Original Article

Clinical Assessment and Medicinal Management of Extrapyramidal Symptoms Induced by Some Antipsychotics in Iraqi Patients

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Abstract

Background: The extrapyramidal symptoms represent one of the most dramatic drug-induced side effects including *Parkinson's-like symptoms*, dystonia, and akathisia that can be associated with the use of all typical antipsychotic agents. **Objectives:** Assessment of the extrapyramidal symptoms induced by typical antipsychotics and their medical management with anti-Parkinsonian drugs. **Materials and Methods:** Fifty psychotic patients among those attending the outpatient clinic of the psychiatric unit in the Al-Sadiq Teaching Hospital in Babylon province were enrolled in this retrospective case–control study, from the period August 2021 to February 2023. Demographic data (age, gender, and marital status), medical, and psychiatric history (such as suicide attempts, time and location of the incident) were collected. Chlorpromazine, haloperidol, and trifluoperazine were used as antipsychotics. Through 1 month of follow-up, the anti-Parkinsonian drugs trihexyphenidy and procyclidine were prescribed to patients who experienced extrapyramidal side effects. **Result:** Fifty-two percent of the patients experienced extrapyramidal side effects (24% Parkinson-like symptoms, 18% dystonia, and 10% akathisia), which were mild, moderate, and severe in 13%, 12%, and 27% patients, respectively. All dystonic reactions were treated with procyclidine and trihexyphenidy. Patients not controlled by these treatments were changed to another neuroleptic drug with less extrapyramidal side effects. **Conclusion:** Extrapyramidal side effects are the most frequent medical disorders that are associated with antipsychotic usage, and they can be managed by anti-Parkinsonian drugs.

Keywords: Anti-Parkinsonian drugs, antipsychotics, extrapyramidal symptoms

Introduction

Antipsychotics classification based on clinical indication and a shared pharmacological mechanism of dopamine D2 receptor antagonism are related to clinical efficacy.[1] Older neuroleptic drugs "Typical Antipsychotics" are competitive blockers of dopamine receptors (D2) newer agents "Atypical Antipsychotics" are blockers of serotonin receptors (5HT2A) and to a lesser extent dopamine receptors (D2). The antipsychotic drugs also relieve the manic phase of bipolar affective disorder. Many also block muscarinic, alpha-adrenergic, and histamine receptors to varying degrees.[2,3] The most dramatic and theoretically important group of side effects that can occur with the use of the typical antipsychotic agent is the extrapyramidal reaction, which is most severe with haloperidol, Thiothixene, Trifluoperazine, and Fluphenazine, while it is intermediate with chlorpromazine, and mild with Thioridazine.[3]

The antipsychotics-associated extrapyramidal side effects are classified into three arbitrary categories including Parkinsonian-like symptoms, dystonia, and akathisia. The Parkinsonian-like symptoms consist of mask-like

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face, tremors at rest, rigidity, shuffling gait, and motor retardation.[4] Dystonia consists of a wide range of bizarre movements of the tongue, face, and neck including buccofacial movements with salivation, torticollis, oculogyric crisis, and opisthotonus.[5] Akathisia is the motor restlessness in which the patient manifests a great urge to move about and has considerable difficulty in sitting still.[4,5]

Diagnosis of these manifestations is important because their increase indicates an increase in the psychosis then the dose of the antipsychotic medication should be increased, while if one of them is diagnosed as extrapyramidal side effect then either the dose of the antipsychotic treatment should be decreased or an anti-Parkinsonian drug should be added.[6]

The therapeutic trial with anti-Parkinsonian agents such as procyclidine is particularly helpful in making correct diagnoses, especially in dramatic dyskinesias, which responded within minutes to intramuscular or intravenous treatment with anti-Parkinsonian medication.[4]

The acute dystonia typically occurs in the first few days or weeks of treatment, it can appear in patients receiving even a small amount of antipsychotic. It is not uncommon in children treated with a single dose of prochlorperazine for nausea. Dystonia may disappear spontaneously. Generally, it is advisable to treat dystonia with anti-Parkinsonian medication because it is often painful and is always psychologically harmful and upsetting.[7,8]

Acute dystonic reaction is resistance to treatment with such usual anticholinergic anti-Parkinsonian medication. The patient who does not respond to the usual anti-Parkinsonian medication may respond to either diazepam, methylphenidate, caffeine, or barbiturate.[9] It has been suggested that dystonic reactions can occur frequently in patients with hyperparathyroidism a condition indecently associated with basal ganglion disease, hypocalcemia itself may reduce the central nerve system threshold to diskinetic phenomenon.[10]

Patients who appear apathetic, lacking in spontaneity unable to participate in social activities lifeless, or drowsy may be demonstrating subtle extrapyramidal effects. One should be alert to these Parkinsonian-like symptoms because they can be confused with emotional withdrawal or retardation. This Parkinsonian-like syndrome poorly responds to anticholinergics but does respond rapidly to amantadine.[11]

Akathisia can be confused with psychotic agitation. In Akathisia, the patient is driven by motor restlessness and is not verbally preoccupied with the motor restlessness and is not verbally preoccupied with psychological content of whatever he is agitated about.[12] The symptoms are primarily motor and cannot be controlled by the patient. Akathisias are worsened by increasing the antipsychatic dose; they are benefited by decreasing the dose and adding an anti-Parkinsonian medication; however, diazepam and propranolol can also be used.[13]

This study was conducted to assess the presence of some extrapyramidal reactions in Iraqi patients and their susceptibility to major tranquilizers. Also to assess the effectiveness of the anti-Parkinsonian drugs.

Materials and Methods

Study design and patients

In this study, 50 patients with extrapyramidal syndrome who were admitted to Al-Sadiq Teaching Hospital in Babylon City, Iraq were enrolled.

Study design

Retrospective case–control study design of patients with extrapyramidal syndrome admitted to the emergency room, burn unit, and psychiatric unit at Al-Sadiq Teaching Hospital in Babylon City, Iraq. The study was conducted over a period of 2 years, from August 1, 2021, to February 1, 2023.

Treatment evaluation

Three types of neuroleptics including chlorpromazine (100–600 mg/day), haloperidol (4.5–15 mg/day), and trifluoperazine (15–20 mg/day) were examined in this study [Table 2]. Each patient was commenced on one type of neuroleptic drug and in a dosage range, which was periodically reconsidered according to the individual variation and the personal experience of the psychiatrist with each of his patients.[2] All further adjustments of dosages were decided on an individual basis by the treating physician. Individual variations are decided by the body weight, the body surface, and degree of general health in addition to age and sex of each patient.

All dystonic reactions were treated with procyclidine 5 mg I.V. repeated in 2 h if there was no response and the patient was commenced at the same time on oral anti-Parkinsonian drug (trihexyphenidyl 4–6 mg/day) for 2 weeks. Sometimes we used diazepam 10 mg I.V. to control these dystonic reactions if they were accompanied by psychological manifestations such as fear [Table 3].

The decision concerning the initial regime was entirely empirical.

If any patient experiences extrapyramidal side effects, two policies were adopted to abolish these symptoms:

I. Either anti-Parkinsonian drugs was prescribed to control the side effects, (4–6 mg/day) of trihexphenidyl and (10–15 mg/day) of procyclidine were used as anti-Parkinsonian drugs (as shown in Table 3).
II. Or the dose of the neuroleptic was reduced until the extrapyramidal side effects disappeared or the psychotic features reappeared.
III. Severe side effects present: When there is restriction of the usual lifestyle, stopping some normal important or social functioning.

Table 1: Age and sex of the studied patients with the duration of observation

Number of patients	50
Age range	18–63 years
Mean age	40 years
Number of males	25 (50%)
Number of females	25 (50%)
Duration of observation	1 month

Table 2: Types of drugs and range of dosage

Chlorpaomazine (largactil)	100–600 mg/day
Haloperidol (Serenace)	4.5–15 mg/day
Trifluoperazine (Stelazine)	15–20 mg/day

Table 3: Types of oral anti-Parkinsonian drugs and range of dosage

Trihexphenidyl (Artane)	4–6 mg/day
Procyclidine (Kemadrin)	10–15 mg/day
Diazepam	10 mg iv

Table 4: The extrapyramidal side effects development and their severity

Number of patients who develop extrapyramidal symptoms	26 (52%)
Mild	13%
Moderate	12%
Severe	27%*
Total	52%

*P value = 0.004

Data analysis

The data were analyzed using descriptive statistics, including frequency and percentages for categorical variables. Bivariate analyses, including Chi-square and *t* tests, were used to compare demographic and clinical characteristics of patients with extrapyramidal symptoms. The level of significance was set at $P < 0.05$.

Ethical Approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 213 including the number and the date on 14/04/2021.

Results

Table 1 shows the age, sex, and duration of observation of the patients included in this study. Table 4 shows that 52% of the patients experienced extrapyramidal side effects, which is a significant value among whole patients involved.

Table 5: Types of extrapyramidal side effects

Symptoms	Number of patients	Males	Females	Total %
Parkinsonism	12	2	10	24 %*
Dystonia	9	5	4	18 %
Akathisia	5	3	2	10 %
Total	26	10	16	52 %

*P value = 0.003

Table 6: Sex distribution among the patients with extrapyramidal symptoms

Sex	Number
Female	16 (61.54%)
Male	10 (38.46%)
Total	26 (100%)

Regarding its severity, 13%,12%, and 27% of patients experienced mild, moderate, and severe extrapyramidal side effects, respectively. The number of patients who developed severe symptoms was significantly (P value > 0.05) higher than those who showed mild or moderate [Table 4].

The types of extrapyramidal side effects are shown in Table 5. All Parkinson-like syndrome reactions occurred within 72 h of the first dose. They comprise 24% from all patients with extrapyramidal symptoms, which is significantly (P value < 0.05) higher than other symptoms (dystonia and akathisia which was 18% and 10%, respectively)

Extrapyramidal symptoms was more in female [Table 6]. It was more common in females. The patients did not always complain of akathisia although it was distributed in more or less equal percentages between the two sexes.

Discussion

Published studies indicate that between 20% and 40% of patients treated with oral neuroleptics exhibit extrapyramidal effects.[5,6] A single study reported a prevalence of 88% of patients manifesting some form of motor disturbance on trifluoperazine after prolonged use.[7]

The figure reported in the present survey was 52% which is likely to be an underestimate, since patients over 65 years of age had been excluded. This figure still is higher than in some other studies mentioned above.

Our study may indicate that Iraqi patients are more susceptible to the neuroleptic group of drugs, and this is why they showed more extrapyramidal side effects. This can be explained partly because of the pharmacogenetics (or racial difference) in basic pharmacokinetics and pharmacodynamics of some neuroleptic drugs, but the definite answer needs a more elaborate method. Also, it might have some implications over the dose regime or the potential for the manipulation of the medication.

The total dose tolerated over a given time may be significantly raised if smaller doses are administered more frequently.[10] This method of administration possibly prevents the serum level from rising above a theoretical threshold level. It has been suggested that whilst extrapyramidal features are common during the early days of treatment with phenothiazines they gradually decrease in incidence.[11] This was shown to be true in this study. This must emphasize the need to keep the regime of administration and the type of drug as well as the occurrence of new side effects under constant review. When a dose-dependent side effect is present, the treatment of choice is a reduction in the dose of the phenothiazine. The prescription of a further drug should be considered only if the former treatment fails or is considered clinically inappropriate. So, the present study demonstrates that almost half of the patients who experienced major psychiatric illness did not require anticholinergic drugs [Table 5], that is, only 52% experienced side effects.

It is suggested that anti-Parkinsonian drugs should only be prescribed when the side effects appear and to be continued until the symptoms are abolished depending on the individual variation.[12-15] However after this interval, anti-Parkinsonian drugs need to be used only for the duration of the morbidity. The reappearance of the extrapyramidal symptoms after discontinuation of anti-Parkinsonian drugs needs to be further studied as the period of the follow-up was short. In our practice, however, we have noticed that some patients especially those from rural areas are put on a substantial dose of neuroleptics and a prophylactic anti-Parkinsonian drugs in order to prevent the occurrence of extrapyramidal reactions, while they are away and far from psychiatric help and that is because (especially in dystonic reactions) the patient and his family will be seriously alarmed and frightened and this will make stop all medications.

Conclusion

Extrapyramidal side effects are the most frequent acute medical disorder that is associated with the antipsychotic usage and they can be managed by anti-Parkinsonian drugs.

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Conflicts of interest

There are no conflicts of interest.

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