than olanzapine alone in improvement of the 'mental component summary', 'general health perception', 'mental health', 'role limitations due to emotional functioning', 'social functioning', and 'vitality'. In the second 8-week study of 542 patients with bipolar I and bipolar II depression, quetiapine administration resulted in a statistically significant improvement of the health-related quality of life measured by the change of the baseline total scores of the Quality of Life Enjoyment and Satisfaction Questionnaire (Calabrese et al, 2005). Both dosages of quetiapine used in this study (300 and 600 mg) were more effective than placebo, no significant difference was detected between the active treatment arms.

Quetiapine also improved global functioning more than placebo in acute mania, as assessed by the indirect measure of quality of life, Global Assessment of Functioning in a 12-week randomized trial (Bowden et al, 2005). GAF was used to evaluate impact of risperidone on the global functioning of patients with acute mania over a 3-week double-blind treatment period and 9-week open-label extension (Hirschfeld et al, 2006), or ziprasidone in a short 3-week study in acute mania (Keck et al, 2003). Similar to quetiap-

ine, both risperidone and ziprasidone improved functioning of patients with mania significantly better than placebo.

4.4.6. Expectations and reality

Second-generation antipsychotics indisputably represent significant progress in long-term treatment of schizophrenia and bipolar disorder, not just objectively, but also from the patients' perspective. Therefore, it may be somewhat surprising that a review of published studies in schizophrenia investigating their effects on patients' quality of life may indicate that our hopes and expectations fall short of real life. However, the closer scrutiny reveals that glass is indeed rather half-full than half-empty: in half of the reported studies SGA improved quality of life of schizophrenia patients more effectively than conventional treatment and in none of them SGA were inferior. Moreover, in all studies with bipolar disorder SGA were consistently superior to placebo in the measures of quality of life.

If the contrast between negative study results and overall positive clinical impression in schizophrenia can be attributable to the imperfections and variations in study designs, then more better designed, double-blind controlled trials are necessary. Research in bipolar disorder is hampered by the heterogeneity of the illness with suggested negative impact of depressive symptomatology. There is also a lack of long-term observation and absence of direct between-drug comparisons in bipolar research. So far just a single long-term, one-year study (49 weeks of open-label observation) with olanzapine was published. Some of the drugs were evaluated using only indirect measures of global functioning; studies using standard instruments for assessment of health-related quality of life are necessary.

Further research in both schizophrenia and bipolar disorder could also uphold or overcome preliminary results suggesting that there might be differences among antipsychotics in their impact on quality of life, favoring olanzapine. Investigators then should focus on finding response predictors: to identify who may benefit most from a long-term treatment with a specific drug. These issues are important in translating research results into the clinical practice

where the improvement of quality of life index is reflected in a real functional outcome of patients with schizophrenia and bipolar disorder.

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