



## RECURRENCE OF SCHIZOPHRENIA IN ANTIPSYCHOTIC DRUG DEFAULTER PATIENTS OF RURAL HOSPITAL OF JAWAHARLAL NEHRU MEDICAL COLLEGE, SAWANGI, MEGHE, WARDHA.

### Medicine

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### ABSTRACT

**Background** – In India many schizophrenic patients do not complete the course of

Anti psychotic medications and discontinue it due to poor financial condition which results in early recurrence of schizophrenia.

**Aims** – 1. To know factors influencing 'Time Interval' between discontinuation of

Antipsychotic drugs and recurrence of Schizophrenia.

**Method** – A total of sixty (n=60) schizophrenic patients having active signs and symptoms were cross sectionally studied from First October 2007 to July 2008 in terms of dose, duration of Antipsychotic drugs, equivalent to Chlorpromazine received in last episode. For assessment of Positive and Negative symptoms of Schizophrenia the Positive and Negative Syndrome Scale (PANSS) was applied.

**Result.** – One day of Antipsychotic medication provides protection from recurrence of schizophrenia for 0.4417 day and 637.91 mg Chlorpromazine equivalent of Antipsychotic medications per day provides protection for 0.3715 days.

**Conclusions** – As the schizophrenia is not curable but highly treatable disease, long term Pharmacotherapy and consultation with psychiatrist is mandatory.

### KEYWORDS

Recurrence, Schizophrenia, Time interval, Antipsychotic, Defaulter.

### INTRODUCTION

Schizophrenic patients becomes drug defaulter due to many reasons (i) financial, (ii) Lack of awareness of relative and patients about illness, and (iii) troublesome side effect of antipsychotic medications. Recurrence of schizophrenia occur if patient stops taking medications before completing its course. In general for first episode of Schizophrenia Antipsychotic medications should be continued for two years and for second episode for five years and for subsequent episodes, for life long. Kraepelin revised his original recovery rate of 13% to less than 4% ultimately suggesting that the full recovery brought the original diagnosis into question. Relapse rates after hospital discharge were higher in patients who had been ill for more than a year before treatment. In that group only 18% remained free of relapse after two years. Approximately one third of first admission patients with schizophrenia were relapse-free during first two years after admission. The relapse rate after two years of illness was around 60% (1). Weiden *et al.* (2004), reported that Antipsychotic gap as short as 10 days can double the risk of re-hospitalization for Schizophrenia and there is a steady, nearly linear increase of risk as the gap widens (2). Ioannis A. Parashos *et al.* (2000) studied 22 non compliance schizophrenic patients at Mental health centre of Volas, Greece and found that reason for noncompliance were lack of knowledge about the disease and specifically its course and management, in 60% of schizophrenia patients, 20% had to do with lack of insight, 10% had social pressure and 10% had drug side-effect., Overall 50% of the case were related to the use of medication. The major reason of compliance (54%) was the feeling of trust in doctor (3.). Because relapse typically occur weeks to months of discontinuation of medication, patients rarely attribute it to non compliance (Chien 1975 Herz and Melville 1980). (4,5). Kashner *et al.* found that substance abusing patients with Schizophrenia were 13 times more likely than non substance abusing patients to be non compliant with Antipsychotic medication (6).

Substance abuse increased the risk of non compliance eight folds and result in poor clinical outcome (Dixon *et al.*, 1992), (7). Rhobinson *et al.* (2005) reported that 23% of patients who relapsed were on First Generation Antipsychotics as compared to 15% who were on Second Generation Antipsychotics (8). Knights *et al.* (1974) followed Schizophrenic patients for 6 months who were either on Fluphenazine decanoate or Flupenthixol decanoate and found that only 7% of patients relapsed (9). Roberta Friedman (2000) found that post hoc analysis of a trial of long acting antipsychotic drug Paliperidon given by injection appear to decrease the likelihood of recurrence in schizophrenic patients. Larry Alphs (2009) told that evidence exist to support limiting recurrence in Schizophrenia because brain mass seems to decrease over time in patients with the disorder. The brain deteriorates with each progressive relapse (10).

Medication non compliance rate of 55 to 71 percent have been reported for patients with arthritis (Berg *et al.* 1993), 54 to 82 percent for patients with seizure disorders (Shope 1988), 20 to 57 percent for people with bipolar affective disorder (Elixhauser) and 19 to 80 percent for patients with diabetes (Friedman 1988). Half of patients with hypertension drop out care with in one year and only two-third of those who remain take adequate medication (Eraker *et al.* 1984), (11,12,13, 14, 15). A 1986 review of 26 studies using a variety of definitions and detection methods to assess medication use among outpatients with schizophrenia reported a median default rate of 41 percent (range 10% to 76%) with oral medication and 25 percent (range 14% to 35%) with depot injection over time period up to one year (Young *et al.*, 1986). Fifteen subsequent studies using varying definitions of non compliance and many patients taking oral and depot medications reported a median one month to two years, non compliance rate of 55% (range 24% to 88%) (Hogan *et al.*, 1983, Ayers *et al.*, 1984), (16,17.). Cooper S.J. (200) studied the effect of Zotepine in prevention of recurrence in randomized double blind placebo controlled study for Chronic Schizophrenia and found that Zotepine 300 mg daily for 26 weeks had approximately 5 times less relapse rates (4 versus 21) than placebo. (18). According to Bottai (2009) relapse prodromal signs are similar to the initial prodromal sign as well as in symptomatology than as their chronological apparition (19). Srinivas T, N, *et al.*, (1994) found that a female patients experienced a vague pain, discomfort and sensitivity to cold and hot objects in her teeth, sleeplessness, restlessness and irritability (20).

Majority of people coming in OPD of Department of Psychiatry, Jawaharlal Nehru Medical College (JNMC), & Acharya Vinoba Bhave Rural Hospital, Sawangi Meghe, Wardha were poor. Many Schizophrenic patients came with recurrence of this disorder due to early discontinuation of medication, due to financial problem.

### AIMS AND OBJECTIVES

1. To know factors influencing 'Time Interval' between discontinuation of Antipsychotic drugs and recurrence of Schizophrenia.

**MATERIAL & METHODS** – All schizophrenic patients having active signs and symptoms either came themselves or brought by relatives in the Psychiatry OPD, JNMC, Sawangi Meghe wardha on fixed OPD days, were enrolled for the study. Approval of Institutional Ethical Committee and written informed consent were taken either from patients or from their relatives. The patients were interviewed by using semistructured proforma by psychiatrist and the diagnosis was made according to DSM IV criterion. Total sixty (n=60) schizophrenic patients having active signs and symptoms, were examined in cross-sectional way, from first of October 2007 to July 2008. Factors like (a) Drugs in Chlorpromazine equivalent, received in the past and (b) Time interval between Antipsychotic drug discontinuation and onset of

first sign and symptoms of schizophrenia were recorded. For assessment of Positive and Negative symptoms of Schizophrenia the Positive and Negative Syndrome Scale (PANSS) was used. Patients were divided into four groups (i) Patients who had 'Time interval' between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 1 day to 6 months. (ii) Patients who had 'Time interval' between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 6 month to 1 year.

(iii). Patients who had 'Time interval' between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 1 year to 1 year and 6 months. (iv), Patients who had 'Time interval'

between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 1 year and 6 months to 2 years.

**INCLUSION CRITERION -**

1. Schizophrenic patients who themselves or their relatives agreed to participate in Study.

**EXCLUSION CRITERION -**

1. Schizophrenic patients who either themselves or their relatives refused to participate in study.
2. Those who had received Electro Convulsive Therapy in the past.

**TABLE No. 1, Time interval between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 1 day to 6 months, (n=40)**

Sl No.	Age (years)	Gen Der	Chlorpromazine Equivalent (mg)	Duration of Treatment	Time Interval	PANSS score (Total)	Positive	Negative	General Psycho pathology
1	50	M	125	3years	2months	96	18	38	40
2.	40	F	150	6month	4months	82	30	16	36
3.	44	F	200	6year	1month	83	18	21	44
4	26	F	750	10d	2mo,15d	100	22	24	54
5.	34	F	100	3y	2mo	92	30	27	35
6	23	F	300	3m	2mo	107	17	33	57
7	20	F	700	1m	2m	100	18	32	50
8	30	M	200	2y	25d	97	24	19	54
9	25	F	530	1y	2m	107	34	19	57
10	30	F	1500	2m	2m	120	24	37	59
11	32	F	1250	4m	1m15d	120	32	26	62
12	40	F	150	2y	1m	73	23	21	39
13	56	M	70	2y6m	5m	97	36	14	47
14	28	F	1050	6m	1m15d	101	17	37	47
15	18	F	1950	1m	4d	89	27	19	43
16	45	F	500	4m	3m	108	12	39	57
17	43	F	750	1m	4m	121	27	36	58
18	33	M	800	2y	2m	91	19	29	43
19	33	M	600	6y	4m	113	27	31	55
20	50	F	500	4M	15d	115	26	31	58
21	36	F	600	4m	15d	85	24	15	46
22	30	F	850	2m	5m	70	18	16	36
23	62	F	600	2m	20d	121	35	25	61
24	44	M	600	1y	6m	81	13	29	39
25	30	F	200	1y	6m	89	17	31	41
26	45	F	800	8m	3m	56	11	12	33
27	28	M	200	2y	2m	65	19	15	31
28	25	M	300	2m	2m	58	23	26	19
29	24	F	600	6m	2m	48	16	11	16
30	23	M	600	3y	3m	69	20	16	33
31	36	F	300	1y	6m	59	11	16	32
32	35	F	400	1y6m	2m	55	10	18	27
33	45	F	600	10m	6m	74	20	20	34
34	20	F	1500	5y	15d	61	9	24	28
35	35	F	200	3y	6m	90	24	21	45
36	28	M	400	10m	3m	104	32	16	56
37	30	F	500	2y	1m	76	14	30	32
38	31	F	1500	4y	2m	124	30	38	56
39	34	M	800	6y	3m	93	26	27	40
40	27	M	1000	2y	6m	93	24	28	41
Total			24725	23830days	3259days				

Time interval = Time interval between discontinuation of Antipsychotic drug and onset of symptoms of Schizophrenia. y= year, m=month

**TABLE No. 2, Time interval between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 6 month to 1 year (n= 11)**

Sl No.	Age	Gen Der	Chlorpromazine Equivalent mg	Duration of Treatment	Time Interval	PANSS score (Total)	Positive(PANSS)	Negative (PANSS)	General Psycho Pathology
1	18	F	600	20d	11m	93	30	19	44
2	30	M	700	4m	8m	82	21	20	41
3	65	F	600	1m	8m	103	20	30	53
4	26	F	500	1y	1y	100	25	31	44
5	35	F	400	2y	1y	57	14	18	25

6	50	M	500	3Y	1Y	76	15	25	36
7	42	M	350	1y6m	1y	81	13	33	35
8	45	F	800	1y	9m	74	18	28	28
9	27	F	1400	2y	1y	117	30	32	55
10	35	F	1000	1y	8m	108	29	32	47
11	30	M	600	1y6m	10m	106	25	28	53
Total			7650	4912	3120				

**TABLE No. 3, Time interval between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 1 year to 1year and 6 months .**

Sl No.	Age	Gen Der	Chlorpro mazine Equivalent	Duration of Treatment	Time Interval	PANSS score (Total)	Positive (PANSS)	Negative(PANSS)	General Psycho Pathology
1	42	F	100	2y6m	1y6m	85	23	23	39
2.	22	F	700	2y	1y, 6m	115	28	36	51
Total			800	1642	1095				

**TABLE No. 4, Time interval between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 1 year and 6 months to 2years.**

Sl No.	Age	Gen Der	Chlorpro mazine Equivalent	Duration of Treatment	Time Interval	PANSS score (Total)	Positive	Negative	Gen ,psychopathology
1	25	F	900	1y	2y	102	18	34	50
2	45	F	700	2y	2y	112	39	24	49
3	28	F	500	3m	2y	67	17	20	30
Total		2100	1185	2190					

**TABLE No. 5, Time interval between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia, from 2 year to 5 years.**

Sl No.	Age	Gen Der	Chlorpro mazine Equivalent	Duration of Treatment	Time Interval	PANSS score (Total)	Positive	Negative	Gen. Psychopathology
1	50	F	900	1m	2y,6mo	102	22	40	42
2	50	M	500	1m	4y	89	21	22	46
3	35	M	500	1 m	3y	105	23	29	53
4	20	F	1100	1y6m	3y	68	11	22	35
Total		3000	637	4562					

**TABLE No. 6, Overall ‘Time interval’ between discontinuation of Antipsychotic medication and onset of recurrence of schizophrenia,**

Table No.	Chlorpro mazine Equivalent	Duration of Treatment	Time Interval
1	24725	23830days	3259days
2	7650	4912	3120
3	800	1642	1095
4	2100	1185	2190
5	3000	637	4562
<b>Grand Total</b>	<b>38275</b>	<b>32206</b>	<b>14226</b>

**RESULTS** – Total 40 patients received 23830days Antipsychotic medication and got protection for 3259days . It means if a patient received medication for one day then he got protection from recurrence of schizophrenia for 0.1367 day ( 3259/ 23830 = 0.1367 day) . Similarly 40 patients consumed 24725 mg Chlorpromazine equivalent of Antipsychotic medications per day to get protected for 0.1318 day ( 3259 / 24725=0.1318) (Table -1).Table no 2 shows that Total 11 patients received 4912 days Antipsychotic medication and got protection for 3120 days . It means if a patient received medication for one day then he got protection from recurrence of schizophrenia for 0.6351 day ( 3120/ 4912 =0.6351 day) . Similarly 11 patients consumed 7650 mg Chlorpromazine equivalent of Antipsychotic medications per day to get protected for 0.4078 day ( 3120 / 7650=0.4078) . Table no 3 shows that Total 2 patients received 1095 days Antipsychotic medication and got protection for 1642 days . It means if a patient received medication for one day then he got protection from recurrence of schizophrenia for 0.6668 day ( 1095 / 1642 = 0.6668 day) . Similarly 2 patients consumed 800 mg Chlorpromazine equivalent of Antipsychotic medications per day to get protected for 1.36 day ( 1095/800= 1.36).Table no 4 shows that Total 3 patients received 1185 days Antipsychotic medication and got protection for 2190 days . It means if a patient received medication for one day then he got protection from recurrence of schizophrenia for 1.84 day ( 2190/1185=1.84 day) . Similarly 3 patients consumed 2100 mg Chlorpromazine equivalent of Antipsychotic medications per day to get protected for 1.04 days ( 2190 /2100 = 1.04 days).Table no 5 shows that Total 4 patients received 637 days Antipsychotic medication and got protection for 4562 days . It means if a patient received medication for one day then he got protection from recurrence of schizophrenia for

7.16 days (4562/637= 7.16 days) . Similarly 4 patients consumed 3000 mg Chlorpromazine equivalent of Antipsychotic medications per day to get protected for 1.52 days (4562/3000 = 1.52 days).

Table no 6 shows that total 60 patients received 32306 days of Antipsychotic medication and got protection for 14226 days . It means if a patient received medication for one day then he got protection from recurrence of schizophrenia for 0.4417 days (14226/32206= 0.4417 days) . Similarly 60 patients consumed 38275 mg Chlorpromazine equivalent of Antipsychotic medications per day to get protected for 0.3715 days (14226/38275 = 0.3716 days).

**DISCUSSION -**

Our finding suggest that if schizophrenic patient takes antipsychotic medications for 3 days the he gets protection from schizophrenia for approximately 4 day. The protection is not long lasting. Kaplan and Sadock also reported relapse rates after hospital discharge within two years is 82% (1). Our finding was in concordance with findings of Kaplan and Sadock. Our findings are similar to the findings of Weiden *et al*, (2004), who reported antipsychotic gap of as short as 10 days can double the risk of re- hospitalization in schizophrenic patients. In our study also 40 patients became symptomatic with in 6 months of discontinuation of antipsychotic drugs (Table 1) .Our findings were similar to findings of Cooper *et al*, (2000), who found Zotepine 300mg (Chlorpromazine equivalent 600mg) per day was required for prevention of relapse. In our study on an average one patient received 637.91 mg ( 38275 mg/ 60 = 637.91mg) of Chlorpromazine equivalent of medication every day (18). Though the mathematical calculations used in this study is not perfect but still it gives rough idea about recurrence of schizophrenia.

Our finding was similar to the findings of Sadia *et al*, (2014) who also found lack of knowledge about need to use regular medication was the most common reason of non compliance followed by financial difficulty in psychiatric patients(21) .

Carpenter *et al* (1991), Atwood (1985) and Nose (2003) also found that non compliance was more common in low socioeconomic status (22, 23, 24).

### Limitations

- (i) Number of previous episodes were not reported in current study.
- (ii) Compliance with Oral Antipsychotic and compliance with Long acting depot preparation was not studied separately.

### CONCLUSION:

Our findings suggest that Antipsychotic medications do not provides protection from recurrence of schizophrenia for long time. Patients must continued the medication for long time as advised by doctors. Government should have policy to provide free medication for long time. As the schizophrenia is not curable but highly treatable disease long term consultation with psychiatrist is mandatory.

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