The Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) Study: Baseline Clinical and Functional Characteristics and Antipsychotic Use Patterns in Turkey*

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ABSTRACT:

The intercontinental schizophrenia outpatient health outcomes (IC-SOHO) study: Baseline clinical and functional characteristics and antipsychotic use patterns in Turkey

Objective: In this study, our main objective is to describe the baseline findings of the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study in Turkey.

Method: The IC-SOHO study is an ongoing prospective, three-year non-interventional observational study of schizophrenia treatment, clinical characteristics and mental health services utilization in Turkey. The study population consisted of non-hospitalized patients who had started or switched into a new antipsychotic.

Results: The baseline findings of the IC-SOHO study (Turkish Subset) appear to reflect clinical features of schizophrenia patients in Turkey (n=692). Overall the patients were moderately to markedly ill (66.7%) and already overweight (46.4%) and obese (7.3%) when they entered the study. Functionally the majority of patients were not involved in social activities, could not care for themselves and were unemployed. Substance and alcohol dependency/abuse was not a major problem in this study population. The majority of patients at baseline were treated with an antipsychotic (86.1%) and oral typicals antipsychotics were the most commonly used drugs 6 months prior to the study. Sexual adverse events were the most frequently reported amongst the surveyed adverse events and overall compliance/adherence was moderate.

Conclusion: The baseline IC-SOHO findings highlighted various clinical and functional characteristics and antipsychotic use patterns in a group of schizophrenic outpatients in a naturalistic setting in Turkey. Once completed, the IC-SOHO study will add further information to this knowledge base.

Key words: schizophrenia, outpatients, antipsychotic agents, clinical characteristics, functional characteristics, IC-SOHO

Bull Clin Psychopharmacol 2004;14:132-142

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* This paper is similar to two other papers reporting aspects of the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) Study. The other 'Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) Study: Baseline Clinical and Functional Characteristics and Antipsychotic Use Patterns in the Central and Eastern Europe (CEE) Region' has been accepted for publication in Psychiatria Danubina. The other paper reporting on the African and Middle Eastern Area (AMEA) results has been accepted for publication in the South African Psychiatry Review.

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Kabul tarihi / Date of acceptance: 15 Ağustos 2004 / August 15, 2004

Introduction

The emphasis in evaluating drug treatment benefits is shifting from 'efficacy' to 'effectiveness'. Efficacy is defined as the desirable effect of an intervention, where effectiveness is the extent to which a product works in the patients to whom it has been offered. This meaning is slightly different from 'efficacy', which can be measured in those who were actually treated. 'Efficacy' relates to explanatory studies and 'effectiveness' to pragmatic studies (1). Therapeutic efficacy (effectiveness) is often studied with observational surveys of patients whose treatments were selected nonexperimentally. New methodological strategies are being developed that may improve the quality of observational studies, often based on the design principles and patient assembly procedures of the randomised trial (2).

Randomised clinical trials (RCTs) have been considered the 'gold standard' for establishing safety and efficacy due to a strong internal validity. Given a set of assumptions RCTs are designed to achieve a valid comparison of alternative treatments. The process of randomisation reduces bias in order to compare and equalize treatment and control groups with respect to all variables except the assignment of treatment. In this way a causal relationship between treatment and outcome can be established. RCTs are usually conducted under strict protocol and regulatory guidelines. For these reasons RCTs have been criticized

for lacking in external validity. This implies that results obtained from RCTs can often not be generalized to the actual effects seen when the drug is used in clinical practice (3,5).

RCTs have been the cornerstone for pharmaceutical drug development as well as the eventual drug registration and regulation process. The call for new methods for the monitoring of drug safety, efficacy and effectiveness has gone to the extent where the discontinuation of phases III and IV of placebo controlled trials and the enhancement of the use of post marketing surveillance have been suggested (4). When a drug is commercialised the question turns from one of safety and efficacy ('can it work'?) to one of effectiveness ('does it work'?) (3).

Observational studies examine natural variations in exposure to treatments and describe associated outcomes (1). The major criticism against observational studies is that for potential allocation bias and risk adjustment (5). In order to control for these factors observational studies can be designed with rigorous methodology and statistical methods that mimic those of clinical trials (7,9). Recent studies conducted across multiple therapeutic areas comparing RCTs and observational study findings found no major differences among estimates of treatment effects (6-8,10-14). In conclusion, both RCTs and non-randomised (observational) studies can provide complimentary evidence.

Increasingly more observational studies are being published assessing the treatment effects of the atypical antipsychotics in schizophrenia: clozapine (15), sertindole (16,22), risperidone (17-20,22) and olanzapine (18-22). Brambilla et al (15) reviewed 50 experimental and observational studies evaluating clozapine-treated subjects in treatment-resistant schizophrenia. They reported that most studies enrolled a small sample of patients (less than 50 patients) and were retrospective in design. Overall the vast majority of RCTs and observational studies (both prospective and retrospective in design) were of short duration (less than 8 and 12 weeks respectively). Observational trials also adopted implicit criteria for patient selection.

New observational studies are thus needed incorporating a larger sample group, being prospective in design, longer in duration and with explicit selection criteria. The Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study has been initiated to address this need. The IC-SOHO study was designed to assess antipsychotic medication therapy outcomes for schizophrenia patients in actual clinical practice. This paper reports the IC-SOHO study baseline findings in Turkey. The primary objective of the analyses reported here was to determine the antipsychotic usage patterns of schizophrenia patients in an outpatient setting. In addition, the baseline clinical and functional characteristics were examined in these patients.

Material and Methods

Study Design and Patients:

The IC-SOHO study is a longitudinal (3-year), non-interventional, prospective, observational, open-label study of the treatment of schizophrenia in Turkey. The primary objective of the study is to understand the comparative outcomes associated with antipsychotic medication therapies initiated or changed during outpatient treatment for schizophrenia. The secondary objective of the study is to understand the pharmacological treatment patterns for schizophrenia. The study is currently being conducted in 25 countries from 4 continents. This article will report on a subset of results taken from the larger Intercontinental SOHO study.

Participating psychiatrists offered enrolment at their discretion to patients who met the following criteria: (1) present within the current course of care, (2) will initiate or change antipsychotic medication for the treatment of schizophrenia (ICD-10 or DSM-IV Criteria), (3) will initiate or change the antipsychotic medication in the outpatient setting or in the hospital when the admission was planned for the antipsychotic initiation or change, (4) at least 18 years of age, and (5) will not be simultaneously participating in a different study that includes a treatment intervention and/or an investigational drug. Patients were included regardless of whether the new antipsychotic drug substituted a previous medication or was an addition to existing treatment and regardless of the reason for the treatment change. Newly diagnosed and neuroleptic naïve patients were also included in the study. All patients were informed about the study and at least

oral consent that is documented in the clinical report forms were required to enable the release of their personal medical information. There was not any local ethical review regulation for observational studies when the study has been implemented in Turkey.

The IC-SOHO study was designed to provide two patient cohorts of approximately equal size: the first group of patients who were initiated or changed to olanzapine, and the second group of patients who were initiated or changed to non-olanzapine antipsychotic therapy.

While each participating psychiatrist was requested to enrol at least one block of 10 patients, with 5 patients in each cohort, a minimum number of patients per psychiatrist was not required. This was done by allocating alternate patients to each cohort in order to provide approximately equal numbers in each cohort. Investigators were instructed to make treatment decisions independent of the study and then evaluate whether patients were eligible for inclusion based on entry criteria and the alternating structure of enrolment..

Data were collected on a standardised collection form and took approximately 15 to 20 minutes to complete. The data collected were similar to those usually collected in routine clinical practice, including patient demographics, medical resource use, clinical, functional and social status, antipsychotic and other co-prescribed medication use, tolerabilitypatient and physician reported compliance, sexual function, alcohol and substance abuse, and quality of life. Tolerabilty data was collected by using an adverse event questionnaires that included a list of the most frequently observed ones with typical and atypical antipsychotics (EPS, TD, hyperprolactinemia symptoms/sexual dysfunction, and weight and height measurements). The missing data of the respective cases were not included in the analysis. However, investigators continued to use the standard procedures to make reports to the company the adverse events that were not listed in the clinical report forms. As SOHO study is an observational study and measurements as like serum lipid/glucose levels would require laboratory test that are out of the standart practice in Turkey, this laboratory information were not collected. Clinical status was assessed using the Clinical Global Impression - Severity (CGI-S) Scale (24). For the brevity purpose of this study the schizophrenic symptom domains measured on the CGI-S included overall symptom severity. According to the logic used in other psychiatric disorders (25), specific, single-item scales to assess positive , negative depressive symptoms and cognitive symptoms have been developed based on the CGI scale. Health-related Quality of Life was assessed using the EuroQol (EQ-5D) scale consisting of five items and the Visual Analogue Scale (23,24).

Statistical Analysis:

The first step in the evaluation of the study data was to use exploratory and descriptive analyses to gain an understanding of the qualitative and quantitative nature of the data collected and thus also the characteristics of the sample studied. Part of the baseline analysis described patient characterists by sociodemographic, clinical and functional status for the total group of patients as well as by gender. For all the groups parameters means and percentages were calculated. A Cochran-Mantel-Haenszel test was used to calculate differences between the categorical variables. Weighted Kappa test is used to determine any evidence of agreement between two ordinal variables. Chi-squared test and Fisher Exact test are used to detect any evidence of an association between two categorical variables.

Results

A total of 692 patients were enrolled in the study at baseline. Patients from seven geographic regions of Turkey were enrolled in the study (Table 1). The study population consisted of 409 (59,1%) male and 283 (40,9%) female patients with a mean age of 33,8 (SD: 10,6) years (Table 2).

Table 1. Enrolment by Regions in Turkey

Regions	n (%)
Marmara	186 (27)
Central Anatolia	200 (28)
Black Sea	122 (18)
South Eastern Anatolia	49 (7)
Mediterranean	30 (4)
Eastern Anatolia	25 (4)
Aegean	80 (12)
TOTAL	692 (100)

Table 2. Patient Characteristics (Turkish Subset)

Characteristic	
Number of Patients Enrolled (%)	692 (100)
Gender (%) Male	409 (59.1)
Female	283 (40.9)
Mean Age (SD)	33,8 (10,6)
Percent of patients neuroleptic naïve	13,9
CGI overall symptoms: mean (SD)	3,7 (1,08)
CGI positive symptoms: mean (SD)	3,5 (1,47)
CGI negative symptoms: mean (SD)	3,1 (1,40)
CGI cognitive symptoms: mean (SD)	2,8 (1,39)
CGI depressive symptoms: mean (SD)	2,4 (1,45)
Patients who have attempted suicide: (%) (n=160):	
Ever (%)	15,7
Subjects with suicide attempts in the previous 6 months (%)	5,8

mostly with positive (CGI-S mean score 3,5), negative symptoms (CGI-S mean score 3,1) (Table 2). Females had significantly more positive symptoms (Table 3) than the male group, and males tended to have slightly more negative symptoms (Table 3). Cognitive symptoms were less severe with depressive symptoms the least severe (Table 2). Both cognitive (Table 3) and depressive (Table 3) symptoms appear to be equally distributed amongst males and females. A good proportion of patients (15,7%) reported that they have attempted suicide in the past, with 5,8% of the attempts being in the last 6 months prior to the baseline visit (Table 2).

Table 3. Symptom Severity (%) by Gender (Turkish Subset)

	Normal	Borderline	Mild	Moderate	Marked	Severe	Most
Severe							
Overall Symptoms							
(p=0.1075)*	0	2,2	10,0	34,3	33,8	16,4	3,2
Male	0,4	2,8	9,6	23,4	41,1	17,7	5,0
Female							
Positive Symptoms							
(p=0,0007)*	4,2	8,1	15,0	22,5	26,5	18,6	5,1
Male	2,8	5,0	9,2	21,6	30,1	22,0	9,2
Female							
Negative Symptoms							
(p=0.0390)*	2,9	9,3	16,6	30,6	24,4	12,2	3,9
Male	5,3	12,8	16,3	29,8	21,6	12,1	2,1
Female							
Cognitive Symptoms							
(p=0.3556)*	5,4	11,8	22,5	29,2	20,6	9,6	1,0
Male	8,9	12,8	18,9	28,5	21,0	9,3	0,7
Female							
Depressive Symptoms							
(p=0.0090)*	10,0	16,4	21,8	24,0	18,6	8,1	1,0
Male	14,2	17,8	22,4	27,4	12,1	6,0	0,0
Female							

*Cochran Mantel-Haenszel Mean Score Test, p<0,005

Clinical Characteristics

The CGI-Severity scores ranges from 1 to 7, with 1 being 'normal/not at all ill', and 7 'among the most severely ill'. The CGI-S overall mean score was between mild to moderately ill (Table 2). Males tended to be more moderately ill while the females tended to be more markedly ill at baseline (Table 3).

Symptom severity (CGI-S) was also individually measured for the four symptom clusters associated with schizophrenia. At baseline, patients presented

Functional Characteristics

In terms of functional status, one third of patients were involved in a relationship (married or in a permanent relationship) with a spouse or partner, and more than half had no social activities with friends or family in the 4 weeks before the study (Table 4). Most of the Turkish-SOHO patients were in residence as a dependent family member, (Table 4). The rate of unemployment was also high for the patients in the Turkish-SOHO study. (Table 4). Statistically significant

Table 4. Work Status and Social and Living Conditions in the past 4 weeks (%) (Turkish Subset)

Employment	
Employed	22,8
Able but no job	16,9
Unable	43,9
Social Status	
Relationship*	33,4
Socially Active	45,2
No socializing	54,7
Living Conditions	
Independent	27,9
Dependent	67,6
Supervised	2,7

*Relationship=married or in a permanent relationship

differences were observed between males and females in terms of employment status and alcohol abuse in the past; more males (28,6%) were employed than females (14,6%; p<0.0001) and more males (8.1%) suffered from alcohol abuse than females (0.,4%; p<0.0001)

Patient behaviour was also assessed at entry into the IC-SOHO study. The vast majority (97,5%) of Turkish patients with schizophrenia reported that they never suffered from or have been diagnosed with substance dependency/abuse in the past. Only a few percentage of the patients reported that they suffered from or have been diagnosed with substance dependency/abuse in the past. The rate of current substance dependency/abuse diagnosis was also very low. A similar pattern is observed for alcohol dependency/abuse (Table 5).

Table 5. Patient Behaviour (%) (Turkish Subset)

Antisocial Behaviour (Past 6 months)	
Arrested/Jailed	17,2
Verbal/Physical Aggression	39,4
Victimized	1,3
Substance Abuse	
Never	97,5
In the past	2,5
Current	0,7
Alcohol Abuse	
Never	95,1
In the past	4,9
Current	0,4

Finally Antisocial behaviour was recorded. Almost forty percent of the patients reported that they exhibited verbal or physical hostility/aggression in the past 6 months. Furthermore, 17,2% of the schizophrenic patients were compulsorily admitted, arrested or spent at least one night in a jail in the past 6 months. A minority of schizophrenic patients has also been a victim of violent crimes (e.g. robbery, mugging, assault or rape) in the past 6 months (Table 5).

Patient care and resource utilization

Information related to outpatient psychiatrist visits and hospital admissions were retrospectively collected with reference to the last 6 months before enrolment. One third of the patients were at least hospitalised once during the 6 months The mean number of schizophrenia related hospitalisations for the Turkish-SOHO patients was 1,98 (S.D: 2,18) and average stay in hospital was 39,4 days (S.D: 31,47). The median number of outpatient psychiatrist visits were 4,0 and two thirds of the patients visited a psychiatrist at least one to six times (Table 6).

Table 6. Schizophrenia related hospitalisations and psychiatrist visits (Turkish Subset)

Schizophrenia related admissions*	
Number of patients who had schizophrenia related admissions (%)	206 (35%)
Mean number of schizophrenia related admissions (S.D)	1,98 (2,18)
Median	1,00
Days of schizophrenia related hospitalisation	
Mean (S.D)	39,5 (31,47)
Median	30,0
Outpatient visits(last 6 months)	
Number of patients who had outpatient visits	558
Mean (S.D)	8,98 (13,31)
Median	4
% patients visiting a psychiatrist 1-6 times	67.7
% patients visiting a psychiatrist 7-30 times	23.2
% patients visiting a psychiatrist ≥31 times	5.9

*(at least one overnight stay, but not in emergency room)

Antipsychotic Drug Use

Table 7 summarizes the pattern of antipsychotic and concomitant drug use. At the Turkish-SOHO

baseline visit more than half the patients were being treated with a typical oral antipsychotic for the last six months. A further one quarter of the patients were on a depot typical antipsychotic. Conversely half of the patients was receiving an oral atypical antipsychotic agent while 18,3% of the patients was neuroleptic naïve.

Table 7. Pattern of Antipsychotic and Concomitant Drug Use (%) at enrollment (Turkish Subset)

Antipsychotics	
Oral Typical	55,2
Depot Typical	24,6
Oral Atypical	48,8
No Antipsychotic	18,3
Concomitant Drugs	
Anticholinergics	39,2
Antidepressants	8,7
Anxiolytics/Hypnotics	9,2
Mood Stabilizers	5,2
None	49,4

In this SOHO sample the daily starting mean doses of the most frequently prescribed antipsychotics were similar to what has been recommended by the manufacturers for schizophrenic outpatients (Table 8).

Table 8. Daily starting dose of most frequently prescribed antipsychotics as monotherapy (Turkish Subset)

Antipsychotics	n	Daily Starting Mean Dose (S.D) mg	Daily Starting Dose Median&Mode
Clozapine	35	194 mg (202)	100&25
Haloperidol	15	16.5 mg (9,1)	15&10
Olanzapine	304	13 mg (5.3)	10&10
Risperidone	90	5 mg (1.9)	4&4
Amisulpride	10	404 mg (179)	400&400
Quetiapine	45	348 mg (196)	400&400

Concomitant medications upon entry into the study were also recorded. While almost half of the patients were not on any concomitant medication. Anticholinergics were most commonly used concomitant medication followed by anxiolytics/ hypnotics, antidepressant and mood stabilizers (Table 7).

Weight was recorded and body mass index (BMI) was calculated for all patients that entered the study (Table 9). More than half the patients enrolled in the Turkish-SOHO study were already overweight or obese.

Table 9. Body Mass Index (%) (Turkish Subset)

Mean BMI (S.D) kg/m^2	24.73(3.89)
Underweight (BMI<19)	4,4
Normal (19=<BMI<24)	41,9
Overweight (24=<BMI<31)	46,4
Obese (BMI>=31)	7,3

When patients entered the IC-SOHO study an assessment was made regarding current adverse events associated with antipsychotic drug therapy The most frequently reported adverse event was that of loss of libido (46,8%, n=635), followed by impotence and sexual dysfunction (39,9%, n=579), menstrual disturbance and amenorrhoea in woman (36,2%, n=260), extrapyramidal symptoms (dystonia/akathisia/ parkinsonism) (34,6%, n=688), galactorrhoea (4,9%, n=506), and the lowest reported adverse events tardive dyskinesia (3,5%, n=688) and gynocomastia (2,5%, n=550). Some patients did report multiple adverse events resulting in the total percentage being 165,9%. It is also recognized that patients being treated with neuroleptics medication might have other side-effects not recorded in the IC-SOHO study. The focus on the typical and atypical antipsychotics has been weight, EPS, sexual dysfunction and prolactin therefore these have been selected and included in the study.

A detailed additional analysis was performed to understand the attributes of the most frequently reported sexual adverse events. There was a significant increase in the frequency of sexual adverse events in patients on antipsychotic treatment. Antipsychotics can be classified as prolactin sparing (clozapine, olanzapine, quetiapine, ziprasidone) and prolactin elevating (typical antipsychotics, amisulpiride, risperidone) (37). Albeit reaching statistical significance, all reported sexual adverse events were at least 1,5 times more frequent with prolactin elevating treatment (Table 10).

Sexual adverse events were already present in early and late phases of the illness at similar rates and were not affected by duration of the illness (Table 11).

Compliance/adherence in the 4 weeks prior to the baseline visit was recorded from both the psychiatrist as well as the patients' point of view (Table 12). The results were very similar with half of the patients and psychiatrists reporting that the patient almost always

Table 10. Baseline sexual dysfunction by prior antipsychotic use

	Amenorrhea	Galactorrhea	Gynecomastia	Loss of libido	Impotence
Overall	36.20%	4.90%	2.50%	46.30%	39.90%
Without antipsychotic treatment	11.10%	1.40%	1.80%	30.10%	22.90%
With antipsychotic treatment	45.70%	6.30%	2.80%	53.70%	46.70%
Prolactin-sparing (PS)	25.90%	1.80%	1.60%	37.10%	28.60%
Prolactin-elevating (PR)	49.10%	7.20%	3.10%	56.70%	50.00%
PR/PS	1.9	4	1.9	1.5	1.7
Without vs with antipsychotic treatment (p)	<0.001	0.022	0.496	<0.001	<0.001
PRL-sparing vs PRL-elevating (p)	0.026	0.123	0.700*	0.003	0.002

*Fisher Exact chi-square test, other tests are chi-square tests, p<0.005

Table 11. Recent diagnosis of schizophrenia by sexual dysfunction

	Time of diagnosis				
	<1 year		>1 year		p value*
	n	% Present	n	% Present	
Loss of libido	131	45,8	405	43,8	0,3911
Impotence/ Sexual Dysfunction	128	35,9	402	35,5	0,1719
Patient reported sexual dysfunction	130	36,2	407	34,9	0,6096

*Cochran Mantel-Haenszel mean score test, p<0.005

Table 12. Compliance to Prescribed Antipsychotic Medication (In the past 4 weeks for patients already undergoing antipsychotic therapy) (Turkish Subset)

	Psychiatrist's view	Patient's report
Almost Always	52,3	56,1
Half the Time	14,7	11,9
Almost Never	6,1	5,7

complies/adheres to antipsychotic medication treatment. This amount decreased to 11,9% of patients and 14,7% of psychiatrists reporting that their patients only complies/adheres to treatment about half the time. Finally 6,1% of psychiatrists reported on their patients and 5,7% of patients admitted that they almost never comply/adhere to their antipsychotic medication. The weighted kappa test showed a strong and significant correlation between the patient's view and the physician's view of compliance (K=0,85; p<0,0001)

Finally psychiatrists were requested to record the reasons for changing or initiating antipsychotic therapy at the baseline visit prior to continuing with the study .Almost two thirds (60,4%) of the psychiatrists reported a lack of or incomplete effectiveness with previous antipsychotic medication. This was followed by intolerability to previous antipsychotic medication (29,5%) and lack of or incomplete compliance/ adherence with previous antipsychotic medication at 14,8%. Patients requested a change in medication in 11,3% of cases. These findings were similar to those reported in other studies (27,28).

Physicians most frequently preferred to change medication for patients using quetiapine due to inefficacy .Haloperidol was the antipsychotic most frequently changed to others because of intolerability. The lack of efficacy and patient request for change of therapy was most frequently attributed to chlorpromazine (Figure 1).

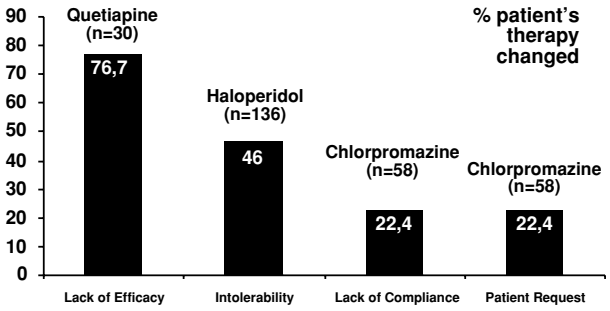

Figure 1. Reasons for therapy change by most frequently attributed drug

Discussion

The IC-SOHO study is a prospective, three-year non-interventional observational study of schizophrenia

treatment, clinical and functional characteristics. This report includes a subset of Turkish results. A total of 692 patients were enrolled from seven regions in Turkey. To our knowledge, this is the largest schizophrenia study done in Turkey to date. The Turkish SOHO study baseline results provides useful information about clinical and demographical characteristics of patients with schizophrenia and how they are treated in actual practice in Turkey. The ratio of males to females as well as the mean age of patients enrolled in the study was consistent with prevalence-based samples of individuals with schizophrenia treated in outpatient facilities (20,25,27-31). However, the mean age of the patients enrolled in Turkish sample was lower than the European SOHO sample (32) that may be also a reflection of the relative younger population of Turkey.

The baseline CGI-Severity scores of the patients enrolled in the Turkish-SOHO study were generally lower than those reported in other studies (20,28,29). This might be understandable in the light that the patients enrolled in the study consisted of non-hospitalised schizophrenic patients and by nature of this group of patients would be less severely ill than those hospitalised. Other studies do not report a difference in overall symptom severity by gender.

The symptom severity for the four symptom clusters associated with schizophrenia follows the same pattern as reported in other similar studies. Positive and negative symptoms are usually more severe than cognitive and depressive symptoms, with the depressive symptoms the least severe (30). The results of studies about specific symptom clusters by gender are contradictory (27,39,42-44). In most of the studies negative symptoms tend to be more prevalent in males (27) and positive symptoms are equally distributed between two genders in contrast with our results. Many other factors (age, social status, current treatment setting, duration of illness) between two groups explain the differences between this and previous studies (44). Schizophrenic patients remain at risk for suicide attempts, even though they are being treated with antipsychotic medication with improvement in clinical symptoms.

The Turkish-SOHO sample reported here had considerable functional impairment on various levels. Although more than 80% of the patients were already on active antipsychotic treatment more than half had no social activities with friends or family and only a third of the study population were involved in a relationship. These results are slightly higher than previously reported (30,31). Only about a quarter of the Turkish-SOHO patients could care for themselves in independent living conditions and is again consistent with other results (31). As can be expected from a debilitating disease like schizophrenia about two-thirds of the study group was in the care of a family member or supervised residence. Although the proportion of patients that were employed was relatively high (22,5%) than generally reported (30,31), it must be remembered that this figure includes paid and unpaid employment (e.g. sheltered programmes and volunteer work).

Generally substance and alcohol dependency/abuse has been reported to be high in schizophrenic patients (27). The fact that over 95% of patients in this study reported that they never suffered from or has been diagnosed with substance and alcohol dependency/abuse might be understandable in terms of the cultural and religious characteristics of the sample. On the other hand this high figure might be an underestimation of the problem by the study. However, previous naturalistic study with Turkish schizophrenic patients showed similar alcohol dependency/abuse rate (40). A further explanation of the finding can either be due to denial on the part of the patients regarding the extent of their problem, or a lack of insight into the problem as well as its dangers and consequences.

Agitation, aggression and hostility, both verbal and physical, have typically been associated with schizophrenia (29). It is therefore not surprising that one third of the patients included in the study reported this kind of behaviour. More so, over fifteen percent of the patients also recognized that they were compulsorily admitted, arrested or spent at least one night in a jail because of this behaviour.

Comprehensive and recent acceptable schizophrenia treatment guidelines recommend the use of second-generation (atypical) antipsychotics both for first-line treatment and in patients where a typical antipsychotic has failed (36,37). This was not found to be the situation at baseline in this Turkish-SOHO patient group where 80% of the patients still

received either an oral or depot typical agent. This pattern of antipsychotic use might also be typical of countries in the developing world where there are also financial implications. It was however encouraging that a third of the patients received a newer atypical agent which might indicate a shift in prescribing patterns. At baseline a significant group of patients (18,3%) were also neuroleptic naïve opening the possibility to study these patients.

Due to the complexity and symptom extent of schizophrenia as well as the often-emergent side-effect profile of currently used antipsychotics these patients are commonly prescribed adjunctive medication (19,20,29,32,33). This phenomenon was also confirmed in the Turkish-SOHO baseline data where more than half of the patients received concomitant medication and where the anticholinergics comprise the majority (39,2%) of those used. This high rate of anticholinergic use can be understood in the light of the high rate of typical antipsychotic usage in this sample where the old antipsychotics have been associated with a higher rate of extra-pyramidal adverse events. This is in line with published data (19,20,29,32,33). The concomitant use of anxiolytics/hypnotics, antidepressants and mood stabilizers were much less, reflecting the predefined study population (e.g. non-inclusion of schizoaffective and/or bipolar disorder) (33).

In contrast to the existing literature the most frequent reported adverse event in this Turkish-SOHO sample was loss of libido in almost half the study patient group (20,28). Impotence, sexual dysfunction (39,9%) and menstrual problems (36,2%) were also reported at much higher rates as previously published (17,20,28). A recent review about sexual adverse events of antipsychotics highlights the neglect of reporting in clinical practice and in research, as well as relatively low rates of sexual adverse events with prolactin sparing antipsychotics (41). Extrapyramidal symptoms (dystonia/akathisia/parkinsonism) have been the focus in antipsychotic treatment and rates reported in just over a third of patient in this study is compatible with the literature (19,20,29). Although this data does not differentiate emergent EPS between the typical and atypical groups of patients, it is expected that the atypical group of patients should have a lower incidence of reported EPS (18,20,28,29)

Weight gain is an important and potentially manageable problem in patients being treated with antipsychotics. Weight gain can either be related to the disease and inherent inactivity of schizophrenic patients or on the other hand to the antipsychotic medication itself. Weight gain on antipsychotics with a possible differentiation between the various groups of drugs has been repeatedly reported in many studies (29,34). The Turkish-SOHO results did indicate that more than half of the patients at baseline were either overweight or obese. Due to the nature of the study it was not possible to establish the exact origin of this weight gain.

Compliance/adherence is essential in the medical management of schizophrenia. The Turkish-SOHO baseline data confirms that only about half of treated schizophrenic patients almost always complies/adheres to antipsychotic medication treatment. Good tolerance of medication is often linked to compliance/adherence (18). Medication adverse events are distressing to patients and linked to non-compliance. These adverse events include extrapyramidal adverse events, neuroleptic dysphoria, akathisia, sexual dysfunction, and weight gain (35). Treatment adherence may also be improved by the use of atypical antipsychotics with few perceived adverse events (30).

Conclusions

Although we recognize that naturalistic observational studies may have several limitations, they could also offer new insights. By its nature observational studies can evaluate drug use in everyday clinical practice settings and avoid protocol-induced bias, however unlike in blinded randomised controlled trials, selection and evaluation biases can not be excluded This kind of study can provide clinicians valuable information about the relationship between the patient, the illness and the drug and doing so it can address the needs and concerns of both the patient and the clinician. Naturalistic studies do however not rule out conventional studies (RCTs) that are essential to establish the efficacy and safety of new chemical compounds. The IC-SOHO study thus address other clinical issues in order to achieve optimal clinical stability and patient satisfaction

Patients with schizophrenia from 7 different geographic regions and from different treatment settings (private and public) of Turkey are included in IC-SOHO study in order to maximize the external validity of the data obtained. Although an inter-rater reliability analysis is not performed, internal validity is also warranted by The IC-SOHO study design, its comprehensiveness and size. To our knowledge, this is the largest schizophrenia study done in Turkey to date. Specific clinical and functional characteristics compared to antipsychotic use patterns can produce valuable information in the short and long-term for the optimal treatment of schizophrenia. Specific themes discussed above started emerging from the baseline results that will need further exploration. Ultimately it is hoped that the complete IC-SOHO study will contribute to this knowledge base.

Acknowledgement / Teşekkür: *This study was supported by a research grant from Lilly İlaç Tic Ltd ıirketi in Turkey.*

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