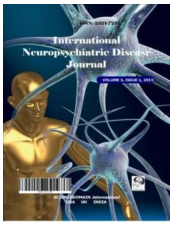

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Subjective Experiences of Antipsychotic Treatment: A Comparison of First- and Second-generation Medications among Patients with Schizophrenia

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Authors' contributions

This work was carried out in collaboration between all authors. Author NW was involved in planning of the study, carrying out assessments, analysis of data and writing the first draft of the manuscript. Authors SC and SG designed the study, supervised the assessments, analyzed the data further and wrote the final versions of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The patient's perspective of antipsychotic treatment has been a relatively neglected area of research. Whether subjective experiences of antipsychotic treatment are better among patients on second-generation antipsychotics (SGAs), than those on first-generation antipsychotics (FGAs) has also evoked some controversy. This study attempted a longitudinal comparison of attitudes toward treatment, subjective well-being and quality of life (QOL) between patients on SGAs and FGAs. Socio-demographic and clinical correlates of these subjective experiences were also examined.
Methodology: Standardised ratings of insight, psychopathology, side-effects, attitudes, subjective well-being and QOL were carried out among 40 patients with schizophrenia on SGAs and 30 on FGAs, over a 6-month period.
Results: Both groups were similar in the first 3-month period, apart from the slightly greater severity of illness in the FGA group. Differences in symptom-severity and side-effects emerged

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between the groups over the course of follow-up. Moreover, as the study progressed, differences also became apparent in subjective experiences; patients on SGAs had significantly better attitudes, subjective well-being and QOL than those on FGAs. However, differences between individual SGAs (olanzapine and risperidone) on these indices were minimal. The three indices of subjective experience were highly correlated with each other. Older age, being employed, greater insight, lower symptom-severity and the absence of side-effects demonstrated significant positive associations with different aspects of subjective experiences.

Conclusions: Patients on SGAs had a more favourable profile of subjective experiences with treatment than those on FGAs. These differences seemed to be determined mainly by differences in symptom-severity and side-effects.

Keywords: Subjective experiences; antipsychotics; schizophrenia.

1. INTRODUCTION

The patient's perspective of antipsychotic treatment was largely neglected till the introduction of atypical or second-generation antipsychotics (SGAs) in the 1990s [1,2]. Since then, subjective experiences of antipsychotic treatment including constructs such as attitudes toward medications, subjective well-being on antipsychotic treatment, and quality of life (QOL) on these medications have been increasingly acknowledged as being critical to the outcome of treatment [1,2].

It was anticipated that SGAs, which promised a similar efficacy along with an improved side-effect profile than first-generation antipsychotics (FGAs), would have a more benign profile of subjective effects [1]. Indeed, early clinical trials seemed to suggest a trend towards superiority of SGAs in this regard [2-4]. However, the spectrum of evidence ranging from randomized clinical trials, naturalistic comparisons, reviews and meta-analyses to large-scale effectiveness trials in "real world" settings has been somewhat inconclusive. The more recent large-scale effectiveness studies have also included these variables as secondary outcomes of interest. While some of these studies have not found any differences in patients' attitudes, subjective well-being, or QOL between SGAs and FGAs [5,6], others have reported greater and clinically relevant improvement on these parameters among patients on SGAs [7,8]. Finally, surveys of patients' views on the matter have usually revealed a strong preference for SGAs, despite side effects such as weight gain or sexual dysfunction [9].

The present study attempted a longitudinal comparison between SGAs and FGAs on three major aspects of subjective experiences with antipsychotics including attitudes toward treatment, subjective well-being, and QOL, among patients with schizophrenia being treated with these medications. The relationships between these three aspects of subjective experiences, as well as their correlates were also examined.

2. MATERIALS AND METHODS

2.1 Approval-consent

The study-protocol was approved by the research and ethics committees of the institute. Written informed consent was obtained from all participants prior to inclusion. Other ethical safeguards were also maintained during the study.

2.2 Participants

The study was conducted in the psychiatry department of a multi-specialty hospital in north-India. Patients aged 18-60 years with a diagnosis of schizophrenia, as per the Structured Clinical Interview for DSM-IV Axis I Disorders-Clinical Version I [10] were included if they were on treatment with the same antipsychotic for at least 3 months before inclusion. Patients were not included if they had organic brain syndromes or comorbid psychiatric illnesses and substance dependence (apart from nicotine). Patients being treated with combinations of antipsychotics, or depot injections were also excluded.

One hundred and forty patients with schizophrenia on clozapine, olanzapine, risperidone, quetiapine, aripiprazole and ziprasidone were screened over a 6-month period. Of these patients, 49 did not fulfil selection criteria; 10 did not consent and 26 patients did not complete their baseline assessments. Of the 55 patients who remained, 40 completed both baseline follow-up

assessments. Thus, these formed the study group. A control group of 30 patients on FGAs were also recruited simultaneously, from a sample of 50 patients on these medications. They had fulfilled all selection criteria and completed their assessments. Matching of the 2 groups was done on age, gender, marital status, education of patients, and the duration of their illnesses.

2.3 Assessments

The following assessments were carried out:

1. Psychopathology - the Positive and Negative Syndrome Scale (PANSS) [11]
2. Side-effects – the Udvalg for Kliniske Undersogelser Side Effect Rating Scale (UKU) [11]; the Barnes Akathisia Rating Scale (BARS) [11] and the Abnormal Involuntary Movements Scale (AIMS) [11]
3. Insight - Scores on the PANSS General Psychopathology item 12 (G12)
4. Attitudes towards antipsychotics - the Drug Attitude Inventory-10 item version (DAI-10) [3,11,12]
5. Subjective well-being on antipsychotics - the short form of the Subjective Well-being under Neuroleptic Medication scale (SWN-K) [3,11-13]
6. Self-rated QOL - the World Health Organization Quality of Life-Bref scale (WHOQOL-Bref, Hindi) [14].

All assessments were carried out twice. Baseline assessments carried out at intake covered the preceding 3-month period. A second assessment after 3 months of follow-up covered the interim three-month period between baseline and follow-up assessments.

2.4 Data Analysis

Data were analysed using the Statistical Package for Social Scientists, version fourteen. Chi-square, Student's *t* and Mann-Whitney tests were used to compare the two groups on different parameters. Repeated-measures ANOVAs were used to compare the rate of change in the SGA and FGA groups and olanzapine and risperidone subgroups between baseline and follow-up assessments. Finally, three stepwise multiple regression analyses were carried out for the whole sample to determine the influence of socio-demographic and clinical variables on attitudes, subjective well-being and QOL respectively.

3. RESULTS

3.1 Patient Profiles

Patient profiles are depicted in Tables 1 and 3. Significant differences between the two groups were:

1. Patients on FGAs came from low-income families. These differences in income were most probably a reflection of the prevailing prescribing practices. Since only FGAs are available from the hospital free of cost, clinicians usually tend to prescribe these medications as a first option to patients with low incomes, who would be unable to afford the more expensive SGAs.
2. Patients on FGAs had higher number of past relapses and hospitalizations.
3. Patients on FGAs had been on treatment for a longer period.
4. Patients on FGAs were on a higher number of psychotropics; this was due to a greater number of patients on anticholinergics in the FGA group (X^2 = 27; $P < .000$) and suggested a higher prevalence of extrapyramidal side effects among them.

3.2 Results of Repeated-measures ANOVAs

Table 2 depicts the rate of change in different parameters in the SGA, FGA, olanzapine and risperidone groups over two time periods; one at baseline consisting of the 3-month period prior to intake and another after 3 months of follow-up. The principal findings here were the significant decline in PANSS scores in the SGA group over this period along with significant improvements in SWN-K and WHOQOL-Bref scores, while DAI scores did not change much in either group. The findings in olazapine and risperidone subgroups were more mixed, though significant changes were observed in a greater number of parameters in the olanzapine subgroup.

Table 3 depicts the comparisons of symptom-severity, insight, side effects and subjective experiences with antipsychotics between the SGA and FGA groups, as well olanzapine and risperidone subgroups versus the FGA group.

3.3 Symptom-severity

PANSS scores did not differ significantly between the two groups in the three-month period prior to

intake, apart from the significantly higher positive scores of the FGA group. Over the next 3 months there was a significant decline (*P < .05*) in all subscale scores and the total PANSS scores among patients on SGAs. At the end of 3 months of follow-up and over the 6-month study-period, the FGA group had significantly higher total scores and higher scores on all 3 subscales of the PANSS.

3.4 Insight

No differences were noted on the G12 PANSS scores between SGAs and FGAs at any assessment.

3.5 Side-effects

Patients on FGAs had significantly higher scores on "Neurological" side-effects of the UKU, including rigidity (*P < .001*), tremors (*P < .05*), hypokinesia/akinesia (*P < .01*) and hyperkinesias (*P < .01*) in the 3 months preceding intake, over the next 3 months of follow-up, and over the 6-month study-period. Patients on FGAs also had significantly greater scores on the "Autonomic" side-effects of the UKU after 3 months of follow-up, and for the 6-month study-period, resulting mainly from higher scores on orthostatic hypotension (*P <.01*). Patients on FGAs had significantly higher scores on the "Psychic" side-effects, including asthenia/lassitude (*P <.01*), sedation (*P < .05*), depression (*P< .05*) and tension/inner unrest (*P < .05*) at the 3-month follow-up assessment. Patients on SGAs had significantly higher scores on the "Other" side-effects subscale of the UKU after 3 months of follow-up, and for the 6-month study-period, due to significantly higher weight gain (*P< .000*) and erectile dysfunction (*P < .05*).

Table 1. Demographic, clinical and treatment details

	SGAs N=40	**FGAs N=30**
Age – Mean (SD)	35.8 (10.2) years	37.4 (8.8) years
Male/female	29/11	20/10
Married/single	25/15	19/11
≤8 years of schooling	13	14
> 8 years of schooling	27	16
Employed	20	16
Unemployed/housewives	20	14
Family income – Mean (SD)	12092 (13282) Rupees/ month	5157 (4034) Rupees/ month *
Urban/rural residence	31/9	21/9
Illness duration—Mean (SD)	69.3 (35.7) months	78.9 (30.3) months
No. of hospitalizations in the past – Mean (SD)	0.3 (0.5)	0.7 (.9) *
No. of relapses in the past – Mean (SD)	15 (37.5)	19 (63.3)*
Type of antipsychotics		
Risperidone	14	-
Olanzapine	23	-
Quetiapine	03	-
Trifluoperazine	-	23
Chlorpromazine	-	07
Dose in chlorpromazine equivalents – Mean (SD) [a]	310 (172) mgs/day	333 (86) mgs/day
Duration of treatment with current medications – Mean (SD)	12.3 (12) months	39.4 (30.8) months*
Total number of psychotropics -–Mean (SD)	1.5 (0.7)	2.3 (0.7) *

*Abbreviations: SD – standard deviation; SGAs – second generation antipsychotics; FGAs – first generation antipsychotics; [a] Doses of antipsychotics represent average doses over 6 months of the study; * P < 0.05 (Mann Whitney U or Student's t values)*

3.6 Attitudes towards Antipsychotics

Patients on SGAs had significantly higher DAI-10 scores after 3 months of follow-up and for the 6-month study-period. Patients on SGAs had significantly higher scores among on the following items: "For me, the good things about medication outweigh the bad" (*P < .05*); "By staying on medications, I can prevent getting sick" (*P < .001*); and, "I take medications on my own free choice" (*P < .05*).

3.7 Subjective Well-being on Antipsychotics

Total scores on the SWN-K were significantly higher among patients on SGAs in the 3 months preceding intake, as were the scores on the subscales of "Mental functioning", "Emotional regulation," and "Physical functioning." At the end of 3 months of follow-up and for the 6-month study-period the two groups differed significantly not only on the total SWN-K scores, but also on all 5 SWN-K subscales.

3.8 QOL

Total WHOQOL-Bref scores and scores on 3 of the 4 subscales (apart from "Environmental health") did not differ significantly between SGAs and FGAs in the 3 months prior to intake. However, the SGA group registered a significant increase (*P <.05*) in QOL scores (total, "Psychological" and "Social health") over the next 3 months of follow-up, while the total scores declined significantly (*P < .05*) in the FGA group. Thus, at the end of this period, as well as for the entire study-period, patients on SGAs had significantly higher total WHOQOL-Bref scores and higher scores on subscales of "Psychological health," "Social health" and "Environmental health."

Table 2. Results of the repeated-measures ANOVAs

Comparison of baseline (covering 3 months before intake) and follow-up assessments (after 3 months of follow-up)				
Mean (SD) of scores	**SGA**	**FGA**	**Olanzapine**	**Risperidone**
PANSS positive	F=53.07 ***	F=0.89	F= 44.83 ***	F=29.13 ***
PANSS negative	F= 8.59 **	F=0.01	F=10.47 ***	F=1.76
PANSS GP	F= 14.21**	F=0.36	F=14.17 **	F=5.68*
INSIGHT (GP12)	F=5.87*	F=6.43*	F=3.72	F=2.51
UKU psychic side effects	F=1.88	F=38.07***	F=0.176	F=2.43
UKU neurological side effects	F=14.91 ***	F=22.98***	F=6.32*	F=5.61*
UKU autonomic side effects	F=1.68	F=0.05	F=3.22	F=0.042
UKU other side effects	F=4.1	F=0.079	F=4.02	F=0.869
UKU total score	F=3.01	F=19.66 ***	F=0.785	F=3.30
BARS	F=0.004	F=3.56	F=2.21	F=3.05
AIMS facial & oral movements	F=0.494	F=3.18	F=1.03	F=1.00
AIMS extremity movements	-	-	-	-
AIMS trunk movements	-	-	-	-
AIMS global judgments	F=2.36	F=8.43*	F=2.42	-
DAI-10	F=1.17	F=0.32	F=5.15*	F=2.16
SWN-K mental functioning	F=2.04	F=1.285	F=6.360*	F=0.107
SWN-K self control	F=0.051	F= 5.897*	F=1.79	F=0.653
SWN-K emotional regulation	F=0.178	F=5.338*	F=0.234	F=3.024
SWN-K physical functioning	F=2.72	F=2.76	F=9.50*	F=0.024
SWN-K social interaction	F=2.54	F=1.39	F=3.70	F=0.295
SWN-K total score	F=1.45	F=10.02 **	F=6.18 *	F=0.170
WHOQOL physical	F=20.69 ***	F= 2.23	F=10.31**	F=13.03**
WHOQOL psychological	F=23.81 ***	F=0.529	F= 8.37 **	F=15.20 ***
WHOQOL social	F=6.97 *	F=3.49*	F=10.70**	F=0.650
WHOQOL environmental	F=9.793	F=11.21**	F=18.02 ***	F=2.94
WHOQOL total score	F=8.88 **	F=16.54 ***	F=6.44**	F=3.20

*Abbreviations: SD - standard deviation; SGAs-second generation antipsychotics; FGAs-first generation antipsychotics; PANSS-Positive and Negative Syndrome Scale; GP-General psychopathology; UKU-Udvalg for Kliniske Undersogelser Side Effects Rating Scale; BARS -Barnes Akathisia Rating Scale; AIMS-Abnormal Involuntary Movements Scale; DAI- 10-Drug Attitude Inventory- 10 item version;SWN-K -Subjective Well-being under Neuroleptic Medication scale (20-item version); WHOQOL -Bref,- WHO Quality of Life-Bref, Hindi version. * P < 0.05 ** P < 0.01*** P < 0.001*

Table 3. Symptom-severity, insight, side effects and subjective experiences with antipsychotics

Mean (SD) of scores	Baseline assessments (covering three months prior to intake)				Follow-up assessments (after three months of follow-up)				Average of both intakes (over six months of the study-period)			
	SGAs (N=40)	FGAs [a] (N=30)	Olanz [b] (N= 23)	Risp [c] (N=14)	SGAs (N=40)	FGAs [a] (N=30)	Olanz [b] (N= 23)	Risp [c] (N=14)	SGAs (N=40)	FGAs [a] (N=30)	Olanz [b] (N= 23)	Risp [c] (N=14)
PANSS positive	15.8 (3.1)	17.7 * (3.4)	14.9** (3.0)	17.0 (3.1)	12.7 (3.3)	17.2 *** (4.03)	11.8 **** (3.1)	13.6 ** (2.3)	14.3 (2.1)	17.4 * (3.4)	13.3 **** (2.8)	15.3 * (2.4)
PANSS negative	15.8 (4.8)	17.1 (3.9)	15.9 (4.3)	16.2 (6.1)	14.6 (3.8)	17.1 * (3.8)	14.5 * (3.7)	14.9 (4.5)	15.2 (4.1)	17.1 * (3.5)	15.2 (3.9)	15.6 (5.0)
PANSS GP scores	29.5 (5.2)	31.2 (6.1)	29.2 (4.6)	30.4 (6.6)	27.0 (5.7)	31.0 * (8.1)	25.6* (5.3)	28.4 (6.4)	28.2 (5.0)	31.1 * (6.8)	27.4 * (4.4)	29.4 (6.3)
INSIGHT [d]	2.80 (0.8)	3.0 (1.1)	2.7 (0.9)	2.9 (0.5)	2.4 (1.2)	2.5 (1.2)	2.3 (1.3)	2.6 (0.9)	2.6 (0.9)	2.8 (1.1)	2.5 (1.0)	2.7 (0.6)
UKU Psychic side effects	7.1 (3.1)	6.8 (2.7)	7.6 (3.1)	6.4 (3.5)	7.8 (3.0)	10.2** (3.8)	8.0 * (3.0)	7.6 * (3.4)	7.5 (2.7)	8.5 (2.9)	8.0 (2.6)	7.3 (3.1)
UKU neurological side effects	2.4 (1.8)	3.5 * (1.7)	2.4 * (1.8)	2.9 (1.7)	3.6 (1.9)	5.1 ** (1.7)	3.5 ** (2.1)	3.9 * (1.5)	3.0 (1.6)	4.3 ** (1.5)	3.3 * (1.7)	3.7 (1.4)
UKU Autonomic side effects	3.6 (2.7)	4.4 (2.9)	3.9 (3.1)	3.2 (2.3)	3.0 (2.1)	4.3 * (2.4)	2.8 * (2.3)	3.4 (2.0)	3.3 (1.9)	4.3 * (2.40)	3.7 (2.3)	3.6 (1.8)
UKU Other side effects	3.4 (3.1)	2.8 (1.8)	3.2 (3.6)	3.8 (2.4)	4.6 (1.8)	2.8 *** (1.9)	4.3 *** (2.0)	4.5 * (1.8)	4.0 (1.9)	2.9 * (1.6)	4.3 ** (2.0)	4.4 ** (1.5)
UKU Total score	16.6 (8.0)	17.5 (6.2)	17.2 (8.8)	16.3 (7.6)	18.9 (5.2)	22.5 * (5.9)	19.1* (4.9)	19.4 (6.2)	17.7 (5.3)	20.0 (5.2)	18.1 (5.0)	17.8 (6.2)
BARS	3.0 (5.2)	2.3 (2.8)	2.0 (3.2)	3.4 (3.4)	3.0 (3.8)	2.8 (3.1)	2.8 (3.9)	3.9 (3.9)	3.0 (3.8)	2.5 (2.9)	2.4 (3.3)	3.6 (3.6)
AIMS facial & oral movements	0.3 (0.9)	1.0 (1.6)	0.5 (1.1)	0.1 (0.3)	0.4 (1.1)	1.4 (2.5)	0.6 (1.4)	0	0.3 (0.9)	1.2 (2.0)	0.6 (1.3)	0.1 (0.3)
AIMS extremity movements	0	0.03 (0.18)	0	0	0	0.03 (0.2)	0	0	0	0.03 (0.2)	0	0
AIMS trunk movements	0	0	0	0	0	0	0	0	0	0	0	0
AIMS global judgments	0.3 (1.1)	1.1 (1.8)	0.6 (1.5)	0	0.5 (1.5)	1.5 (2.3)	0.9 (1.9)	0	0.4 (1.2)	1.3 (2.1)	0.8 (1.8)	0
DAI-10	1.8 (1.7)	1.0 (1.9)	1.5 (1.8)	2.6 *	2.2 (2.1)	0.9 **	2.5 ** (2.2)	1.9 (2.1)	2.0 (1.6)	0.9** (1.2)	2.0 *	2.0 *

Mean (SD) of scores	Baseline assessments (covering three months prior to intake)				Follow-up assessments (after three months of follow-up)				Average of both intakes (over six months of the study-period)			
	SGAs (N=40)	FGAs [a] (N=30)	Olanz [b] (N= 23)	Risp [c] (N=14)	SGAs (N=40)	FGAs [a] (N=30)	Olanz [b] (N= 23)	Risp [c] (N=14)	SGAs (N=40)	FGAs [a] (N=30)	Olanz [b] (N= 23)	Risp [c] (N=14)
				(1.4)		(1.2)					(1.7)	(1.7)
SWN-K mental functioning	15.3 (3.4)	12.8 *** (2.3)	15.3** (3.1)	14.6 (3.7)	15.9 (2.7)	12.4**** (2.5)	16.5**** (3.0)	14.9** (1.9)	15.6 (2.7)	12.6 **** (2.1)	15.9**** (2.8)	14.8 ** (2.5)
SWN-K self control	14.6 (2.5)	13.5 (2.3)	14.9 (2.8)	14.2 (2.2)	14.8 (2.3)	12.5**** (2.5)	15.9**** (2.0)	13.6 ** (2.3)	14.7 (1.9)	13.1** (2.1)	15.3 *** (1.9)	13.9** (1.7)
SWN-K emotional regulation	15.3 (4.0)	12.9 * (2.3)	14.9 (4.6)	16.1 ** (3.3)	15.2 (2.8)	11.9 **** (3.0)	15.2 *** (3.0)	15.0 ** (2.4)	15.2 (3.0)	12.4**** (2.6)	15.0 ** (3.5)	15.4 *** (2.5)
SWN-K physical functioning	15.2 (3.1)	13.6 * (3.4)	15.6 * (3.2)	14.3 (3.1)	16.0 (2.6)	12.7 **** (2.6)	17.1**** (2.7)	14.4* (1.6)	15.6 (2.5)	13.1**** (2.7)	16.3 **** (2.7)	14.4 (1.8)
SWN-K Social interaction	14.7 (3.8)	13.0 (3.3)	14.4 (4.2)	14.8 (3.0)	15.3 (3.1)	12.7*** (2.8)	15.3 * (3.9)	15.1 ** (1.2)	15.0 (3.2)	12.8** (2.8)	14.8 * (3.9)	14.9 * (1.7)
SWN-K Total score	75.2 (12.9)	66.1** (10.3)	75.1 * (14.9)	73.9 * (10.4)	77.1 (10.1)	62.0**** (9.8)	79.7**** (11.4)	72.9 *** (5.5)	76.2 (10.5)	64.0**** (9.4)	77.4**** (12.5)	73.4 ** (6.8)
WHOQOL physical	19.6 (3.5)	19.0 (2.9)	18.8 (4.1)	20.3 (2.4)	22.2 (3.5)	18.0 (3.5)	19.3 (3.9)	23.1 ** (3.3)	19.8 (3.6)	18.9 (2.6)	19.0 (3.8)	20.8 * (2.7)
WHOQOL psychological	16.2 (2.8)	16.0 (2.4)	15.6 (3.0)	16.8 (1.8)	18.9 (4.2)	15.7*** (2.8)	18.0* (4.7)	20.0**** (3.1)	17.6 (3.1)	15.9* (2.3)	16.8 (3.4)	18.3** (2.0)
WHOQOL social	8.7 (2.1)	8.5 (2.0)	8.0 (2.2)	9.4 (1.7)	9.7 (2.0)	7.8**** (1.5)	9.4 *** (1.8)	10.0 *** (2.4)	9.2 (1.7)	8.1* (1.5)	8.7 (1.8)	9.7 ** (1.6)
WHOQOL environmental	27.0 (8.9)	19.8**** (3.4)	25.4**** (5.3)	29.8*** (13.2)	28.2 (7.9)	21.0**** (4.6)	27.2*** (6.7)	32.0*** (10.8)	27.6 (8.4)	20.4**** (3.8)	26.3**** (6.3)	30.9**** (11.9)
WHOQOL total score	77.0 (13.4)	75.6 (8.7)	74.4 (15.3)	79.0 (9.6)	84.0 (14.3)	69.9 **** (8.4)	81.2 *** (12.3)	88.2 **** (17.6)	80.5 (11.6)	72.7 ** (7.7)	77.8 (12.3)	83.6 *** (10.4)

Abbreviations: see footnote to table 2

[a] Significant differences between SGAs and FGAs; [b] Significant differences between olanzapine and FGAs ; [c] Significant differences between risperidone and FGAs; Olanzapine and risperidone differed significantly only on PANSS positive scores over six months (p < 0.05), total SWN-K scores at three months (p <0.05), SWN-K-self control scores at three (p <0.01) and over six months (p <0.05), and SWN-K-physical functioning scores at 3 (p <0.001) and over 6 months (p <0.05); [d] Insight was rated on the GP 12 item of the PANSS

** P < 0.05 ** P < 0.01*** P < 0.001**** P < 0.00001*

3.9 Olanzapine and Risperidone

The number of significant differences with FGAs was more for the olanzapine group, and their pattern was more or less similar to the SGA-FGA differences. Differences between the risperidone and the FGA group were fewer and mainly restricted to the SWN-K and QOL scores.

3.10 Correlates of Attitudes, Subjective Well-being and Quality of Life

Three separate stepwise multiple regression analyses were carried out for the whole sample to examine the correlates of attitudes, subjective well-being and QOL. For these regression analyses, demographic variables (age, gender, marital status, education, occupation, income and residence), clinical variables (duration of illness, antipsychotic dose, PANSS, G12, UKU, AIMS and BARS scores) and subjective parameters (two of the three parameters of attitude, well-being and QOL as applicable) were treated as independent variables, while average 6-month scores on each of the three aspects of subjective experiences constituted the dependent variables.

DAI-10: Higher age (14%) and greater total SWN-K scores (6%) emerged as the significant correlates of DAI-10 scores, contributing to 20% of the variance in these scores ($F = 8.5$; $P < .01$).

SWN-K: Greater WHOQOL-Bref scores (38%), higher DAI-10 scores (9%), lower average PANSS scores (6%), and higher G-12 scores (3%) were the principal correlates of SWN-K scores, and explained 56% of the variance in these scores ($F = 20.9$; $P < .001$).

WHOQOL-Bref: Higher SWN-K scores (37%), employment (9%), and total UKU scores (5%) contributed to 51% of the variance in WHOQOL-Bref scores ($F = 25$; $P < .001$).

4. DISCUSSION

Whether patients on SGAs have more positive subjective experiences of taking these medications than those on FGAs has been a matter of some controversy [2-9,15,16]. Though initial clinical trials seemed to suggest a trend towards superiority of SGAs in this regard [2-4,15-18], this assumption has not been consistently supported by empirical data and meta-analyses [19]. The issue of differences between FGAs and SGAs on these parameters does not seem to have been resolved despite recent large-scale effectiveness studies; while some of these have not found any differences in patients' attitudes, subjective well-being, or QOL between SGAs and FGAs [5,6,20-22], others have reported greater and clinically relevant improvement on these parameters among patients on SGAs [7,8,23-25]. Moreover, patients seem to prefer SGAs despite side effects such as weight gain or sexual dysfunction [9]. Studies comparing individual SGAs on attitudes, subjective well-being and QOL are similarly inconsistent; while some have found one or the other medication (mostly olanzapine) to be better [7,8,13], most others have not been able to find any differences between different SGAs [3,4,7,18].

However, the present study found a significantly favourable profile of subjective experiences among patients on SGAs, including better attitudes to treatment as well as improved QOL, and, particularly marked differences in subjective well-being between SGAs and FGAs. Though olanzapine appeared to contribute more often to these differences between SGAs and FGAs, there were very few differences on different aspects of subjective experiences between olanzapine and risperidone when these two SGAs were compared directly.

Then again, these findings need to be interpreted with caution because of certain methodological concerns. These included the small numbers involved, particularly in the individual SGA groups. The duration of the study was also relatively short. Moreover, patients were drawn from a single centre and all assessments were non-blind. The differences between FGA and SGA groups on demographic and clinical factors could have biased the findings in favour of SGAs as well. Patients on FGAs were more likely to belong to low-income families, which could have affected their QOL. However, (as mentioned above) these differences could have been an artefact of prescribing practices and income levels did not correlate with any of the subjective parameters on regression analyses. Additionally, patients on FGAs had higher number of past relapses and hospitalizations, were on longer periods on treatment with antipsychotics, and the PANSS-positive scores were higher in this group at baseline. Then again, none of these indicators of severity and chronicity correlated with the three subjective experience variables, apart from average PANSS scores which explained about

6% of the variance in subjective well-being scores. Thus, differences between the two antipsychotic groups on severity and chronicity were not likely to have contributed a great deal to the differences in subjective parameters.

Alternatively, the more favourable profile of subjective experiences among patients on SGAs could be attributed to other causes. In the current study, while differences between the two groups were not marked in the 3 months prior to intake, over the subsequent 3 months scores on all 3 subjective parameters continued to improve among patients on SGAs, whereas they declined in the FGA group. It has been noted earlier that, since these subjective parameters vary with time, longitudinal comparisons such as the present one, are more likely to reveal differences between the SGAs and FGAs, than cross-sectional studies [7,8,13,26,27]. Moreover, the sensitivity of the instruments used could have also made a difference. While the DAI-10 and the SWN-K have proved to be valid and sensitive tools [13,27,28], there is some evidence to suggest that patient-rated QOL instruments (such as the WHOQOL-Bref) are more sensitive measures of QOL, than clinician-rated ones used in some of the earlier studies [4,18]. Differences on subjective well-being were the most marked, and were present on all four subscales of the SWN-K. This pattern is thought to reflect differences between SGAs and FGAs in social functioning, effect on depressive and negative symptoms, neurocognition and the lack of motor symptoms [7,13,27]. The differences on QOL and attitudes essentially mirrored these differences and were similar to the findings of other SGA-FGA comparisons using the WHOQOL-Bref [4]. Although differences on the DAI-10 were less obvious, they suggested that a weighing of positive and negative aspects of medications and the need for relapse prevention were the attitudes that best discriminated patients on SGAs from those on FGAs. Finally, correlates of subjective experiences also indicated the possible reasons for the differences between the two antipsychotic groups. Firstly, there were significant correlations between the three indices of subjective experience. Such relationships between attitudes, subjective well-being and QOL have been found in several [1,2,18,27,29,30], though not in all studies [13]. This suggests that though these 3 aspects of subjective experience are relatively independent constructs, there is some degree of overlap between them [12,27]. Symptom-severity (based on total PANSS scores) was associated with lower subjective well-being scores. This was similar to other studies, which have found severity of illness to be correlated with subjective well-being scores; however, such correlations have often been modest and only with negative or depressive symptoms in most of these studies [2,12,13,31]. Greater awareness of illness has been found to be associated with improved attitudes and QOL in other studies [1,32,33], but was only associated with enhanced subjective well-being in the present study. Side effects were associated with poorer QOL in the present study. The majority of earlier studies have found side-effects to adversely affect not just the QOL of patients, but also their subjective well-being and attitudes toward medications [3,4,7,9,29-31]. However, most of them have focused on the negative impact of extrapyramidal side-effects on subjective experiences. In keeping with recent literature the profile of side-effects in this study indicated that not just extrapyramidal side-effects, but also postural hypotension, negative mood effects, sedation and lethargy discriminated FGAs from SGAs [34-36]. Additionally, the findings of this study suggested that weight gain and sexual dysfunction could have a similar adverse influence on subjective experiences among patients on SGAs, since they were more common in this group. This reflects the growing literature on the association between metabolic and sexual side-effects and compromised QOL among patients on SGAs [4,35-37].

5. CONCLUSIONS

Despite its methodological limitations, the results of this study suggested that patients on SGAs had a more favourable profile of subjective experiences with treatment in terms of attitudes, subjective well being and QOL than those on FGAs, over 6 months of treatment and follow-up. These differences seemed to be determined mainly by differences in symptom-severity and side-effects, which emerged between the groups over the course of follow-up. Accordingly, these findings imply that antipsychotic treatment, which is effective in ameliorating symptoms, enhancing patients' awareness of the illness and minimising side-effects is more likely to be associated with favourable subjective experiences among patients. Attempting to improve the subjective experience of treatment among patients is of particular significance, because among the many factors which determine adherence with treatment, they represent the most suitable targets for intervention [1-3]. Though much of the

extant literature finds no differences in subjective experiences between patients on SGAs and FGAs, it appears that there is still scope for further methodologically sound research in this area of immense clinical relevance.

ETHICAL APPROVAL

Ethical approval was obtained from the Research and the Ethics Committees (IRB) of the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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