The Relationship Between Antipsychotic Treatment and Quality of Life for Patients With Dementia Living in Residential and Nursing Home Care Facilities

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For any treatment, the impact on quality of life (QoL) is a key consideration. These issues are particularly important in the pharmacologic management of behavioral and psychological symptoms in patients with dementia (BPSD). Although these symptoms can be very distressing for some patients, the overall relationship of the symptoms with QoL is far less clear. In addition, although antipsychotic agents have moderate efficacy in the short- to medium-term management of these symptoms, it cannot be assumed that symptom resolution automatically equates with improved QoL. This is of particular concern in light of the adverse side effect profiles of many of these agents. Indeed, the only empirical study in this area conducted to date indicated that antipsychotics are associated with a worse QoL for nursing home patients. Unfortunately, none of the placebo-controlled trials of antipsychotics for the treatment of BPSD have included formal QoL measures, although preliminary evidence indicates that atypical antipsychotics such as quetiapine may result in QoL improvements. The inclusion of systematic QoL measures in future clinical trials is imperative in order to provide evidence to enable the clinician to make informed judgments regarding the potential benefits or risks of pharmacologic treatment for individual patients. In addition, such information will facilitate a better understanding of the likely factors that may contribute to the impact of treatment on QoL (e.g., side effects) and hence enable physicians to make rational treatment choices between different pharmacologic agents.

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More than 50% of patients with dementia experience behavioral and psychological symptoms of dementia (BPSD), such as psychosis, agitation, and mood disorders.[1] BPSD can be distressing for patients[2] and problematic for their caregivers,[3] for whom BPSD are associated with clinically significant depression.[4] BPSD are frequently the trigger for placement in residential or nursing home care.[5] These symptoms are even more frequent among patients residing in care facilities, with point prevalence frequencies of agitation alone exceeding 50%.[6] There are particular concerns regarding the management of BPSD among this group, as more than 40% of patients with dementia living in residential or nursing home care facilities are prescribed antipsychotic drugs.[7] Prescriptions for antipsychotics are often issued uncritically[8] and inappropriately,[9] with little relationship existing between the types of symptoms patients experience and the drugs that they are prescribed.[10] In addition, subsequent monitoring and treatment reviews are often inadequate[7] and prescriptions are rarely discontinued. The clinical importance of the problem is such that in the United States legislation has been introduced to improve prescribing practice for nursing home patients,[11] while in the United Kingdom the Chief Medical Officer has highlighted the importance of caution when prescribing antipsychotic drugs to patients with dementia.[12]

Although the evidence is limited for many individual drugs, several meta-analyses of the literature have indicated a class effect of significant but moderate efficacy for antipsychotics used for the short- to medium-term (6–12 weeks) management of BPSD. In general, this approximates to a 60% response to active drug compared with a 40% response to placebo (Table 1[13–26]).[27,28] The demonstration of only moderate efficacy is probably due, at least in part, to the fact that some BPSD (e.g., psychotic symptoms) have high rates of spontaneous resolution.[1,29–31] Psychological interventions may also be effective in the man-

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Table 1. Double-Blind, Placebo-Controlled Trials of Antipsychotics for Behavioral and Psychological Symptoms in Patients With Dementia[a]

Study	Sample Size	Active Agent	Patients With Improvement, %, Active Agent/Placebo
Abse et al, 1960[13]	32	Chlorpromazine	No significant difference
Hamilton and Bennett, 1962[14]	27	Trifluoperazine	22/0
Sugarmann et al, 1964[15]	18	Haloperidol	89/67
Hamilton and Bennett, 1962[16]	19	Acetophenazine	64/20
Cahn and Diesfeldt, 1973[17]	36	Penfluridol	No significant difference
Rada and Kellner, 1976[18]	42	Thiothixene	59/55
Petrie et al, 1982[19]	61	Haloperidol	65/36
		Loxapine	58/36
Barnes et al, 1982[20]	53	Thioridazine	59/47
		Loxapine	68/47
Teri et al, 2000[21]	149	Haloperidol	32/31
Finkel et al, 1995[22]	33	Thiothixene	65/19
Satterlee et al, 1995[23]	238	Olanzapine	No significant difference
Katz et al, 1999[24]	435	Risperidone	68/61
De Deyn et al, 1999[25]	344	Risperidone	72/61
		Haloperidol	69/61
Street et al, 2000[26]	206	Olanzapine	
		5 mg/d	65/36
		10 mg/d	57/36
		15 mg/d	43/36

[a]Reprinted with permission from Ballard and O'Brien.[27]

agement of BPSD.[32,33] Therefore, the optimal treatment approach for individual patients is far from clear, particularly as conventional antipsychotic drugs have substantial adverse effects, such as an increased risk of falls, drowsiness, parkinsonism,[34] akathisia, tardive dyskinesia, antipsychotic sensitivity reactions,[35] and QT prolongation.[36] These agents may also accelerate cognitive decline,[37] with increased loss of nicotinic receptors in the caudate and putamen probably reflecting greater loss of dopaminergic neurones.[38] The established atypical antipsychotics, such as risperidone, olanzapine, and quetiapine, may offer a better treatment option (reviewed by Tariot et al.[39] in this supplement) because of their improved tolerability profiles. However, the difficult management conundrum faced by clinicians is that they must balance a variety of complex issues and needs in determining whether a pharmacologic intervention with an antipsychotic agent is the best treatment for a particular patient. There are probably 3 main considerations: the risk to the patient and others, the quality of life (QoL) of the patient, and the QoL of the caregiver or others in the same living environment.

QoL: GENERAL ISSUES

There is an increasing need to find QoL measures suitable for the assessment of patients with dementia in residential care, particularly as the disabilities resulting from cognitive impairment can cause disempowerment and can preclude the use of the usual forum for complaints if a patient's care or treatment falls below an acceptable standard. One of the reasons for the slow evolution of this work relates to the obvious methodological problems of obtaining reliable subjective reports from individuals with dementia who have compromised cognitive abilities, often in combination with impaired communication skills. In a review of conceptual and methodologic issues facing researchers engaged in QoL work, Selai and Trimble[40] have highlighted the difficulties posed by issues such as change in cognitive function, communication, subjective and objective viewpoint, and loss of insight.

Broadly speaking, QoL can be measured using 3 different approaches: self-rating, proxy rating, and observational methods. A variety of scales have been developed, with different scales focusing on different aspects of QoL. Some concentrate on physical factors and activities of daily living (e.g., the Short Form [SF-36] Health Survey[41] and the Nottingham Health Profile[42]), while others focus on emotional factors[43] or social factors (e.g., the Blau QoL scale).[44] Other scales incorporate a global measure of all these factors, e.g., the Duke Health Profile[45] and the Dementia QoL rating scale.[46]

Probably the most widely used tool with respect to outcome studies in nursing home settings has been Dementia Care Mapping (DCM), an observational method based on Kitwood's psychosocial theories of dementia.[47–49] With this method, residents' well-being and activities such as articulation, feeding, and walking are recorded every 5 minutes over a period of 6 hours.[50] Well-being is measured on an ordinal scale from –5 to +5 (Table 2) and a mean well-being score is derived from these data. Activities are rated according to 24 behavioral category codes, which are subdivided into 4 categories for coding purposes with operationalized rules for assignment. The emphasis is on recording activities that promote or sustain well-being if they occur during the coding epoch. For group data, a Dementia Care Index score can be calculated by combin-

Table 2. Dementia Care Mapping Scale for Well-Being[a]

Score	Level of Well-Being
+5	Exceptional well-being with high levels of engagement, self-expression, and social interaction
+3	Considerable well-being, interaction or initiation of social contact
+1	Coping adequately with present situation, no signs of ill-being observable
–1	Slight ill-being visible, e.g., boredom, restlessness, or frustration
–3	Considerable ill-being, e.g., sadness, fear, or sustained anger
–5	Extremes of apathy, withdrawal, grief, or despair

[a]Based on Kitwood and Bredin.[50]

ing the well-being/ill-being and Behavior Category Code scores. This combination then serves as a condensed piece of information about the quality of care. The information derived from this evaluation relates to patients' experience, which contributes a major component to their QoL. As a research tool, the method has the advantage of excellent interrater reliability,[51] good agreement with audit measures[52] as a global assessment of quality of care, good concurrent validity with an established informant scale,[53] and good test/retest reliability.[53]

QoL AND BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA

It is often assumed that BPSD have a negative impact on QoL, but there are very few empirical studies to support this. Several studies have reported that approximately one third of patients with various psychiatric or behavioral symptoms experience distress as a consequence of these symptoms.[2,54] This could be considered a coarse indication that, at least in patients experiencing distress, QoL is likely to be compromised. In support of this, one study highlighted the finding that the frequency with which psychiatric symptoms were experienced by individual patients showed the strongest association with distress.[54] This is consistent with clinical experience and common sense in suggesting that distress is more likely in the context of severe symptoms.

A recent cross-sectional study focusing on 112 patients with dementia residing in care facilities in the United Kingdom evaluated the relationship between individual BPSD symptoms (measured using the Neuropsychiatric Inventory [NPI]) and key indices of QoL (evaluated using DCM).[10] More than 50% of the residents had 1 or more BPSD symptoms at a clinically significant level, and 40% had at least 1 severe BPSD symptom. However, there was no significant association between any of the QoL parameters (well-being, social withdrawal, or participation in activities) and any of the NPI symptom domains. Although on first consideration this is surprising, it is likely to reflect the general impoverishment of the care environment, in which residents spend more than 85% of the time disengaged from any constructive activities or interaction.[55] In this milieu, the additional impact of behavioral or psychiatric symptoms on overall QoL is probably small for the majority of individuals. The importance is likely to be much greater, however, for the proportion of individuals with very severe BPSD who are clearly distressed by their symptoms.

QoL AND ANTIPSYCHOTICS IN DEMENTIA

Potentially, there are a number of ways in which antipsychotic agents could impact positively or negatively on QoL. If distressing behavioral symptoms, such as agitation, are improved with treatment, the potential QoL benefits for the person with dementia are clear. This has been illustrated in a recent placebo-controlled trial of aromatherapy with *Melissa* (lemon balm) that demonstrated a significant improvement in symptoms and QoL (well-being and activities measured using DCM) over a 4-week, double-blind treatment period.[56] In addition, if behavioral or psychiatric symptoms are resulting in stress for a family or professional caregiver, successful resolution of the symptoms may result in indirect QoL benefits for the patient if the caregiver-patient relationship is improved. Treatment may also create new opportunities for activities or interaction for the patient that would otherwise be precluded by the severity of BPSD.

However, there is also the potential for treatment to have a detrimental impact. For example, side effects such as extrapyramidal symptoms, tardive dyskinesia, or falls may cause distress. Falls may also lead to serious injury, which could further impair QoL. Parkinsonism and sedation may reduce an individual's potential to engage socially or to participate in activities. Different antipsychotic agents vary considerably in their side effect profiles (reviewed by Baskys[57] in this supplement). Therefore, it is likely that individual drugs will also vary in their detrimental impact on QoL, and this has key implications for the choice of treatment.

None of the placebo-controlled trials evaluating the efficacy of antipsychotics for the treatment of BPSD has specifically determined the benefits or detriments on QoL, a very serious omission. Hence, the evidence base for determining the impact of antipsychotic treatment on QoL is minimal. Some data were provided by the aforementioned study of the relationship between BPSD and QoL in nursing home patients, as this study also evaluated the impact of antipsychotic drugs on the DCM indices.[10] Overall, 46% of residents with dementia were taking antipsychotics, either conventional agents or risperidone. In a logistic regression analysis examining differences in specific activities, patients taking antipsychotics spent less time passively engaged in activities ($p = .03$), less time eating ($p = .01$), and less time performing work or work-like activity ($p = .04$). In addition, ill-being (well-being

score < 0) was significantly more frequent in patients taking antipsychotics (ill-being: taking antipsychotics, N = 9 [18%]; not taking antipsychotics, N = 3 [5%]; odds ratio = 4.0, 95% confidence interval = 1.03 to 15.64). Ill-being was especially frequent in those taking conventional antipsychotics compared with those taking risperidone (N = 7 [22%] vs. N = 2 [10%], respectively).

These findings are of potential importance for 2 reasons. First, the antipsychotic agents had a more detrimental impact on QoL than the symptoms for which they were prescribed, yet for many of those patients who were receiving antipsychotics, clinically significant BPSD were not present. This implies that either the treatment was initiated inappropriately or it had not been reviewed following resolution of the target symptom. Second, there appeared to be a difference between conventional and atypical antipsychotic drugs. However, this study must be interpreted with caution as it was a cross-sectional evaluation and there may have been important unidentified confounding effects. The relationship between impaired QoL and medication side effects was not examined, and there was no subanalysis focusing specifically on patients with very severe BPSD.

A subsequent randomized, placebo-controlled study determined the impact of discontinuing antipsychotic agents in 100 patients with dementia residing in care facilities.[58] The patients were receiving long-term antipsychotics, either conventional agents or risperidone, and were without active severe behavioral disturbances. During the 3-month evaluation period, there was no difference in the severity of BPSD between patients taking antipsychotics and those taking placebo. However, there was a 15% improvement in DCM well-being scores in patients withdrawn from antipsychotic treatment, compared with a slight worsening in patients who continued to take antipsychotics. Although this difference was not statistically significant, it certainly does not indicate any beneficial effect of these antipsychotics on QoL.

At the conclusion of this placebo-controlled study, patients who had received antipsychotics and for whom ongoing antipsychotic therapy was clinically indicated (N = 48; mean ± SD age = 83.6 ± 7.2 years; mean ± SD Mini-Mental State Examination score = 2.1 ± 4.1; 80% assessed as Clinical Dementia Rating Scale stage 3) were changed from their previous antipsychotic, in the majority of cases to quetiapine (N = 27). Several residents remained on their original antipsychotics, i.e., a conventional antipsychotic (N = 11) or risperidone (N = 10), based on a strongly expressed preference of the primary care physician. The change of antipsychotic was undertaken as a rapid conversion, with no tapering of the prior agent. Quetiapine was initiated at a dosage of 25 mg twice daily, which was increased as clinically indicated. The dosages of the other antipsychotic agents were continued unchanged. The DCM evaluation was completed prior to the change of medication and repeated after a further 6 weeks. The differences in well-being and daytime sleep between the 2 timepoints were evaluated using paired-sample t tests.

Table 3. Changes in Well-Being and Daytime Sleep After 6 Weeks in Care Facility Patients With Dementia Whose Antipsychotic Therapy Was Either Changed to Quetiapine or Continued With Risperidone or Conventional Antipsychotics[a]

Variable	Quetiapine (N = 27)	Risperidone (N = 10)	Conventional Antipsychotics (N = 11)
Well-being	↑ 16%	↓ 1%	↓ 2%
Daytime sleep	↓ 29%	↓ 43%	↑ 11%

[a]M.L.M.; L. Lee, R.M.N.; unpublished data, 2000–2002.
Symbols: ↑ = increased, ↓ = decreased.

Overall, there was an improvement in well-being scores and a reduction in daytime sleep with quetiapine (Table 3), although these differences did not reach statistical significance. Patients who continued to receive risperidone showed no improvement in well-being, but did show a reduction in daytime sleep. Those who continued to receive conventional antipsychotics did not improve in either well-being or daytime sleep (see Table 3). Although none of these differences were statistically significant, these data provide some very preliminary evidence that QoL improvements may be gained in individuals who require ongoing pharmacotherapy for BPSD by changing the antipsychotic used to a drug with a better side effect profile. This hypothesis needs to be investigated systematically in an adequately powered placebo-controlled trial. It is imperative that future trials of antipsychotic agents in patients with dementia include QoL measures as an integral part of their design to enable clinicians to make fully informed decisions about the likely benefits for their patients.

DISCUSSION

When deciding on the optimal management approach for dementia patients with behavioral or psychiatric symptoms, clinicians are often left with a difficult decision. They must balance the potential risks, detrimental consequences, and possible benefits of both the symptoms and the available treatment options. When deciding whether a pharmacologic treatment approach for BPSD is necessary or preferable, the potential risk to the patient and others is probably the largest single factor, although this is only applicable to a small minority of patients. In the absence of high levels of risk, whether a treatment improves or impairs the QoL of the individual patient is of prime importance. It is clear that we cannot assume that symptom resolution automatically equates with improved QoL, but unfortunately there is a complete lack of information pertaining to QoL from placebo-controlled treatment trials of

BPSD with antipsychotic agents. Pharmacologic treatment with antipsychotics in patients with dementia should be targeted toward the resolution of specific symptoms, and the atypical agents are a more favorable option than conventional drugs, given the vulnerability of dementia patients to serious adverse events.

Due to the relatively modest efficacy of most antipsychotic agents and the potential for adverse effects, the side effect profile of the drug and the impact of QoL are critical factors in selecting an individual drug and, more generally, in deciding the role of pharmacotherapy. Preliminary evidence from a pilot crossover trial suggests that changing treatment from a conventional antipsychotic to the atypical antipsychotic quetiapine, which has a very favorable side effect profile, may lead to some improvements in QoL. It is essential that future trials determine differences between individual antipsychotics in their impact on QoL before clear treatment recommendations can be developed.

Most of the evidence reviewed in the current article focuses on patients with dementia living in care facilities. The potential impact of antipsychotic treatment on QoL may be very different among patients living in their own homes. This aspect needs to be investigated as a separate but equally important issue.

In summary, QoL is a critical outcome measure for determining the value of pharmacologic treatments for BPSD, especially as preliminary studies indicate a significant capacity for a detrimental effect of some of the available antipsychotics. QoL measures should be core to future trials of atypical antipsychotics in this area.

Drug names: chlorpromazine (Thorazine, Sonazine, and others), haloperidol (Haldol and others), loxapine (Loxitane and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), thiothixene (Navane and others), trifluoperazine (Stelazine and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, chlorpromazine, haloperidol, loxapine, olanzapine, quetiapine, risperidone, thiothixene, and trifluoperazine are not approved by the U.S. Food and Drug Administration for the treatment of behavioral and psychological symptoms in dementia, and penfluridol and acetophenazine are not approved for use in the United States.

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