World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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ECG pattern among adult patients on antipsychotic medications at the university of port Harcourt teaching hospital, River State, Nigeria

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World Journal of Biology Pharmacy and Health Sciences, 2024, 17(02), 312–322

Publication history: Received on 07 January 2024; revised on 17 February 2024; accepted on 20 February 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.17.2.0079

Abstract

Background: Antipsychotic medications treat neuropsychiatric disorders like Schizophrenia and Bipolar disorder. Despite their symptom management benefits, they carry cardiovascular risks. Electrocardiogram (ECG) monitoring is crucial for detecting abnormalities. This research aims to identify and understand these risks, aiding healthcare professionals in implementing effective monitoring for better patient outcomes.

Methods: A retrospective study on subjects who are patients on Antipsychotic medications from the University of Port Harcourt Teaching Hospital (UPTH).

Results: In a study with 100 patients on antipsychotic medications, 68% displayed abnormal ECG changes during treatment, while 32% had normal patterns. Left Ventricular Hypertrophy (LVH) and Atrial Enlargements were common, affecting 30% and 26% respectively, while QT interval prolongation was rare (2%). Risperidone, Sodium Valproate, and Trihexyphenidyl showed the most abnormal ECG changes, whereas Olanzapine, Fluoxetine, and Escitalopram were relatively safer.

Conclusion: ECG monitoring is an essential component of the management of patients on antipsychotic drugs. It enables the early detection of QT interval prolongation and other cardiac abnormalities, allowing for timely interventions and personalized treatment plans. Our study showed just 2% of the patient had QT interval prolongation, however Left Ventricular Hypertrophy was a common finding in the ECG of the patients, 30%.

Keywords: Antipsychotics drugs; Tertiary hospital; UPTH; Electrocardiogram; Pyschatric

1. Introduction

Antipsychotic medications are used in the treatment of various neuropsychiatric disorders, such as schizophrenia, bipolar disorders, and anxiety disorders. These medications help alleviate symptoms associated with these conditions, including hallucinations, delusions, and mood disturbances. However, antipsychotic drugs are not without their potential side effects, particularly in relation to cardiovascular health.

One major concern linked to antipsychotic medications is their adverse effect on cardiac function regardless of whether the patient has a history of cardiac disease (1). Patients with psychiatric disorders have been reported by various studies to have a heightened risk of cardiovascular morbidity and mortality (2–4). Approximately 70% of fatalities in

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individuals with mental illnesses are attributed to physical ailments, with cardiovascular diseases (CVDs) accounting for 17.4% to 22.0% of the overall decrease in life expectancy (5). On a worldwide scale, more than 80% of individuals diagnosed with bipolar disorder experience some form of medical comorbidity, with a significant number either grappling with or succumbing to CVDs (6). Furthermore, those with schizophrenia are documented to have a threefold higher risk of dying from a heart attack compared to the general populace (7,8).

Certain medications within this class have been found to cause electrocardiogram (ECG) abnormalities such as prolonged QT interval, sinus tachycardia, sinus bradycardia, widening QRS complex, and premature atrial contraction (2,9). Additionally, antipsychotic drugs may also contribute to other cardiovascular effects, such as orthostatic hypotension, myocarditis, and cardiomyopathy (10–12).

Several factors play a role in the onset of CVDs in individuals with psychiatric disorders. These include inherent biological shifts observed during episodes of psychosis and a heightened occurrence of controllable cardiovascular risk elements like obesity, smoking, diabetes, and dyslipidemia. These factors collectively contribute to the elevated prevalence of CVDs among psychiatric patients (13).

Although CVD is widely prevalent, roughly 80% of individuals with mental health conditions face restricted access to primary healthcare and fewer chances for CVD assessments (14). Additionally, those with mental disorders often struggle to express their health worries, exhibit limited awareness of their condition, and frequently overlook cardiovascular symptoms like chest pain and palpitations. This oversight can lead to a diminished detection rate of CVDs (15). Consequently, the combination of underdiagnosed CVDs and constrained healthcare access heightens the potential for sudden cardiac fatalities among these individuals (16).

Given these potential risks, ECG monitoring becomes crucial in patients receiving antipsychotic medications. By regularly assessing cardiac function through ECG, healthcare professionals can detect any abnormalities or changes in the ECG patterns of these patients, allowing for timely intervention and modification of treatment plans to ensure patient safety.

In Nigeria and other African countries, there is a significant underreporting of cardiovascular diseases and associated electrocardiographic changes among psychiatric patients. Those in Nigeria and similar developing nations often do not undergo initial or subsequent ECG screenings when prescribed psychiatric medications. Also, there is a scarcity of research in Africa that examines ECG changes in individuals taking antipsychotic medications, emphasizing the need for more studies on the cardiac side effects faced by these patients.

By consolidating the available knowledge on ECG monitoring in patients on antipsychotic drugs, this research work aims are to identify the cardiovascular risk factors associated with antipsychotic medications, contribute to a better understanding of the associated risks and guide healthcare professionals in implementing effective monitoring strategies to optimize patient outcomes.

2. Materials and methods

This research is a retrospective study conducted at the University of Port Harcourt Teaching Hospital (UPTH), River State, Nigeria, comprising of both outpatient and inpatient adults who are receiving antipsychotic medications.

A total of 100 patients aged 18 to 73 years with various psychiatric diagnosis established through clinical evaluation and clinical records were included in this study. This included patients who has been on psychotropic medication for at least 5months.

Convenience sampling was employed.

Demographic data (age, gender, duration on medication, etc.) and information on other potential confounding variables like other medical conditions were retrieved from the health record of the patients.

Standard 12-lead ECG recordings were obtained from each participant using a digital ECG machine. The ECGs results were interpreted by qualified cardiologists blinded to the participants' clinical data.

Demographic and clinical characteristics of the participants was summarized using means, standard deviations, frequencies, and percentages as appropriate.

The prevalence of abnormal ECG patterns, such as QT prolongation, ST-segment changes, and arrhythmias, was determined. Associations between ECG abnormalities and duration of antipsychotic medication use, or other potential risk factors was assessed using Statistical Package for Social Sciences (SPSS) version 21.0.

3. Results

Selected baseline characteristics of the patients are shown in Table 1.

The male and female patients are same in proportion (50% each). Majority (58%) of the patients were within the age range of 18-39 years, 33% were within 40-59 years while 9% were within 60-79 years. The body mass index (BMI) of the patients shows that 35% of the patients had normal BMI, 26% were obese, a slight majority 38% were overweight and just 1% were underweight.

The mean age of the patients was 38.92 years ± 13.08, mean BMI was 27.35 Kg/m^2 ± 5.59 and mean duration was 3.36 years ±3.69.

Table 1 Baseline characteristics of study population

Characteristics	**Patients (100) n (%)**
Gender	
Male	50 (50%)
Female	50 (50%)
Age group	**N (%)**
18-39	58 (58%)
40-59	33 (33%)
60-79	9 (9%)
BMI group	**N (%)**
Normal	35 (35%)
Obese	26 (26%)
Overweight	38 (38%)
Underweight	1 (1%)
Characteristics	**Patients (100) mean ± sd**
AGE (YEARS)	**38.92 ± 13.08**
BMI (Kg/m2)	**27.35 ± 5.59**
Duration on treatment	**3.36±3.69**

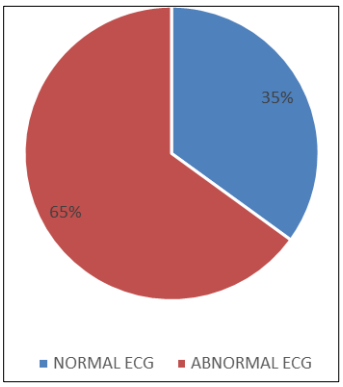

Figure 1 ECG findings comparison

Figure 1 is a bar chart showing the ECG distribution of the patients, majority (65%) had abnormal ECG while 35% had normal ECG.

The psychaitic diagnosis amomg patients is shown in Table 2. Depression was the most common diagnosis found in 29% of the patients, schizophrenia 28%, Bipolar disorder 23%, psychosis 18%, substance disorder 12%, anxiety 10%. The least occuring diagnosis are dementia, somatoform disorder, OMD, PTSD and tourret syndrom with occurrence of 1% each.

Table 2 Distribution of psychaitic diagnosis amomg patients

Psychiatric diagnosis	Percentage(%)
Depression	29
Schizophrenia	28
Bipolar	23
Psychosis	18
Subtance related disorder	12
Anxiety	10
Dementia	1
Somatoform disorder	1
Omd	1
Ptsd	1
Tourrete syndrom	1

Table 3 shows a comparative of ECG finding among the anti-psychotic patients. Patients with abnormal ECG includes 68.3% of patients on risperidone, 61.9% on Na Valproate, 67% on Trihexyphenidyl, 66.7% on Aripiprazole, 68.8% on Sertraline, 76.5% on Carbamazepine, 73% on Haloperidol, 69.2% on Amitriptyline. Majority (66.7%) of patients on Olanzapine had abnormal ECG, also the same majority (66.7%) on Fluoxetine had abnormal ECG.

Table 3 Comparative distribution of ECG findings among various anti-psychotic medications

Anti-Psychotic	Normal ECG	Abnormal ECG	Percentage of Patients medication
Risperidone	31.7%	68.3%	41%
Na Valproate	38.1%	61.9%	21%
Trihexyphenidyl	32.1%	67.9%	28%
Aripiprazole	33.3%	66.7%	9%
Sertraline	31.3%	68.8%	16%
Carbamazepine	23.5%	76.5%	17%
Haloperidol	26.3%	73%	19%
Olanzapine	66.7%	33.3%	15%
Amitriptyline	30.8%	69.2%	13%
Fluoxetine	66.7%	33.3%	6%
Escitalopram	100%	0%	4%
Chlorpromazine	33.3%	66.7%	6%
Flupentixol	0%	100%	2%
Paroxetine	40%	60%	5%

Antipsychotic usage by gender is shown in a chart in Fig 2. Males are the majority of patients on Risperidone (26%), NA Valproate (15%), Trihexyphenidyl (16%), Carbamazepine (13%), Haloperidol (11%) and CPZ (chlorpromazine) (6%). Females on Sertraline, Amitriptyline and Fluoxetine are more than the males, 11%, 9% and 4% respectively.

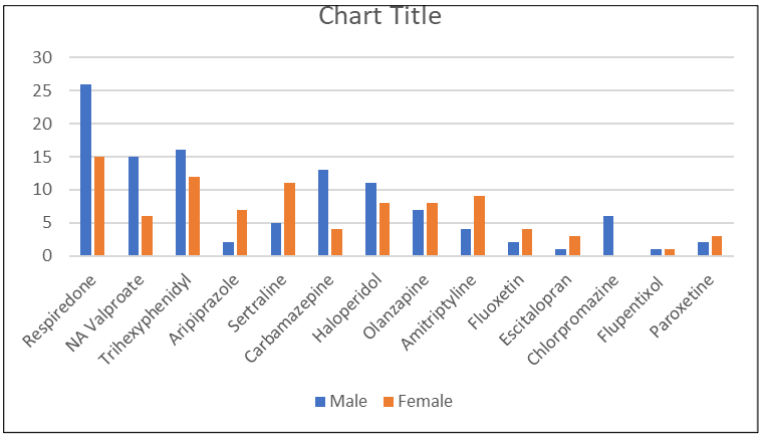

Figure 2 Antipsychotic medication usage by gender

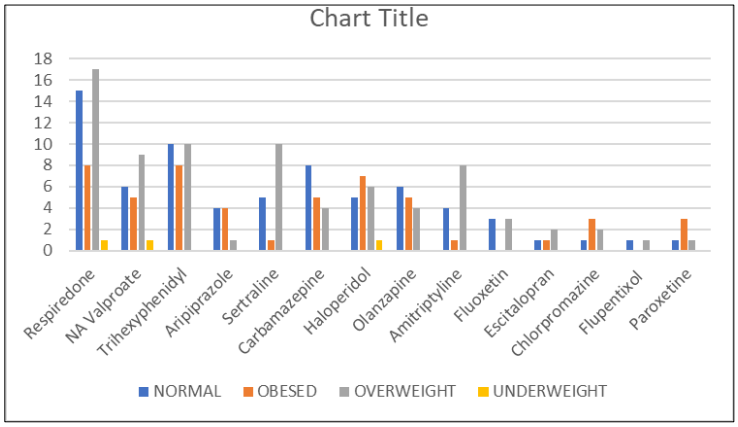

Figure 3 The effect of various antipsychotic medication on BMI

Fig 3 is a chart showing the distribution of medication by BMI. Majority of people on Risperidone, NA Valproate, sertraline and amitriptyline are overweight. Majority of patients on Haloperidol, CPZ and Paroxetine are obese. The proportion of obese patients was also high among those who were on Trihexyphenidyl, olanzapine and Aripiprazole.

Table 4 Illustrates the impact of antipsychotic medication on BMI across different durations

Duration of medication	Normal weight	Obese	Overweight	Underweigt	Total patient count
<5 YEARS	26	18	26	1	71
5-10 YEARS	8	6	9	0	23
>10 YEARS	1	2	3	0	6

Majority (71%, n=71) of the patients were treated for less than 5 years (Table 4). 26% of the total patients had normal weight and were treated for less than 5 years. Another 26% were overweight and treated for less than 5 years. The proportion of total patients who were treated for 5 -10 years and were obese was 6%, overweight 9%, normal weight 8% and underweight 0%. The least (6%, n=6) number of patients were treated for more than 10 years. The proportion of the total patient who were treated for more than 10 years and were obese are 2%, overweight 3%, normal weight 1% and underweight 0%.

Table 5 The various ECG changes in relations to various Anti-Psychotic medication

ECG Changes	**Anti-psychotics**													
	Risperidone	**Na Valproate**	**Trihexyphenidyl**	**Aripiprazole**	**Sertraline**	**Carbamazepine**	**Haloperidol**	**Olanzapine**	**Amitriptyline**	**Fluoxetine**	**Escitalopram**	**Chlorpromazine**	**Flupentixol**	**Paroxetine**
Normal ECG	13	8	9	3	5	4	5	10	4	4	4	2	-	2
Sinus Rhythm	34	19	24	10	16	15	19	14	11	6	4	5	2	6
LAD	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RAD	1	1	1	-	-	-	-	-	-	-	-	-	1	-
LVH	16	6	9	2	5	6	7	2	3	2	-	3	2	2
RAE	5	-	3	3	-	2	3	-	1	-	-	-	-	1
LAE	6	3	4	4	4	3	3	1	2	-	-	3	-	-
QT Prolongation	2	-	1	-	-	1	-	-	-	-	-	-	-	-
Sinus Tachycardia	1	-	2	-	-	1	-	1	-	-	-	-	-	-
Sinus Arrhythmia	1	2	1	-	-	-	1	-	-	-	-	-	-	-
Sinus Bradycardia	3	-	1	-	1	2	1	-	2	1	1	-	-	-
Abnormal T-wave	4	-	-	-	-	-	-	-	-	-	-	-	-	1

Ventricular Ectopic	1	-	-	-	-	-	-	-	-	-	-	-	-	-
Early Repolarization	4	1	3	1	-	2	1	-	2	-	-	-	-	-
RBBB	-	-	-	1	-	1	-	-	-	-	-	-	-	-
LBBB	1	-	-	-	1	-	-	-	-	-	-	-	-	-
Poor R-wave Progression	-	2	2	-	1	-	1	-	-	-	-	-	-	-
Pre-excitation	-	1	1			1	1	1	-	-	-	1	-	-
Tall T-wave	-	3	3	2		1	5	-	-	-	-	1	-	-
ST Abnormality	-	1	-	-	1	-	1	1	-	-	-	-	-	-
Atrial Enlargement (Non-specific)	-	-	-	-	2	-	2	-	-	-	-	-	-	-

Table 5 shows the various ECG changes in relations to various Anti-Psychotic medication. The proportion of the total patients in the study who were treated with anti-psychotic medication and has Left ventricular hypertrophy (LVH) includes 16% on risperidone, 6% on Na Valproate, 9% on trihexyphenidyl. Right atrial enlargement (RAE) was seen patient treated with risperidone (5%), trihexyphenidyl (3%), aripiprazole (3%). Left atrial enlargement was seen in patients on risperidone (6%), Na valproate (3%), trihexyphenidyl (4%), aripiprazole (4%), sertraline (4%), carbamazepine (3%). Sinus bradycardia was seen in patient with risperidone (3%), carbamazepine (2%), amitriptyline (2%). Other ECG changes in relation to anti-psychotic medication are shown in Table 5.

4. Discussion

The mean age of the patients from this study was 38.92 ± 13.08 years. Mean duration of intake of antipsychotic medication was 3.36 ± 3.69 years.

The prevalence of abnormal ECG in this study was 65% (fig1). This finding is similar to a study conducted at Jimma Medical Center psychiatric Clinic Ethiopia where the prevalence of abnormal ECG from their findings was 60.6%(17) but lower than the findings in a study conducted at Ekiti State University Teaching Hospital (EKSUTH) Ado Ekiti, Nigeria where the prevalence of abnormal ECG was 35.8% (18). This inconsistency may be due to study population, dosage and types of antipsychotic medications, patients' comorbidities, duration of antipsychotic medications and difference in socio economic status.

The most prevalent psychiatric disorder from our findings is Depression (29%). This could be due to economic challenges in Nigeria, PTSD and cultural factors which may in include social expectation and gender roles (19,20).

From our findings, patients on Risperidone had the highest number of ECG abnormalities (68.3%) (Table 3) this disagrees with a study conducted at Yong-in Mental Hospital, Gyeonggi, Republic of Korea which concluded that using risperidone to treat acute schizophrenia might increase cardio-vagal activity, potentially improving the balance between sympathetic and vagal functions. However, the reason for the high prevalence of abnormal ECG in this study may be because Risperidone has been associated with QT interval prolongation, a known risk factor for ventricular arrhythmias and sudden cardiac death (21).

This current study revealed that patients on Risperidone were mostly overweight (17%) (fig 3). This agrees with various studies that showed that risperidone is associated with weight gain and dyslipidemia (which are known factors for cardiovascular diseases) in patients on antipsychotic medications (22,23). These metabolic changes may contribute to an increased risk of cardiovascular events and abnormalities in the ECG (24).

According to the findings on this study, patients on antipsychotic medications gained weight within the first 5 years on being on medications (table 4). This could be as a result of several factors such as: hormonal changes, histamine receptor blockade, serotonin receptor modulation and dopamine receptor antagonism.

Antipsychotic medications, particularly atypical antipsychotics such as Risperidone, Aripiprazole and Olanzapine can affect hormonal systems related to metabolism. They may lead to disruptions in insulin sensitivity, increased appetite, and alterations in the balance of hormones such as leptin and ghrelin, contributing to weight gain (25)

Many atypical antipsychotics have histamine receptor-blocking properties, which may increase appetite and lead to weight gain (26).

Serotonin receptors, especially 5-HT2C receptors, play a role in appetite regulation. Antipsychotic medications can interact with these receptors, potentially leading to increased food intake (27).

Dopamine receptors in the brain are also involved in the regulation of appetite and satiety. Antipsychotics that block dopamine receptors such as NA Valproate, Trihexyphenidyl, Aripiprazole among others may interfere with these processes, contributing to weight gain (28).

Several atypical antipsychotic medications have been associated with QT interval prolongation which includes Risperidone. From table 5 we can see that only 2% of the patient had QT interval prolongation on their ECG. The exact mechanisms by which antipsychotic medications prolong the QT interval are not fully understood. However, it is believed that these drugs can block certain cardiac ion channels, particularly the human Ether-à-go-go-Related (hERG) Gene potassium channel, leading to delayed repolarization and QT prolongation (29).

The findings from Table 5 illustrate various ECG changes in patients treated with different antipsychotic medications. The observed prevalence of LVH among patients on antipsychotic medications, particularly risperidone, Na valproate, and trihexyphenidyl, highlights the potential impact of these drugs on cardiac structure. LVH is associated with increased cardiovascular risk and may result from chronic hypertension, which is a common comorbidity in psychiatric patients. Antipsychotics, through various mechanisms such as sympathetic activation or direct cardiotoxic effects, can contribute to LVH development (29).

The presence of RAE and LAE across multiple antipsychotic medications suggests a generalized effect on atrial remodeling. Atrial enlargement is associated with atrial fibrillation and increased risk of stroke and heart failure. Antipsychotics may influence atrial structure and function through autonomic dysregulation or direct effects on cardiac myocytes, leading to atrial dilation (30).

Antipsychotic medications can influence heart rate, leading to both bradycardia and tachycardia. The mechanisms underlying these effects are multifactorial and may involve various physiological pathways.

Antipsychotic drugs can disrupt the balance between sympathetic and parasympathetic activity in the autonomic nervous system. Some antipsychotics, particularly those with strong antagonistic effects on alpha-adrenergic receptors, can lead to increased parasympathetic tone and bradycardia. Additionally, antagonism of histamine H1 receptors by certain antipsychotics may contribute to bradycardia through central and peripheral mechanisms (29). Also, some antipsychotic medications have direct negative chronotropic effects on the heart, primarily through blockade of cardiac ion channels or receptors. For example, antagonism of muscarinic acetylcholine receptors can lead to bradycardia by inhibiting the actions of acetylcholine on the sinoatrial node (31).

Some antipsychotic medications can increase sympathetic activity, leading to tachycardia. This effect may result from the blockade of alpha-adrenergic receptors, which disinhibits sympathetic tone, or from the antagonism of histamine H1 receptors, which can indirectly stimulate sympathetic activity (30). Antipsychotics may also exert direct effects on the central nervous system, altering autonomic regulation of heart rate. For example, dopaminergic antagonism in the hypothalamus or other brain regions can influence sympathetic outflow and cardiac function (32).

Limitations

Despite the valuable insights provided by the research conducted in a psychiatric center, there are challenges and limitations to consider, such as:

Missing Data: Incomplete or missing data in medical record can introduce bias and affect the accuracy and comprehensiveness of the analysis. For example, Data such as BMI should be collected before treatment, during treatment and after treatment to improve the accuracy of the research.

Cost-effectiveness: While ECG monitoring for patients on antipsychotic drugs is an important tool for detecting potential cardiac abnormalities, this procedure can be expensive for some patient. This can lead to some patient refusing to have an ECG done for them regularly and this can reduce the quality of care given to them.

Recommendations

The American Psychiatric Association (APA) has published practice guidelines for the treatment of psychiatric disorders, including schizophrenia and bipolar disorder. These guidelines address the cardiovascular risks associated with antipsychotic medications and provide recommendations for ECG monitoring and risk management. Key recommendations include:

- Baseline ECG assessment for patients with specific risk factors, such as a history of cardiac disease, syncope, or family history of cardiac events.
- Regular ECG monitoring during treatment, particularly for patients on high-potency antipsychotics or those with additional risk factors.
- Consideration of alternative antipsychotic medications with a lower risk of QT prolongation in high-risk patients.
- Awareness of drug-drug interactions that may potentiate QT prolongation and avoidance of concurrent use of medications known to increase QT interval.

5. Conclusion

ECG monitoring is an essential component of the management of patients on antipsychotic drugs. It enables the early detection of QT interval prolongation and other cardiac abnormalities, allowing for timely interventions and personalized treatment plans. Though our study showed just 2% of the patient had QT interval prolongation, Left Ventricular Hypertrophy was a common finding in the ECG of the patients, 30%. Therefore, by integrating ECG assessment into routine clinical practice, healthcare practitioners would be able to mitigate potential cardiac risk, enhance patient safety and optimize the overall quality of individuals with psychiatric conditions.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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