Antipsychotic prescription patterns in Xhosa patients with schizophrenia or schizoaffective disorder

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Abstract
Objective: To examine the degree to which South African physicians use similar treatment guidelines in their prescription of antipsychotic medication. **Method:** Data on the prescriptions for Xhosa patients with schizophrenia and schizoaffective disorder were retrospectively examined to investigate differences between three catchment areas in the Western Cape, especially in terms of clozapine use. **Results:** There was an overall low rate (10.0%) of clozapine use and a relatively high occurrence of polypharmacy (28.6% of 510 patients). There were statistically significant differences between the three catchment areas in terms of clozapine (p=0.002) and haloperidol (p=0.001) use. Valkenberg hospital had the highest number of clozapine prescriptions and the lowest of haloperidol. Prescriptions of depot antipsychotics did not differ between catchment areas. **Conclusion:** Discrepancies in antipsychotic medicine prescription patterns were evident between the examined hospitals. It is becoming paramount for practical implementation of guidelines to be improved in South Africa to address, e.g., low clozapine use and the high frequency of polypharmacy.

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Introduction

Internationally, clinical practice guidelines – such as National Institute for Clinical Excellence (NICE) guidelines[1] and others[2,3] – are widely available for the treatment of mental illness. Although adherence to these guidelines varies[4], their aims are to assist in clinical decision-making and increase the cost-effectiveness of services by reducing unnecessary variations in prescribing practices.[5] In South Africa, mental illnesses such as schizophrenia impose a heavy financial burden on health services[6], but we do not have uniform provincial or national guidelines regulating practices in the treatment of mental illness. We also often have a difference in ethnic background between clinician and patient, a factor that could lead to mistaken assumptions that affect the way in which clinicians adhere to guidelines or make treatment decisions.[7-9] Currently, our standards are international guidelines, which are not specifically adapted to local circumstances.

The aim of this study is to examine the antipsychotic prescription patterns for a population with schizophrenia or schizoaffective disorder, to determine if local practices are comparable with standard international guidelines. In order to limit possible confounding factors an ethnically homogenous group was chosen. We pay particular attention to clozapine prescription as this was at the time of the study the only second generation antipsychotic available to the public service patient population in the Western Cape, where our study took place. We investigated differences between three neighbouring areas in the Western Cape, where we expected treatments to be similar, due to the relatively homogeneous nature of the population.

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Method

Participants

As part of a large Xhosa genetic study taking place between 2002 and 2005[10], 510 subjects were recruited from three ''catchment areas'' in the greater metropole of Cape Town, South Africa. These catchment areas consisted of three hospitals – the Stikland (STH), Lentegeur (LGH) and Valkenberg (VBH) psychiatric hospitals – and their affiliated community healthcare clinics (CHCs). These hospitals form part of one platform of care, namely the Associated Psychiatric Hospitals (APH). Mental healthcare workers from each of these centres were asked to identify all possible participants, who were then screened for suitability based on the following inclusion criteria: (1) diagnosis of schizophrenia or schizoaffective disorder according to DSM-IV criteria[11] and; (2) Xhosa ethnicity (four out of four grandparents reported as of Xhosa origin). Patients were excluded if they had a significant general medical condition.

Data collection

For the original study[10], each subject was interviewed by a psychiatrist or an experienced, trained research sister, using the standardised Diagnostic Interview for Genetic Studies version 2 (DIGS)[12], as well as the Schedule for the Assessment of Negative Symptoms (SANS)[13] and the Schedule for the Assessment of Positive Symptoms (SAPS).[14] To ensure inter-rater consistency over the entire period of recruitment, all participants were assessed by both raters simultaneously during the first year of the study. Each participant was interviewed in their mother tongue, namely Xhosa. The study was approved by the institutional review board of the University of Stellenbosch (97/005).

For the purposes of this study, the DIGS and research folders of all participants were retrospectively examined for demographic details, type, dose and duration of antipsychotic drug prescribed, and the catchment area in which the participant received their treatment. Data were then compared between the three catchment areas, focusing on differences in antipsychotic drug prescription, SANS and SAPS scores. The SANS and SAPS scores of patients using and not using Clozapine were also compared.

General prescription constraints

At the time of collection of study data conventional antipsychotics were the only first line treatment available for prescription to public service patients throughout the Western Cape. Clozapine was the only atypical freely available but due to its side-effect profile is considered to be a third-line treatment (as per international convention), only prescribed for treatment-resistant patients or patients with prominent side-effects on conventional antipsychotics.

Results

Demographics

The demographic structures of participants (n=510) were similar across the three hospitals. Of 510 participants in this study, 426 (83.5%) were male and 84 (16.5%) female. The majority (n=403, 79.8%), had never married, 53 (10.5%) were married, 16 (3.2%), divorced, 18 (3.6%), separated, and 15 (3.0%) were widowed (data on marital status were unavailable for 5 participants). The mean age at interview was 35.0 years (range = 15-70, SD = 11.0), whilst the mean age at onset of illness was 23.3 years (range = 10-55, SD = 6.8). Three hundred and twenty-two (63.1%) participants were receiving a disability grant, 165 (32.3%) were unemployed, 18 (3.5%) were employed, and 1 (0.2%) was a student (data for 4 participants were unknown).

Medication

Fifty-one (10.0%) of the 510 participants were prescribed clozapine, on a mean dose of 318.0 mg (SD = 188.5 mg), at the time of interview. The remaining participants were prescribed as follows: haloperidol 209 (41.0%), chlorpromazine 89 (17.5%), and depot preparation 252 (49.4%). Fluphenazine was the most common depot preparation prescribed (150 or 59.5% of the 252 prescriptions). Zuclopenthixol was used in 64 patients (25.4%) and Flupenthixol in the remaining 38 patients (15.1%).

In those using one or more conventional antipsychotics, the mean dose in chlorpromazine equivalents was 233.2 mg (SD = 220.7 mg). More than one antipsychotic drug was prescribed to 142 (27.8%) of the patients at the time of interview. The most frequently used combination was haloperidol and a depot preparation (n = 77, 54.2%). Of the 51 patients prescribed clozapine, 11 (22.0%) were also prescribed one or more conventional antipsychotic.

Clozapine users – clinical profile

The 51 clozapine users had a mean SANS score of 9.8 (SD = 4.8), and a SAPS score of 7.46 (SD 4.4). Those patients not using clozapine had mean scores of 8.86 (SD 4.1) for SANS and 6.21 (SD 5.1) for SAPS. Clozapine users had significantly higher SAPS scores than the non-clozapine users ($p = 0.013$) but the SANS scores of the two groups were similar ($p = 0.53$).

Comparing the three catchment areas

Overall, 87 (17.1%) patients were receiving their treatment in the STH catchment area. The VBH catchment area consisted of 183 (35.9%) patients, and the LGH catchment area of 240 (47.1%) patients. Thirty-seven (44.6%) of the STH patients were inpatients, 65 (40.9%) of the VBH and 127 (56.7%) of the LGH patients were inpatients. VBH therefore had a significantly lower proportion of inpatients than LGH ($p < 0.05$).

For clozapine and haloperidol prescriptions, there were significant differences between the three catchment areas (Table I). Specifically, VBH had the highest clozapine and

Table I. Main antipsychotic drug prescriptions for Xhosa patients with schizophrenia or schizoaffective disorder, compared between the catchment areas for three psychiatric hospitals in the Western Cape.

Hospital:	*Lentegeur*	*Stikland*	*Valkenberg*
Clozapine***	14 (5.8%)	8 (10.3%)	29 (15.9%)
Haloperidol***	108 (50.2%)	45 (57.7%)	58 (34.7%)
Depot	118 (52.9%)	36 (46.2%)	100 (59.9%)

*** $p < 0.005$
Percentages are the percentage out of each catchment area's total number of participants.
Data were missing for 9-17 patients per hospital

lowest haloperidol prescriptions. Differences in depot antipsychotics use were not significant (p>0.05).

The SANS scores of the three areas were similar, but they differed significantly in terms of SAPS scores (Table II). Patients at LGH had the highest SAPS score, which differed significantly from the scores of VBH patients (post-hoc test: p<0.05). The SAPS scores from STH patients did not differ significantly from either of the other two catchment areas.

Table II. The mean (SD) scores of the Schedule for the Assessment of Negative Symptoms (SANS) and Schedule for the Assessment of Positive Symptoms (SAPS) for Xhosa patients with schizophrenia and schizoaffective disorder, in the catchment areas of three psychiatric hospitals in the Western Cape.

Hospital:	*Lentegeur*	*Stikland*	*Valkenberg*
SANS score	9.09 (3.82)	8.18 (4.4)	8.94 (4.17)
SAPS score*	6.85 (4.98)	6.71 (5.06)	5.47 (5.02)

* p < 0.05

Discussion

This study found an overall rate of 10% clozapine use across three Western Cape hospitals, which is lower than the clozapine rates found in Connecticut, USA – 15%[15] – and Auckland, New Zeeland – 26%.[16] One of the possible reasons for the lower-than-expected rate of clozapine use may be that clinicians in the APH hospitals feel that patients are less compliant when it comes to treatment adherence and regular follow-up. This is an important variable to consider before commencing treatment, as a special feature of clozapine is a requirement of regular leukocyte counts to monitor the risk of agranulocytosis.[17] However, there is no supporting evidence that specifically African patients have poorer treatment adherence rates than patients of other ethnic groups and this possibility requires further research. The low frequency of clozapine use may merely reflect practical implications such as side-effect profile[18], repeated white cell counts and difficulties related to reintroduction of clozapine after discontinuation for longer than 48 hours .

We found a rate of antipsychotic polypharmacy of 28.6% , which compares poorly to studies in New Zealand[16] and the USA[15] that found rates of antipsychotic polypharmacy of 13% and 10%, respectively. Antipsychotic polypharmacy is strongly discouraged in widely-accepted international guidelines, including the NICE guidelines.[1] Polypharmacy may lead to an increased potential for adverse drug effects, unwanted pharmacokinetic drug interactions, and an increase in the cumulative antipsychotic dose increasing the risk of tardive dyskinesia.[2,19]

There were significant differences between the three catchment areas in the use of clozapine and haloperidol. One possible explanation could be that the patients from each hospital differed in their clinical presentations. The patient profiles may differ somewhat between catchment areas, as SAPS scores varied significantly between sites. Interestingly, the lowest SAPS scores were found in VBH patients, which were also the patients with the highest clozapine prescription rates. However, clozapine users overall had significantly higher SAPS scores than non-clozapine users. Part of the reason for this discrepancy may be that clozapine treatment has had an effect in VBH already. These results should be treated with caution, however, as SANS and SAPS scores serve only as proxy markers of actual clinical presentations.

The comparison with international prescription rates, and significant variation within this population suggest a need for improved regulation of treatment through standardized guidelines.

Conclusion

In the interests of mental health care in South Africa, it is becoming necessary for us to implement practical clinical guidelines, and make these readily available in the large variety of settings that characterize this country. An important step is for specialty societies – in our case, the South African Society of Psychiatrists (SASOP) – to brand local guidelines, such as those available at STH, to add the necessary credibility.[21] Local guidelines need to take into account appropriate resource allocation[22], ethnic and racial variations in pharmacokinetics[23,24], patients' personal preferences[9] and the careful monitoring of adverse drug effects.[20] Tools that could enhance the use of these clinical practice guidelines include the provision of a 'clinical practice guidelines summary pocket guide', and clearly visible , 'user-friendly' hospital performance charts and discharge forms on which the reasoning behind decisions are noted.[25] The combination of monitoring and implementation of evidence-based practices is reaching new levels of sophistication, with the introduction of management computer programmes (e.g.[20]) that make it easier to implement guidelines in a structured manner. However, as it can take many years for guidelines to take effect in general practice[26], the time to start addressing this issue, is now.

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