American Journal of Psychiatry and Neuroscience
2014; 2(5): 76-82
Published online October 30, 2014 (http://www.sciencepublishinggroup.com/j/ajpn)
doi: 10.11648/j.ajpn.20140205.12
ISSN: 2330-4243 (Print); ISSN: 2330-426X (Online)

Antipsychotic medication induced movement disorders: The case of Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia

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To cite this article:

Habtamu Taye, Tadesse Awoke, Jemal Ebrahim. Antipsychotic Medication Induced Movement Disorders: The Case of Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia. *American Journal of Psychiatry and Neuroscience.* Vol. 2, No. 5, 2014, pp. 76-82.
doi: 10.11648/j.ajpn.20140205.12

Abstract: Background: Neuroleptic-induced movement disorders constitute a worldwide problem in the treatment of schizophrenia because of the limited affordability of atypical antipsychotic drugs. The observable features of acute Parkinsonism; such as limb stiffness and slowness of movement are a social and functional handicap. The same is true for the restless movements and agitation associated with acute akathisia. Tardive dyskinesia, on the other hand is a permanent condition that affects quality of life. However, very few studies have been conducted to estimate the prevalence of Neuroleptic-induced movement disorders and their associated factors among psychotic patients in Ethiopia. Thus the aim of this study was to determine the prevalence of conventional antipsychotic induced movement disorders and associated factors among psychotic patients treated at Amanuel mental specialized Hospital. Method: Hospital based cross-sectional study was conducted by using established clinical rating scales to identify cases of conventional antipsychotic-induced movement disorders in Amanuel mental specialized Hospital on a sample of 377 psychotic outpatients. Systematic random sampling method was employed to select subjects. Logistic regression was used for comparison of the subjects with and without Neuroleptic-induced movement disorders. Results: the prevalence of Neuroleptic-induced movement disorders, namely; neuroleptic-induced Parkinsonism, neuroleptic-induced Akathisia and neuroleptic-induced tardive dyskinesia were found to be 46.4%, 28.6% and 11.9% respectively. Khat (Catha Edulis) use, AOR=1.93, 95%CI: 1.01-3.66, was factors remained to be associated with the presence of NIA. Alcohol use, AOR = 3.25, 95%CI: 1.04-10.16, was associated with TD. Being on chlorpromazine equivalent dose range of >=400mg/day, AOR =4.32, 95%CI: 2.25-8.30, AOR = 3.677, 95%CI: 1.807-7.482, AOR=4.157, 95%CI: 1.165-14.834 were associated with Parkinsonism, Akathisia and TD respectively. Conclusions and Recommendation: Considerable number of patients with psychotic disorders suffered from a conventional antipsychotic - induced movement disorder. Khat, alcohol and high dose of drugs were found to be associated with conventional antipsychotic Induced movement disorders. Designing treatment guideline, increasing availability of drugs with minimal side effects and psycho-education for patients and their family is essential to reduce these devastating side effects.

Keywords: Parkinsonism, Akathisia, Tardive Dyskinesia, Conventional Antipsychotic, Movement Disorder

1. Introduction

Antipsychotic drugs include dopamine receptor antagonists or conventional antipsychotics, serotonin-dopamine antagonists or atypical antipsychotics and dopamine partial agonists [1].

Since their development in 1950s conventional antipsychotic medications have been a primary component of treatment for schizophrenia and related psychotic disorders [2]. The therapeutic efficacy of these drugs is well established, both for treatment of acute symptoms and in relapse prevention. Unfortunately, they are associated with a broad range of side-effects, the most prominent of which is

the development of a variety of movement disorders [3]. Factors for Tardive dyskinesia were Old age, Female sex, Brain damaged individuals, cumulative neuroleptic dose, duration of exposure, Presence of drug induced Parkinsonism in the early phase of neuroleptic treatment, Primary psychiatric diagnosis of affective disorder and substances including alcohol [3, 4, 5]. The risk factors leading to akathisia were poorly understood; though it is noted more with high potency antipsychotics possibly due to employment of higher doses. Middle aged Women are at greatest risk [6, 7, 8].

Risk Factors for Development of Drug-Induced Parkinsonism were High dose, high-potency drug use; elderly, female sex, hereditary susceptibility and Coexistence with tardive dyskinesia [4, 8].

Cross-sectional Study on institutionalized psychotic patients from Central Estonia reported that, 31.3% had neuroleptic-induced akathisia 23.2% had neuroleptic-induced Parkinsonism and 32.3% had neuroleptic-induced tardive dyskinesia [9]. Previous reports regarding the association of Akathisia with socio-demography were inconsistent. Some of them reported that there was no significant difference in age between the Akathisia and non-Akathisia groups [10, 11, and 12]. The relationship between Akathisia and sex has also been inadequately investigated [14]. Some studies reported higher prevalence is among females [6, 13 and 15]. Most epidemiological studies have not reported any sex differences in the vulnerability to Akathisia [11, 12, and 16]. Another study on the other hand, stated that "Akathisia...tends to prevail in men"[17]. Review article from UK concluded that there was no significant gender difference for development of drug induced Parkinsonism but there are reports that stated the male to female ratio is 1:2 [4, 18]. Nigerian Study done in 1981 reported the prevalence rate of TD was higher among the females (14.5%) than among the males [7%]. All TD cases were found to be of an older age group than the total population [19]. However study conducted in 1989 reported there were no significant differences between the sexes [20].

Search for literature revealed, there was no study that investigated the prevalence of conventional antipsychotic induced movement disorders and associated factors in Ethiopia.

Despite mental health problem was included in national health policy of Ethiopia, interventions against the problem are limited. Among the main reasons, lack of data on the extent of the problem is one. Therefore this study was aimed to determine the prevalence of conventional antipsychotic induced movement disorders and associated factors among Psychotic patients attending treatment at Amanuel Hospital, Addis Abeba, Ethiopia. It was also hoped that this study would increase the awareness of clinicians to critically look and treat patients with antipsychotic induced movement disorders; help administrators to investigate solutions for the problems and serve as base line for those who wish to conduct study on antipsychotic induced movement disorders

2. Methodology

Hospital based cross-sectional study was conducted from February 9 to March 9/2011 among psychotic patients treated at Amanuel mental specialized Hospital. Systematic random Sampling technique was employed. Five experienced psychiatric nurses were hired and assessed all subjects after being trained to identify the movement disorders in accordance with Barnes Rating Scale for Akathisia (8), the Simpson-Angus Rating Scale for Drug-Induced Parkinsonism [9] and Abnormal Involuntary Movement Scale (AIMS) for Tardive dyskinesia [10]. The threshold value for Akathisia was a Barnes scale total score of 2 or more (scale range=0–5); for Parkinsonism, the threshold value was a Simpson-Angus Rating Scale mean global score of 0.65 or more (scale range=0–4). For the diagnosis of Tardive dyskinesia, a minimum global rating of "mild" (i.e. 2 or more on AIMS item no. 8), was used.

For analysis, Coded variables were entered into SPSS version 13.0 window software program. Logistic regression was used for comparison of subjects with and without conventional antipsychotic-induced movement disorders. From the bivariate analysis three different models were fitted for the three outcome variables in relation to each explanatory variable. Those which fulfilled the minimum requirement, 0.2 level of significance; were entered in to multivariate logistic analysis for further assessment. Fitness of model check showed that, the model adequately fitted the data for Neuroleptic Induced Parkinsonism, Neuroleptic Induced Akathisia, and Tardive dyskinesia as P- value from Hosmer and Lemeshow test was 0.86, 0.78 and 0.82 respectively. Written informed consent was obtained from the subjects, and the study was approved by University of Gondar College of medicine and health science ethical committee. The main limitations of this study were: Co-occurrence of spontaneous movement disorders commonly detected in schizophrenic population which could not be excluded.

3. Results

Of the 403 planned participants, 93.5% were involved in the study of which, 65.3 were males. Twenty six patients failed to fulfill the inclusion criteria. The median age of participants was 30.0 years (SD=10.57). Of the total participants the majority; 126(33.4%) were Amhara, 274(72.7%) were Christians, 93(24.7) were jobless, 184(48.8%) were within primary school educational levels and 234(62.1%) were single in marital status. (Table 1)

Of the 377 participants 80.6 % had the diagnosis of schizophrenia, 58.4% had gone <5years with their illness and 9.0% had family history of primary movement disorders. High potent antipsychotic drugs were taken by 41.4% of participants. Patients on Chlorpromazine equivalent dose range of >=400mg/day were 32% and 15.38 % participants took combination of antipsychotic drugs. Of these 13.3 % of them took Fluphenazine and chlorpromazine combination treatment. (Table 2)

Table 1. *Distribution of participants by socio-demographic Characteristics at Amanuel mental specialized Hospital, 2011.*

Characteristics	Frequency (N=377)	Percent (%)
Age		
<30	172	45.6
30-44	142	37.67
>=45	63	16.71
Sex		
Male	246	65.3
Female	131	34.7
Educational status		
Can't read and write	68	18.0
1-6 grades	125	33.2
7-12 grades	71	18.8
>12 grades	113	30.0
Religion		
Christian	274	72.7
Muslim	103	27.3
Marital Status		
Married	103	27.3
Single	234	62.1
Divorced/widowed	40	10.6
Ethnicity		
Oromo	96	25.5
Amhara	126	33.4
Gurage	107	28.4
Others	48	12.7
Occupation		
With job	284	75.3

Table 2. *Distribution of participants by clinical Characteristics at Amanuel mental specialized Hospital, 2011.*

Characteristics	Frequency (N=377)	Percent (%)
Diagnosis of patients		
Schizophrenia	304	80.6
Schizoaffective disorder	22	5.8
Schizophreniform disorder	23	6.1
Others	28	7.4
Family history of primary movement disorders		
Yes	34	9.0
No	343	91.0
Chlorpromazine equivalent dose (mg/day)		
50-<100	118	31.3
100-<400	138	36.6
>=400	121	32.1
High potent antipsychotic drugs		
Yes	156	41.4
No	221	58.6

Among participants using substances; 7.7% consumed alcohol, 24.4% smoked cigarette and 28.1% chewed khat.

3.1. Prevalence of Conventional Antipsychotic Induced Movement Disorders

The overall prevalence of conventional antipsychotic induced movement disorders was 56%: neuroleptic induced Parkinsonism 46.4, Akathisia 28.6 % and tardive dyskinesia 11.9 % respectively. (Fig. 1)

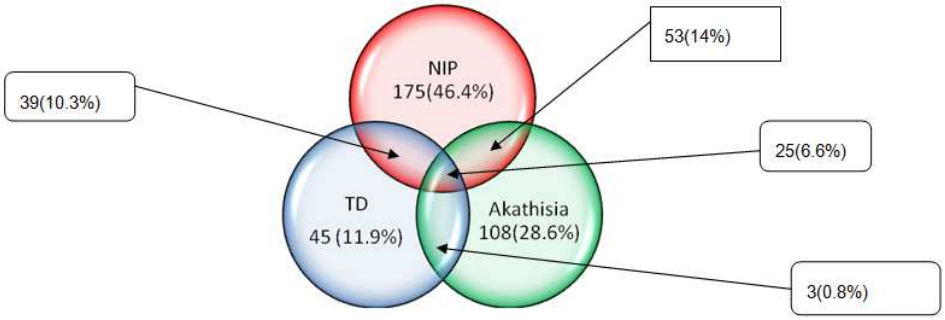

Fig 1. *Prevalence of Neuroleptic induced movement disorders among psychotic patients treated at Amanuel mental specialized Hospital, 2011.*

3.2. Factors Associated with Antipsychotic Induced Movement Disorders

During analysis of neuroleptic induced parkinsonism in relation to all explanatory variables, being on chlorpromazine equivalent dose range of 100-<400mg/day AOR =2.18, 95%CI: 1.22-3.88 and >=400mg/day AOR =4.32, 95%CI: 2.25-8.30 as well as being on high potent conventional antipsychotics AOR= 4.63, 95%CI):1.93-11.13 were factors remained to be statistically significant. (Table 3)

During the multivariate analysis of Akathisia in relation to all exploratory variables, khat use AOR=1.93, 95%CI: 1.01-3.66 and being on chlorpromazine equivalent dose range of 100-<400mg/day AOR=2.27, 95%CI: 1.16-4.43 and >=400mg/day AOR = 3.68, 95%CI: 1.81-7.48 were factors remained to be statistically significant. (Table 4)

During the analysis of TD; age >=45 years AOR =3.45, 95%CI: 1.12-10.63, joblessness AOR=3.19, 95%CI: 1.43-7.16, alcohol use AOR = 3.25, 95%CI: 1.04-10.16, and chlorpromazine equivalent dose range of >=400mg/day AOR=4.157, 95%CI: 1.17-14.83 were the most contributing factors remained to be statistically significant. (Table 5)

Table 3. *Factors associated with neuroleptic induced Parkinsonism (Bivariate analyses and multivariate analysis), at Amanuel mental specialized Hospital, among psychotic patients, 2011.*

Explanatory variable	Parkinsonism (N=377)		COR (95%C.I.)	AOR (95%C.I.)
	Yes	No		
Ethnicity				
Oromo	41	55	1.00	1.00
Amhara	50	76	0.88(0.52, 1.51)	0.71(0.38, 1.30)
Guragie	62	45	1.85(1.06, 3.23)*	1.42(0.74, 2.74)
Others	22	26	1.14(0.57, 2.28)	0.88(0.39, 1.99)
Marital status				
Married	36	67	1.00	1.00
Single	118	116	1.89(1.17, 3.06)*	1.57(0.90, 2.72)
Divorced/widowed	21	19	2.06(0.98, 4.32)	1.54(0.65, 3.65)
Duration of treatment				
1month-<6month	94	138	1.00	1.00
6month-5yr	54	42	1.89(1.17, 3.05)*	1.24(0.70, 2.18)
>=5yrs	27	22	1.80(0.97, 3.35)	1.28(0.58, 2.84)
Alcohol use				
Yes	18	11	1.99(0.91, 4.34)	1.45(0.54, 3.88)
No	157	191	1.00	1.00
Cigarette use				
Yes	57	35	2.31(1.42, 3.73)*	1.29(0.65, 2.53)
No	118	167	1.00	1.00
Khat use				
Yes	65	41	2.32(1.47, 3.68)*	1.45(0.76, 2.75)
No	110	161	1.00	1.00
High potent antipsychotic drugs				
Yes	100	56	3.48(2.26, 5.34)*	2.30(1.400, 3.77)*
No	75	146	1.00	1.00
Chlorpromazine equivalent dose(mg/day)				
50-<100	28	90	1.00	1.00
100-<400	61	77	2.55(1.48, 4.37)*	2.34 (1.31, 4.15)*
>=400	86	35	7.90(4.43, 14.08)*	5.13(2.72, 9.68)*

* Statistically significant

Table 4. *Factors associated with neuroleptic induced Akathisia (Bivariate analyses and multivariate analysis), at Amanuel mental specialized Hospital, among psychotic patients, 2011.*

Explanatory variable	Akathisia(N=377)		COR (95%C.I.)	AOR (95%C.I.)
	Yes	No		
Age				
<30	43	129	1.00	1.00
30-44	42	100	1.26(0.77, 2.08)	1.21(0.69, 2.11)
>=45	23	40	1.73(0.93, 3.20)	1.44(0.72, 2.86)
Sex				
Male	78	168	1.00	1.00
Female	30	101	0.64(0.39, 1.04)	1.01(0.57, 1.78)
Occupation				
With job	74	210	1.00	1.00
Jobless	34	59	1.64(0.99, 2.69)	1.63(0.94, 2.85)
Diagnosis of patients				
Schizophrenia	92	212	1.00	1.00
Others	16	57	0.65(0.35, 1.19)	0.66(0.33, 1.31)
Alcohol use				
Yes	14	15	2.52(1.17, 5.42)*	1.68(0.68, 4.14)
No	94	254	1.00	1.00
Cigarette use				
Yes	37	55	2.03(1.24, 3.33)*	0.93(0.47, 1.85)
No	71	214	1.00	1.00
Khat use history				
Yes	45	61	2.44(1.51, 3.93)*	1.93(1.01,3.66)*
No	63	208	1.00	1.00
Cannabis use history				
Yes	5	1	13.01(1.50, 112.70)*	5.93(0.63,55.63)
No	103	268	1.00	1.00
High potent antipsychotic drugs				
Yes	54	102	1.64(1.04, 2.57)*	1.05(0.62, 1.80)

Explanatory variable	Akathisia(N=377)		COR (95%C.I.)	AOR (95%C.I.)
	Yes	No		
No	54	167	1.00	1.00
Chlorpromazine equivalent dose(mg/day)				
50-<100	16	102	1.00	1.00
100-<400	41	97	2.70(1.42, 5.12)*	2.27(1.16,4.43)*
>=400	51	70	4.65(2.452, 8.80)*	3.68(1.81,7.48)*

*Statistically significant

Table 5. *Factors associated with neuroleptic induced Tardive dyskinesia (Bivariate analyses and multivariate analysis), at Amanuel mental specialized Hospital, among psychotic patients, 2011.*

Explanatory variable	Tardive dyskinesia (N=377)		COR(95%C.I.)	AOR(95%C.I.)
	Yes	No		
Age				
<30	9	163	1.00	1.00
30-44	15	127	2.14(0.91, 5.05)	1.19(0.45, 3.16)
>=45	21	42	9.06(3.87, 21.22)*	3.45(1.12, 10.63)*
Occupation				
With job	27	257	1.00	1.00
Jobless	18	75	2.28(1.19, 4.37)*	3.19(1.43, 7.16)*
Marital status				
Married	15	88	1.00	1.00
Single	21	213	0.58(0.29, 1.17)	0.65(0.25, 1.71)
Divorced/widowed	9	31	1.70(0.68, 4.28)	0.85(0.28, 2.60)
Duration of the psychotic disorder				
<5yrs	10	211	1.00	1.00
5-9yrs	13	58	4.73(1.97, 11.34)*	4.92(0.98, 24.72)
10-19	18	51	7.45(3.24, 17.10)*	3.09(0.44, 21.87)
>=19	4	12	7.03(1.92, 25.74)*	2.45(0.20, 29.74)
Duration of treatment				
1month-<6month	13	219	1.00	1.00
6month-5yr	15	81	3.12(1.42, 6.84)*	0.64(0.13, 3.20)
>=5yrs	17	32	8.95(3.97, 20.15)*	2.06(0.30, 14.35)
Alcohol use				
Yes	10	19	4.71(2.03, 10.92)*	3.25(1.04, 10.16)*
No	35	313	1.00	1.00
Cigarette use				
Yes	19	73	2.59(1.36, 4.95)*	1.54(0.66, 3.55)
No	26	259	1.00	1.00
High potent antipsychotic drugs				
Yes	24	132	1.73(0.93, 3.24)	0.85(0.35, 2.06)
No	21	200	1.00	1.00
Chlorpromazine equivalent dose(mg/day)				
50-<100	5	113	1.00	1.00
100-<400	16	122	2.96(1.05, 8.35)*	2.50(0.77, 8.11)
>=400	24	97	5.59(2.06, 15.22)*	4.16(1.17, 14.83)*

* Statistically significant

4. Discussion

Hospital based cross sectional study was conducted to assess magnitude of conventional antipsychotic induced movement disorders and associated factors by using clinical rating scales (SAS, BAS and AIMS). The overall prevalence of 56%: neuroleptic induced Parkinsonism 175(46.4%), Akathisia 108(28.6%) and tardive dyskinesia 45(11.9%) were found respectively. The results were slightly different from previous studies done abroad [20, 21 and 22]. Some of the variations were probably due to variability of the disorders themselves. Individual patients may show a wide variability in site and severity of involuntary movements, related to adjustment of medication, anxiety, posture and mobility [2].

Even though, giving combination of the same class of drugs was not medically explained; 15.38% of participants took combination of conventional antipsychotic drugs. Of these 13.3 % of them took Fluphenazine and chlorpromazine combination treatment.

During the multivariate analysis of NIP in relation to all explanatory variables, being on chlorpromazine equivalent dose range of 100-<400mg/day and >=400mg/day had 2.18 and 4.32 times more likelihood of inducing NIP than lesser doses. Being on high potent conventional antipsychotics had 4.63 times chance of inducing NIP. This result was consistent with previous studies [17, 22].

Absence of association between gender and Parkinsonism was consistent with other studies [11, 18]. Similar to Estonian study there was no differences between patients with a neuroleptic-induced movement disorder and those

without with respect to sex, smoking status & length of illness and treatment [2].

During the multivariate analysis of NIA in relation to all explanatory variables, khat users had 1.93 times likelihood of having NIA compared to non users.

Possible explanations could be:

1. Akathisia was assumed to be caused by blockage of dopamine D2 receptor in nigrostriatal pathway and khat which is assumed to have similar action with Amphetamine increases striatal dopamine release in acute phase. However, its chronic effects are associated with striatal dopaminergic downregulation which can potentiate antipsychotic action.
2. Patients who took khat may develop symptoms similar with Akathisia on withdrawal phase.

Being on chlorpromazine equivalent dose of 100-<400mg/day and >=400mg/day had 2.27 and 3.68 times chance of inducing Akathisia. This was in line with studies done elsewhere [17, 22]. Absence of statistical difference between patients with Akathisia and those without, with respect to sex, age, ethnicity, education, religion, marital status, occupational status, alcohol use, cigarette use, diagnosis of patient's duration of illness and duration of treatment. This was consistent with previous studies with respect to sex [25, 26, 30], age [25, 26], ethnicity [23] and smoking status [2].

During the analysis of TD in relation to all explanatory variables; age >=45 were 3.45 times more likely to develop TD. This was consistent with multiple studies [19, 22, and 27]. Alcohol users had 3.25 times more likelihood of developing TD. This was consistent with some studies [24, 25] and being on chlorpromazine equivalent dose range >=400mg/day had 4.16 times more likelihood to induce TD. This was similar with other studies [24]. Lack of evidence for diagnostic specificity as a predictor for the occurrence of TD was consistent with some studies [23].

This study was not without limitations. Reports for some of the questions were past history or encounters which are prone to recall bias. Variables like Khat chewing and other substances are by nature a sensitive issue and social desirability bias is unavoidable. Co-occurrence of spontaneous movement disorders, commonly detected in schizophrenic populations, could not be excluded. The temporal connection between NIMD and neuroleptic medication as well as other association was established retrospectively by interview and medical records.

5. Conclusions and Recommendation

In conclusion, many patients with psychotic disorders suffered from a conventional antipsychotic -induced movement disorders which were seen as burdening and stigmatizing phenomena.

All of the antipsychotic induced movement disorders were found to be associated with chlorpromazine equivalent doses. Khat which was thought to be indigenous to Ethiopia is consumed by many patients who had been on antipsychotic drugs and found to be associated with Akathisia; one of distressing side effect.

Designing treatment guideline, increasing availability of drugs with minimal side effects and psycho-education on associated factors (e.g. khat use, alcohol consumption) is essential.

6. Authors' contribution

HT and TA designed the study, collected data and participated on data analysis and preparation of the manuscript. JE participated in analysis, drafted and prepared the manuscript. All the authors approved the final manuscript.

Acknowledgement

The authors would like to acknowledge Amanuel Specialized Mental Hospital for financial support. We also would like to thank the study subjects, data collectors and supervisors for their admirable endeavor during the data collection process.

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