Antipsychotic medications induced extra pyramidal effects

Ali A. AlHamzawi, F.I.C.M.S.

Qadissiya University/ College of Medicine/

Abstract

Background: Antipsychotic drugs are invaluable tools in treating a large variety of patients with schizophrenia, mood disorders with psychotic features, senile and other organic psychoses, psychoses associated with Parkinson's disease. Extrapyramidally mediated movement disorders represent the major set of adverse effects associated with the use of antipsychotic medications.
Objective: Is to assess the size of the problem of extra pyramidal effects among chronic patients taking antipsychotic medications.
Method: 100 chronic psychiatric patients attending outpatient department in Diwania Teaching Hospital to receive their medications were assessed for extra pyramidal side effect of antipsychotic drugs, using the Extrapyramidal Symptom Rating Scale (ESRS). The study was conducted between the 8th of January2009 and the 8th of May 2009.
Results: the study revealed that 38% of patients on antipsychotic medication have extra pyramidal effects. The majority of those patients (80%) were taking anticholinergic drugs.
Conclusion: the study concludes that extra pyramidal effects are common among chronic patients on antipsychotic medications.
Key terms: extra pyramidal symptoms, antipsychotic drugs.

خلاصة

تعتبر الأدوية المضادة للذهان من الأدوات الأساسية في معالجة عدد كبير من المرضى المصابين بالفصام, الاضطرابات الوجدانية المصحوبة بالمظاهر الذهانية, الأمراض العضوية الذهانية والذهانات المصاحبة لمرض باركنسون. تعتبر الأعراض الباركنسونية من الأعراض الأساسية التي تصاحب استخدام الأدوية التقليدية المضادة للذهان,و إن المرضى المعرضين لهذه الأدوية سوف يعانون من هذه المشكلة
الهدف: لتَقييم حجم مشكلةِ التأثيرات الهرمية الإضافية بين المرضى المُزمنين الذين يأخذون الأدوية المضادة للذهان.
الطريقة: أجريت الدراسة على 100مريض مزمن من الذين يراجعون قسم العيادة الخارجية في شعبة الطب النفسي في مستشفى الديوانية التعليمي لاستلام علاجهم،تم تقييم ´الأثر الجانبي الهرمي الإضافي من الأدوية المضادة للذهان بأستعمال مقياس العلامة
. لقد تم إجراء الدراسة بين الثامن من كانون الثاني 2009 والثامن من مايس 2009(إي أس أر.أس)
النَتائِج :
كَشفتْ الدراسة على أن 38 % من المرضى المستمرين على تناول الأدوية المضادة للذهان يعانون من مشكلة التأثيرات الهرمية للأدوية المضادة للذهان.وان 80% من المرضى يتناولون الأدوية المضادة للكولينيرجين
الاستنتاج: تَستنتج الدراسة بأن الأثر الجانبي الهرمي الإضافي شائع بين المرضى المزمنين الذين يتناولون الأدويةِ المضادة للذهان.

Introduction

The term antipsychotic drug is applied to drugs that reduce psychomotor excitement and control some symptoms of psychosis. Alternative terms for these drugs are neuroleptic and major tranquilizer. [1]
Chlorpromazine which was introduced in the mid-1950s was the first drug that significantly and consistently reduced symptoms of psychosis. Other drugs with similar clinical effects were

introduced over the next two decades. Antipsychotic activity was related to high-affinity antagonism of dopamine D2 receptors. Accordingly these agents are called dopamine receptor antagonists. [2].

Soon after the introduction of chlorpromazine its use was noted to be associated with the development of Parkinsonism. Extrapyramidally mediated movement disorders represent the major set of adverse effects associated with the use of standard antipsychotic drugs. These are related to the antidopaminergic action of the drugs on the basal ganglia [3].As this was largely treatable and reversible phenomenon, it was for most psychiatrist a matter of concern. Within a few years however these neurological effects came to be seen as pointing to an essential element of the pharmacology and to offer a window on the drugs mode of action. To reflect these views Jean Delay coined, in 1955, the term by which this new class of drugs has become universally known –neuroleptics, or compound which forcibly grasp or seize neurons or the nervous system. [4].

The text revision of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-1V-TR) includes in the category of medication-induced movement disorders, both such disorders and any medication-induced adverse that becomes a focus of clinical attention [5].The most common antipsychotic drugs related movement disorders are Parkinsonism, acute dystonia, and acute akathesia, and neuroleptic-induced tardive dyskinesia. Neuroleptic-induced tardive dyskinesia is a late appearing adverse effect of neuroleptic drugs and can be irreversible , recent data , however ,indicate that the syndrome, although still serious and potentially disabling, is less pernicious than was previously thought in patients taking neuroleptic drugs[6]. Tardive dyskinesia may occur in cases of dose reduction, discontinuation, or switching from antipsychotic to another.[7,8]The newer antipsychotic drugs, the serotonin-dopamine antagonists, block binding to dopamine receptors to a much lesser degree and thereby are less likely to produce such movement disorders[9].

Exposed patients to standard antipsychotic medications will experience some problems of extrapyramidally mediated movement disorders .These syndromes remain poorly recognized and their full impact is rarely acknowledged. It is important to realize that all these disorders comprise not only objective signs but subjective symptoms [4].

Methods

100 chronic patients on antipsychotic drugs were assessed to determine the size of the problem of extrapyramidal effects of antipsychotic medications, using Extrapyramidal Symptom Rating Scale (ESRS) [10].ESRS includes 12 questionnaire items to identify subjective symptomatology. Eight items are devoted to parkinsonian signs. Each item is rated on a seven-point scale. This scale has a novel approach to resolve the problem of how to judge severity by recommending the rating into two modalities which are: frequency and amplitude. The ESRS has become a very widely utilized instrument in clinical trials to assess the effects of antipsychotic medications. The scale was done as part of a physical-neurological examination; the time to complete the scale is 15-20 minutes. The inclusion criteria were all chronic patients who were on antipsychotics for more than one month duration and they are willing to participate in the study.

Exclusion criteria are: all patients who take other psychotropic medication, all patients who suffer from neurological conditions, or other medical illnesses, and those who refused to participate in this study. The consent of the patients and their relatives and all formal procedures were taken. The purpose of the study was explained to all the participants.

The study was conducted in Diwania Teaching Hospital/ out-patient department of psychiatry during the period between the 8th of January and the 8th of May 2009. 2009.

Table 1. distribution of the patients according to the diagnosis.

Diagnosis	Total Number (No.)of patients	Percent
Chronic schizophrenia	79	79%
Bipolar disorders	14	14%
Delusional disorders	6	6%
Schizoaffective disorder	1	1%
Total	100	100%

Table 2. distribution of patients according to sex.

Sex	Number of patients	Percent
Female	49	49
Male	51	51
Total	100	100

Table 3. distribution of patients according to the development of extrapyramidal effects (EPE).

Type of patients	Male		Female		Total	Total percent
	No.	Percent	No.	Percent		
Those who developed EPE	20	39.22	18	36.73	38	38
Those who don't develop EPE	31	60.78	31	63.27	62	62
Total	51	100	49	100	100	100

Table 4. distribution according to types of movement disorders:

Movement disorders	Male	Female	Total	Total percent
Dystonia	2	1	3	3
Akathesia	10	8	18	18
Parkinsonism	17	16	33	33
Tardive dyskinesia	10	16	26	26

Table 5. distribution of patients with EPE according to the type of antipsychotics:

Type of antipsychotic medications	Male		Female		Total	Total percent
	No.	percent	No.	percent		
Typical	18	47.36	15	39.47	33	33
Atypical	2	5.26	3	7.89	5	5
Total	20	52.62	18	47.36	38	38

Table 6. distribution of the patients according to the type of antipsychotic medications:

Type of antipsychotic medications	No. of patients	Percent
Typical	90	90
Atypical	10	10
Total	100	100

Table 7. distribution of patients who are on anticholinergic drugs according to sex:

Sex	Number	Percent
Male	38	38
Female	42	42
Total	80	80

Table 8. equivalent doses of antipsychotic drugs:

Antipsychotic drugs	daily dose
Chlorpromazine	100
Trifluoperazine	5
Haloperidol	2
Flupentixol	1
Sulpiride	200
Clozapine	60
Risperidone	2
Olanzapine	8
Pimozide	2

Results

The results are shown in the following tables. The equivalent doses of antipsychotic drugs were taken in comparison with chlorpromazine, the mean daily dose of antipsychotic in chlorpromazine equivalent is 300mg. (11)

Discussion

This is the first study which is conducted in Iraq to assess the problem of extrapyramidal effects, in chronic patients, due to the intake of antipsychotic medications.

Antipsychotic medications reflect the importance of the biological perspective in understanding and treating schizophrenia and other psychosis. It will usually be initiated soon after the diagnosis is made, and will often continue for many years (12).

The study used Extrapyramidal Symptoms Rating Scale (ESRS) which measures extrapyramidal symptoms in children, adolescents and adults. The ESRS is considered comprehensive and its statistical properties appear good.

The result of this study showed that the prevalence of extrapyramidal symptoms in global term was 38(38%) of the patients who were on antipsychotic drugs; the number of male and female who developed EPE were 20, 18 (39.22% and 36.73%) respectively as shown in table (3), The results of this study are not much different from previous studies, these studies showed variable rates of extrapyramidal effects of psychotropic medication (13, 14, 15). These variables rates may reflect the differences in the rating instruments used for the assessment of extrapyramidal effects.

Concerning the distribution of patients according to the type of movement disorders, it was noticed that some patients have developed more than one extrapyramidal symptom. The female outnumbered male in regard to the occurrence of tardive dyskinesia. The troublesome Tardive dyskinesia developed in 20 (20%) of chronic patients who were on regular drug intake for more than one year. the female patients were16 (16%) while the male patients were 10 (10%) ,as it is shown in table (4) ,and this is consistent with other studies (3.9,13).

Another striking finding which was noticed is that the majority of the patients who were on typical(older ,traditional, conventional) antipsychotic drugs showed extra pyramidal effects, the total number of those patients were 33 (33%), the number of male patients were 18(47.36%) ,while that of female patients were 15(39.47%). Those who were on atypical antipsychotic (newer antipsychotics) drugs showed reduced liability to cause these effects; their total number was 5(5%), the number of male and female patients were 2, 3(5.26%, 7.89%) respectively as shown in table (5).

Regarding tardive dyskinesia, which is a delayed effect of antipsychotics, none of the (10) patients who were on atypical antipsychotic drugs showed any evidence of such movement disorder, probably the small sample size (10 patients) was the reason beyond their absence. The atypical antipsychotics are associated with less tardive dyskinesia than older (typical) antipsychotics [4, 6]. The concept of drug holiday has not been shown to be of any benefit in preventing and may even enhance the development of tardive dyskinesia. [4, 16]

This reduced liability to cause these side effects (i.e. dystonia, akathesia, parkinsonism, and tardive dyskinesia)is the one advantage of atypical antipsychotic drugs which is agreed upon by all the meta-analyses [6,17,18].

Given their proved efficacy in managing psychotic symptoms and that administration of anticholinergic medication prevents or minimize motor abnormalities traditional (typical) antipsychotic drugs are still valuable. Considerable cost advantage exists to traditional antipsychotic drugs as compared with monotherapy with a newer or atypical antipsychotic. Concern about the development of tardive dyskinesia is the major deterrent to long-term use of these drugs [6, 19].The explanation is that being cheaper than atypical antipsychotic drugs, familiarity with these drugs, and their availability were the reasons behind their frequent uses by those patients and preference by their families.

The extra pyramidal effects and greater tardive dyskinesia risk of the typical antipsychotic drugs, coupled with their lesser efficacy to improve negative symptoms and cognition suggest that newer agents of antipsychotic drugs are preferred [20,21]

Another finding which was revealed by the study is the problem related to the management of these movement disorders. The study revealed that 80% of patients were on anticholinergic drugs (trihexyphenidyl (Artane), benzhexol (Parkisol) and procyclidine (Kemadrin) as shown in table (7). As long as most antipsychotic drugs tend to produce extra pyramidal effects, for this reason some clinicians prescribe anticholinergic drugs routinely. Some of the unwanted effects of antipsychotic medications particularly the extrapyramidal ones are easy for anyone to see. These agents should not be given prophylactically unless it is well established that the patient generally will have extra pyramidal effects at the dose of antipsychotic which is being started. [2, 16] This is not a good practice for a variety of reasons: akathesia and Parkinsonism are the most common and troublesome side effect and there is little evidence that the routine prescribing of anticholinergics reduce them to any worthwhile extent [4, 16]. There is also evidence that the use of these drugs may impair the efficacy of antipsychotic drugs particularly positive symptoms, and increase the incidence of tardive dyskinesia, and because they have mild stimulating properties some patients abuse them, in addition to their own side effects [4, 6, 22].Some studies have found that concomitant treatment with anticholinergics can attenuate the therapeutic effect of antipsychotic drugs treatment. [6, 23].All anticholinergics can exacerbate tardive dyskinesia but are probably not a predisposing factor in its development. [23, 24].

The study concludes those extra pyramidal effects are common among chronic patients on antipsychotic medications.

Recommendations

All patients receiving long-term antipsychotics require periodic evaluation and documentation of continued need and benefit. The benefits and risks of long-term neuroleptic treatment should be discussed with patients and families and their informed consent to treatment documented ,and recommendation for preventing and managing tardive dyskinesia include: using the lowest effective dose of antipsychotics, examining patients on a regular basis for evidence of tardive dyskinesia, and considering discontinuing the antipsychotics or switching to different drugs.

References

1. Michael Gelder, Dennis Gath, Richard Mayou, Philip Cowen, Oxford Text Book of Psychiatry third edition, Oxford University Press 1996:548
2. Marder SR, van Kammen DP, Dopamine receptor antagonist (typical antipsychotic). In: Sadock Bj, Sadock VA, Eds, Kaplan and Sadock's Comprehensive Textbook of Psychiatry, 8th ed. Vol.2 Baltimore: Lippincott Williams & Wilkins; 2005:2817
3. Barnes TR and Spence SA: movement disorders associated with antipsychotic drugs: clinical and biological implication, In MA Reveley and JFW Deakin, Eds. The psychopharmacology of schizophrenia, 2000:178-210. Arnold. London
4. Eve C. John stone, D.G.Cunningham Owens, S.M.Lawrie, M.Sharpe C.P.L. Freeman, Companion to psychiatric studies seventh edition Churchill Livingstone 2004:257-267.
5. DSM-1V-TR: Diagnostic and Statistical Manual of Mental Disorders fourth edition (text revision) Washington DC .American Psychiatric Association..2000.
6. Kaplan & Sadock's Synopsis of Psychiatry tenth edition 2009.992-5.
7. Glazer, WM.expected incidence of tardive dyskinesia associated with atypical antipsychotic. Clin.161 suppl4: 2000, 2-6.
8. Group, BMJ,ed British National Formulary (75 ed) United Kingdom. Royal Pharmaceutical Society of Great Britain p.192 ISBN0260-535X: withdrawal of antipsychotic drugs after long-term therapy should always be gradual and closely monitored to avoid the risk of acute withdrawal syndromes or rapid relapse. March. 2009.
9. Caroff SN, Mann SC,Campell EC, Sullivan KA, movement disorders associated with atypical antipsychotic drugs. J Clin Psychiatry, 2002:63[suppl 4]:12-19
10. Chouinard G, Ross-Chouinard A, Annable L, et al, Extra pyramidal Rating Scale, Can J Neurology Sci, 1980, 7:233.
11. British National Formulary. March. 2008: 189
12. Michael Gelder, Paul Harrison, Philip Cowen, Shorter Oxford Text Book of Psychiatry fifth edition, Oxford University Press 2006: 301.
13. Marsden, C.D.and Schacter, M.: Assessment of extrapyramidal disorders.BrI, J. of CL.Pharmacology, .1981:11,129-51.
14. Kane JM., Smith JM: Tardive dyskinesia: prevalence and risk factors, Ach. Gen.Psychiatry 1982:39:473-81.
15. Abu-Hijleh N. Drug induced extrapyramidal symptoms in psychiatric hospitals. Arab Journal of Psychiatry.1989 Vol .1, No.1.
16. R.E.Kendell, A.K.Zealley, S.M.Lawrie, Companion to psychiatric studies fourth edition Churchill Livingstone 1988:688.
17. Kane, JM.Tardive dyskinesia rates with atypical antipsychotics in adult: prevalence and incidence.Journal of Clinical Psychiatry.2004, 65, 16-20.
18. Jeste, DV. Tardive dyskinesia rates with atypical antipsychotics in older adults. Journal of Clinical Psychiatry.2004, 65, 21-4.
19. Correl CU, Leucht S, and Kane JM: lower risk for tardive dyskinesia associated with second generation antipsychotic: a systematic review of 1-year studies. American Journal of Psychiatry, 2004161.414-25.
20. Meltzer, H. The concept of atypical antipsychotic. In Advances in the neurobiology of schizophrenia (ed. J.A. den Boer, H.G.M. Westerberg, and H.M. van Praag), 1995: 265–73. Wiley, Chichester.
21. Factor SA,Lang AE,Weiner WJ,eds,Drug Induced Movement Disorders.2nd ed. Malden, MA:Blackwell Futura :2005.
22. W. Greil,H.Haag,Rossuagl and

E.Ruther.Effect of anticholinergics on tardive dyskinesia. Br.J.Psychiat.1984:145,304-1.
23. Johnstone, E, Crow, T J, Ferrier, I, et al: adverse effects of anticholinergic medication on positive schizophrenic symptoms. Psychological Medicine, 1983: 13,513-77.
24. Jeste, D, V, and Caligiuri, M, P: tardive dyskinesia. Schizophrenic Bulletin 1993, 19,303-15.