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Tackling myths of common prescribing patterns in schizophrenia amongst Egyptian psychiatrists

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Abstract

Background: There is limited data related to how psychiatrists actually choose amongst different medications, especially in Egypt. Our aim was to survey a sample of psychiatrists regarding common patterns of antipsychotic prescribing practices and review how these vary from the evidence-based. We conducted a qualitative, cross-sectional survey of 124 psychiatrists of different grades from hospitals across Cairo, Egypt. Questions were asked to elicit attitudes towards common antipsychotic prescribing practices and the use of treatment guidelines in schizophrenia.

Results: A total 77.4% participants said they would prescribe atypical antipsychotics as first-line treatment if cost were not an issue, 42.7% said they commonly add anticholinergics from the start with antipsychotics, 50% said they would maintain patients on anticholinergics for as long as they were receiving antipsychotics, 93.5% said they commonly or in some situations combine typical depot antipsychotics with oral atypical antipsychotics, 88.7% said they commonly or in some situations use antipsychotics in small doses for sedation, and 55.6% sometimes add a mood stabilizer to enhance the effect of antipsychotic drugs. Using logistic regression, physician grade significantly predicted whether participants commonly add anticholinergic medication from the start with antipsychotics ($p = 0.001$). Age and gender significantly predicted whether participants sometimes add a mood stabilizer to enhance the effect of antipsychotics ($p < 0.05$).

Conclusions: We demonstrated that several antipsychotic prescribing practices were not evidence-based, yet appeared to be prevalent in a large proportion of participants. A number of demographic and psychiatrist-related factors predicted certain prescribing patterns.

Keywords: Schizophrenia, Antipsychotic, Prescribing, Treatment guidelines, Egypt

Background

Since the emergence of antipsychotics, many expert recommendations and guidelines on the type and the amount of antipsychotic medication to prescribe in schizophrenia have been published to guide physician decision-making [1], yet it seems that prescribing antipsychotic medication is a complex and multifactorial

process subject to a variety of influences at patient, provider, and system levels [2].

Although many clinical practice guidelines for schizophrenia have been published by many countries and organizations, there have usually been discrepancies between the guideline statements and prescription patterns in clinical practice [3–7] with variations in antipsychotic prescribing reported worldwide in the USA [8–11], Korea [3], UK [12, 13], Canada [14], India [15], and the Arab World [16]. These variations include the prevalence of antipsychotics polypharmacy compared to monotherapy, typical versus atypical antipsychotics,

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preference of high-dose antipsychotics or depot antipsychotics, and anticholinergic co-prescribing [17].

A number of studies have examined the impact of patient characteristics on antipsychotic prescribing variations, such as demographic and clinical characteristics as race [6], symptom severity [18], duration of illness [19], or drug-related factors such as the availability and cost in different healthcare settings, the introduction of atypical antipsychotics with improved adverse effect profile, and efficacy or physician-related factors [7] such as order of introduction, ease of use, prescribers' idiosyncratic beliefs, marketing efforts [20], different level of awareness and recognition due to cultural variances, insufficient education regarding the etiology, and management of psychiatric disorders or simply because of differences in diagnosis [21].

The divergence of clinical practices from evidence-based guidelines identifies pressing research questions raised by these variations [20] and leads us to wonder about factors affecting prescribing practices, and why guidelines are followed in some settings but not to others [22].

Surprisingly, to the best of our knowledge, there is limited data related to psychiatrists' decision-making on drug selection and on how psychiatrists actually choose amongst different medications [23], especially in the Middle East in general and Egypt in particular. The limited research done so far points to the fact that current clinical practice in the Middle East differs from clinical recommendations [24].

Lately, this variation in practice has gained attention, partly because of the huge expenditures on antipsychotic medications [20] which is relevant to a country with economic constraints like Egypt. Moreover, it has been suggested that inadequate prescribing is a cause of unnecessarily high relapse rates in patients with schizophrenia [25]. Inappropriate prescribing may not meet patients' needs, and this in turn may contribute to negative attitudes towards treatment and the service provider [26].

Despite a high rate of antipsychotic polypharmacy prescribing in Egypt of 72.9% [27], only one previous study in Egypt has tried to investigate the antipsychotic prescribing attitudes of psychiatrists and their characteristics. This showed that a deep understanding of the content of clinical algorithms for guidelines was limited and did not exceed 37.5% of the psychiatrists surveyed [28]. This raises concerns about some of the prescribing practices and attitudes amongst Egyptian psychiatrists which may not be supported by guidelines. Therefore, the aim of this study was to conduct a qualitative survey in a sample of Egyptian psychiatrists regarding common patterns of antipsychotic prescribing practices, and reviewing how these practices vary from the evidence-base for antipsychotic prescribing. We hypothesized that

there would be a variation between common antipsychotic prescribing practices and the evidence-base for them.

Methods

Participants

We conducted a qualitative, cross-sectional survey of 124 male and female psychiatrists of different grades from 6 universities and public and private psychiatric hospitals from across Cairo, Egypt. These 6 hospitals were the Cairo University Hospital, Ain Shams University Hospital, Abbasiya Psychiatric Hospital, Maadi Military Hospital, Azhar University Hospital, and Okasha Psychiatric Hospital. The inclusion criteria were that participants must be qualified medical practitioners, currently working in psychiatry, and have experience in working and prescribing for patients with schizophrenia.

Tools

Participants were asked to fill out a paper questionnaire designed by the authors. They provided information about their age, gender, current grade, and years of clinical experience in psychiatry and the highest medical qualifications. They then answered a series of 12 questions designed to elicit attitudes towards common antipsychotic prescribing practices and the use of treatment guidelines in schizophrenia. These questions were about the participant's starting choice of antipsychotic medication in schizophrenia, attitude to cost considerations, attitude to dosing, attitude to combining antipsychotics, use of clozapine, use of anticholinergic medication, use of mood stabilizers, and use of antipsychotics for sedation and following treatment guidelines. A number of choices were given for each question, and participants were asked to choose the answer that most closely reflected their prescribing practice.

Procedures

Ethical approval for the study was granted by the Ain Shams University Faculty of Medicine Ethical Committee. A local investigator for each site distributed and retrieved the questionnaires, which were then sent to the principal investigator for data extraction and analysis. Each questionnaire included a page detailing the nature and purpose of the study. The purpose of the questionnaire was explained to each participant and informed consent obtained. Data was collected anonymously between August 2015 and February 2017 with participation being entirely voluntary.

Statistical analysis

Data was recorded and analyzed using the statistical package of social sciences SPSS for Windows, Version 24.0 (2016). All calculations were performed at 95%

confidence intervals, 0.80 power of the study, and alpha error of 0.05. The results were tabulated, grouped, and statistically analyzed using the following tests: mean and standard deviation (SD) for parametric numerical (quantitative) data, frequency, and percentage for non-numerical (qualitative) data. Logistic regression analysis was used to measure the effect of factors that affect the occurrence of selected responses with high frequency. A p value of < 0.05 was considered statistically significant.

Results

Psychiatrists' characteristics

Of the 124 participants in the study, 63 subjects were male (53.8%) and 54 subjects were female (46.2%). The mean age of the sample was 32.81 years ($SD = 7.36$). Table 1 summarizes the sample characteristics also as regards current grade, years of experience, and the highest qualifications in psychiatry.

Patterns of antipsychotic prescribing

Table 2 shows the distribution of responses to each question about common prescribing practices for patients with schizophrenia. This shows a high rate of frequency of responses that are not evidence-based from the current literature or from guidelines. A total of 96 (77.4%) participants said they would prescribe atypical antipsychotics as first-line treatment if cost were not an

issue, 53 (42.7%) said they commonly add anticholinergic medication from the start with antipsychotics, 62 (50%) said they would maintain patients on anticholinergic medication for as long as they were receiving antipsychotics, 116 (93.5%) said they commonly or in some situations combine a typical depot antipsychotic with an oral atypical antipsychotic, 110 (88.7%) said they commonly or in some situations use an antipsychotic in a small dose for sedation, and 69 (55.6%) sometimes add a mood stabilizer to enhance the effect of antipsychotic drugs.

Demographic and psychiatrists characteristics predicting high-frequency responses

Logistic regression analysis was carried out for demographic and psychiatrists-related factors to evaluate whether these factors affect the occurrence of high-frequency responses that are not evidence-based (Table 3). The regression coefficient shows the effect of each variable after controlling the effect of other variables in the model. The current grade was a significant predictor for the response that participants commonly add anticholinergic medication from the start with antipsychotics ($p = 0.001$). Age and gender were significant predictors for the response that participants sometimes add a mood stabilizer to enhance the effect of antipsychotic drugs ($p < 0.05$).

Discussion

This study included 124 psychiatrists from the different public, private, and university hospitals in Egypt. Taking into consideration that the total number of psychiatrists registered in Egypt is around 1100 psychiatrists (Egyptian Psychiatrists Association, personal communication, 2018) with many these working outside the country [29], we could conclude that our results reflect an insight into the common prescribing attitudes amongst Egyptian psychiatrists and might be considered an initial step to generate national-level data to understand the prescription patterns of psychiatrists practicing in Egypt.

Atypical versus typical antipsychotics

The controversy about the marketing claims of the atypical antipsychotics superior efficacy and fewer side effects compared to typicals [30] started around the year 2000 [31] followed by the two effectiveness trials (CATIE and CUtLASS) comparing atypicals and typicals and which provided confirmation that there was no clear difference between both groups either in effectiveness or quality of life [32, 33]. This is reflected in most current international guidelines (e.g., NICE guidelines, Maudsley Prescribing Guidelines) which recommend that no one antipsychotic is preferred over another and that prescribing is based mainly on patient choice and

Table 1 Characteristics of the sample

	Mean	SD
Age (N = 113, missing = 11)	32.81	7.36
Gender (N = 117, missing = 7)	N = 117	%
Male	63	53.8
Female	54	46.2
Current grade (N = 120, missing = 4)	N = 120	%
Resident	49	39.5
Specialist	54	43.5
Consultant	15	12.1
Professor	2	1.6
	Mean	SD
Years of experience (N = 108, missing = 16)	7.24	7.39
Highest qualification (N = 118, missing = 6)	N = 118	%
MBBCh	33	26.6
Diploma	19	15.3
Masters	45	36.3
MD/PhD	13	10.5
MRCPSych/ FRCPSych	3	2.4
Egyptian board	2	1.6
Arab board	3	2.4
American board/others	0	0

Table 2 Frequency of distribution of responses to questions about prescribing practices for patients with schizophrenia

	N = 124	%
Q1 When first prescribing an antipsychotic drug to a patient with schizophrenia, most of the time your choice is primarily guided by:		
a- Your own experience	23	18.5
b- Guidelines	40	32.3
c- Cost of the drug	11	8.9
d- Patient choice	0	0
e- Patients clinical profile	49	39.5
f- Other	1	0.8
Q2 If cost was not an issue, what would be your preferred first line antipsychotic of choice for a patient with schizophrenia:		
a- Oral typical antipsychotic drug	8	6.5
b- Oral atypical antipsychotic drug	96	77.4
c- Combination of oral antipsychotics (eg typical+atypical, 2 typicals, 2 atypicals)	6	4.8
d- Depot antipsychotic—typical/atypical (circle one if preferred)	3	2.4
f- Oral+depot	1	0.8
g- Clozapine	0	0
h- No particular preference.	5	4.0
g- Other	5	4.0
Q3 When prescribing a first line antipsychotic for a patient with schizophrenia, your starting dose is:		
a- The minimum effective antipsychotic dose of the drug.	68	54.8
b- A moderate antipsychotic dose of the drug.	50	40.3
c- The maximum antipsychotic dose of the drug.	4	3.2
Other	2	1.6
Q4 Which of the following most closely reflects your practice in schizophrenia?		
a- I never combine two or more antipsychotic drugs (eg typical+atypical, 2 typicals, 2 atypicals).	8	6.5
b- I commonly combine two or more antipsychotic drugs.	35	28.2
c- In some situations, I can combine two or more antipsychotic drugs.	80	64.5
d- Not stated	1	0.8
Q5 Which of the following most closely reflects your practice in schizophrenia?		
a- I never prescribe antipsychotic medications above the maximum dose.	104	83.9
b- I commonly prescribe antipsychotic medications above the maximum dose.	3	2.4
c- In some situations, I prescribe antipsychotic medications above the maximum dose.	15	12.1
d- Other	2	1.6
Q6 In your practice, when do you most commonly consider prescribing clozapine in schizophrenia:		
a- Never	4	3.2
b- First line	1	0.8
c- Second line	15	12.1
d- Third line	74	59.7
e- Other	30	24.2
Q7 Which of the following most closely reflects your practice?		
a- When prescribing antipsychotic drugs, I commonly add an anticholinergic from the start	53	42.7
b- When prescribing antipsychotic drugs, I never add an anticholinergic from the start	12	9.7
c- In some situations, I will add an anticholinergic from the start	56	45.2
d- Other/not stated	3	2.4
Q8 Which of the following most closely reflects your practice?		
a- If I start an anticholinergic, I mostly maintain patients on them for as long as they are	62	50.0

Table 2 Frequency of distribution of responses to questions about prescribing practices for patients with schizophrenia (*Continued*)

	N = 124	%
receiving an antipsychotic		
b- If I start an anticholinergic, I mostly discontinue them after several weeks while continuing to maintain the patient on an antipsychotic.	58	46.8
c- Other/not stated	4	3.2
Q9 Which of the following most closely reflects your practice?		
a- I never combine typical depot antipsychotic with an oral atypical antipsychotic	6	4.8
b- I commonly combine typical depot antipsychotic with an oral atypical antipsychotic.	47	37.9
c- In some situations I combine typical depot antipsychotic with an oral atypical antipsychotic.	69	55.6
d- Other/not stated	2	1.6
Q10 Which of the following most closely reflects your practice?		
a- I never prescribe an antipsychotic in a small dose for sedation.	12	9.7
b- I commonly prescribe an antipsychotic in a small dose for sedation.	55	44.4
c- I sometimes prescribe an antipsychotic in a small dose for sedation.	55	44.4
other/not stated	2	1.6
Q11 Do you add a mood stabilizer to enhance the effect of the antipsychotics?		
a- I never add a mood stabilizer to enhance the effect of antipsychotic drugs	39	31.5
b- I commonly add a mood stabilizer to enhance the effect of antipsychotic drugs	13	10.5
c- I sometimes add a mood stabilizer to enhance the effect of antipsychotic drugs	69	55.6
d- Other/not stated	3	2.4
Q12 Do you refer to any specific treatment guidelines for your prescribing?		
a- No	44	35.5
b- Yes	73	58.9
c- Other/not stated	7	5.6

medication tolerability rather than specifically recommending a class or individual antipsychotic as a first-line [34, 35].

Yet, our study showed that still 77% of psychiatrists preferred prescribing second-generation antipsychotics as first-line, if the cost was not an issue. This is in line with previous results in other developing countries as in Pakistan and India which showed that risperidone and olanzapine are the two most commonly prescribed antipsychotics by 88.69% of psychiatrists in India with haloperidol being the third most commonly preferred antipsychotic [36]. Furthermore, a survey by Varghese [37] pointed out that amongst recently qualified post-graduate psychiatrists, there were few who were comfortable with using typical antipsychotics. On the other hand, a survey Pakistan reported that 81% of psychiatrists responded by choosing an atypical if they were hypothetically ill themselves [38]. The fact that although some of the newer drugs are associated with lower rates of extrapyramidal side effects (EPSE)/tardive dyskinesia, yet they are also linked to different and equally severe side-effects such as diabetes, with some of the newer drugs having similar rates of EPSE to the older drugs [30], and the absence of routine lab monitoring for

metabolic side effects in Egyptian public hospitals raises some concerns about the appropriateness of this prescribing attitude.

Prophylactic anticholinergic drugs

Approximately half of our subjects declared that on prescribing antipsychotic drugs, they commonly add an anticholinergic from the start and would maintain patients on them as long as they were receiving an antipsychotic. Using logistic regression, the current grade significantly predicted prescribing of anticholinergics from the start with antipsychotics. This might be reflective of the current practice that during psychiatric training, junior doctors routinely add an anticholinergic when prescribing antipsychotics, in order to prevent some of the associated movement side-effects. This is in line with a previous study in Bahrain [17] which showed that anticholinergics are extensively co-prescribed along with both typical and atypical antipsychotics, a finding seen in other studies [39–42].

This might be related to various ideological beliefs and possible cultural and institutional practices [43]. One of these factors is the idea of routinely prescribing an anticholinergic even in absence of extrapyramidal side

Table 3 Logistic regression analysis showing factors predicting responses with high frequency

	B	p
Q2b		
Age	0.015	0.549
gender	0.240	0.581
Years of Experience	-0.054	0.123
current grade	0.163	0.572
highest qualification	0.009	0.937
Q7a		
Age	-0.012	0.598
gender	-0.368	0.338
Years of Experience	0.018	0.620
current grade	-1.341	0.001*
highest qualification	0.298	0.058
Q8a		
Age	-0.020	0.325
gender	-0.007	0.985
Years of Experience	0.041	0.195
current grade	-0.008	0.970
highest qualification	-0.046	0.624
Q9b		
Age	-0.001	0.966
gender	0.440	0.221
Years of Experience	0.025	0.424
current grade	-0.159	0.509
highest qualification	-0.044	0.659
Q10b		
Age	-0.033	0.123
gender	-0.118	0.739
Years of Experience	0.037	0.233
current grade	-0.038	0.864
highest qualification	0.075	0.425
Q11c		
Age	0.061	0.008*
gender	0.741	0.045*
Years of Experience	-0.014	0.678
current grade	-0.011	0.962
highest qualification	-0.044	0.642

B regression coefficient, p p value

*Statistically significant

effects (EPSE) to prevent any possible extrapyramidal symptoms. This commonly occurs in Egypt, especially in the private sector outpatient setting, where prophylactic anticholinergics are prescribed for fear that if any EPSEs occur, then patients would seek out another psychiatrist. Anticholinergics are also added to some atypical antipsychotics such as risperidone where extrapyramidal side

effects appear to occur in 60% to 70% if the patients are taking doses greater than 6 mg/day [44]. Another reason could be the widely held belief amongst Egyptian psychiatrists that the use of multiple drugs with different pharmacological actions is more effective, such as the common practice of adding anticholinergic to clozapine to mitigate clozapine-induced hypersalivation [45]. This therapeutic dilemma has been addressed by Gjerden et al. [46] who viewed that anticholinergic use appears to be superfluous for at least one third of patients, and their use exceeded the incidence of EPSE [47], with chronic administration of anticholinergics contributing to the occurrence of tardive dyskinesia [48].

On the other hand, anticholinergics should be used prudently because in addition to their well-known peripheral side-effects, they may worsen positive symptoms, appear to partially ameliorate negative symptoms, and are associated with impaired cognitive functioning [49], especially in the elderly [50], which may add to the cognitive impairment caused by the illness itself and the use of antipsychotics [51], in addition to the potential for abuse [52].

Use of antipsychotics for sedation

Other questionable practices include the prescribing of antipsychotics for sedation where most participants in our study reported using an antipsychotic in a small dose as a sedative drug. Unfortunately, this is practiced on a large scale amongst Egyptian psychiatrists where one multicentre study [24] showed that clozapine was frequently used in Egypt in comparison to other Arab Countries and especially in lower doses for sedation. It seems questionable at best and unethical at worst to subject patients to the hazards of the side effects (e.g., agranulocytosis, metabolic syndrome) of such a potent drug that is indicated only for use in resistant cases, just for the sake of sedation.

Combining typical antipsychotic depots with atypical oral antipsychotics

Interestingly, approximately about one third (37.9%) of our subjects reported that they *commonly* combine typical depot antipsychotics with an oral atypical one and nearly half (55.6%) reported combining typical depot antipsychotics with an oral atypical antipsychotic *in some situations*. These findings are consistent with other studies and probably stem from the common practice of adding a depot medication in cases of non-compliance to the already given drug. Later, doctors and patients may have unrealistic expectations of benefits of such combinations and may be reluctant to stop the partially effective drug [13]. However, combining typical depot with atypical oral or vice versa, points to the confusion that some doctors have about the mechanism of action

of these drugs, as co-prescribing typicals with atypicals will nullify potential benefits of the atypical drug.

This pattern of prescribing may also be explained by the availability and affordability of antipsychotics. This may differ according to whether patients are seen in the private sector or public sector, where atypical depot medication is very expensive and so are rarely prescribed in public hospitals [24], leaving psychiatrists with little option to using typical depot medications if patients need a long-acting drug.

Adding a mood stabilizer to enhance the effect of antipsychotics

More than half of our subjects responded that they sometimes add a mood stabilizer to the prescribed antipsychotic. This is in line with evidence from the literature that shows that there is a total increase in the use of mood stabilizers in general (carbamazepine, lamotrigine, pregabalin, topiramate) and valproate in particular, for patients with schizophrenia despite there being limited evidence for their efficacy, safety, and regulatory approval [53]. Their use may stem from a desire to control impulsivity and aggression in some patients [54] or to control associated affective symptoms or for use in treatment-resistant cases. However, their effect on core psychotic features remains inconclusive [55–57].

Limitations

Owing to its qualitative cross-sectional nature, our study should be considered primarily as an exploratory and distributive study. It is limited by the subjectivity of the questionnaire, which measures attitudes and not necessarily behavior. Ideally, we would have recruited a representative sample of patients into our study who are being treated by psychiatrists who are solely responsible for decisions about their medication and treatment to explore if there is a dissonance between attitude to prescribing and their practice. However, this was not possible owing to the hierarchical system especially in the educational institute in Egypt, where more than one psychiatrist are usually involved in treatment decision-making.

Conclusions

Our study demonstrated that while attitudes to many prescribing practices for the majority of psychiatrists in this sample were reasonable and evidence-based, some of them were not, yet was prevalent in a large percentage of participants. Future work is required to further understand factors affecting psychiatrists prescribing attitudes in Egypt and if there is clear clinical justification for practices that may vary from international guidelines. It may also point to a need to consider developing local guidelines that address the circumstances of patients

and psychiatrists in Egypt and take into consideration their social and cultural circumstances.

Abbreviations

SPSS: Statistical Package for the Social Science; CATIE: Clinical Antipsychotic Trials of Intervention Effectiveness; CULASS: Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study; NICE: National Institute of Clinical Excellence; EPSE: Extrapyramidal side effects

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Authors' contributions

All authors contributed to the conception and design of the study. SA and HE contributed to the data collection and editing of the manuscript. DAE contributed to the data collection and write up of the manuscript. KAA contributed to the analysis of the data and editing of the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

Available upon request.

Ethics approval and consent to participate

Ethical approval for the study was granted by the Ain Shams University Faculty of Medicine Ethical Committee. Informed consent was obtained for each participant.

Consent for publication

All authors approved the final manuscript for publication.

Competing interests

The authors declare no conflict of interest.

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