



Treatment resistance in individuals with Schizophrenia receiving Clozapine

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Acknowledgment: VSS acknowledges the support of DBT Wellcome Trust India alliance CRC for Neuromodulation in Psychiatry (IA/CRC/19/1/610005)



Introduction:

- Nearly one third of the patients with schizophrenia are treatment resistant.
- The time course to treatment resistance could be a determinant of its mechanism and outcome.
- Treatment resistance duration can be of early (<1 year), medium (>1-5 years), and late (>5 years) onset.

Aim:

Explore the factors associated with the time course to TRS.

Methods:

Retrospective chart-review of 236 patients attending outpatient services of NIMHANS with TRS on Clozapine with approval of the Institute Ethics committee.

Results:

- Onset of treatment resistance ranged from 4 months - 312 months (26 years) with an average of 41.26 months.
- Majority had medium-term onset (134, 56.8%) followed by an equal proportion of (21.6%, 51 patients) of patients with early-onset and later-onset TRS.

	Early onset (N=51) [Mean(SD)/n(%)]	Medium-term onset (N=134) [Mean(SD)/n(%)]	Late onset (N=51) [Mean(SD)/n(%)]	F/ Chi-square	p	Post-hoc
Age	34.82(9.86)	34.79(8.72)	39.74(10.99)	5.40	<0.01	E,M<L
Age at Onset (in years)	24.12(8.63)	22.41(6.03)	23.02(7.61)	1.09	0.33	
Duration of illness (in months)	141.13(108.06)	147.32(81.98)	224.15(89.47)	15.38	<0.01	E<M<L
DUP- Longer (>6 months)	16(31.4%)	55(41%)	27(52.9%)	4.91	0.09	
Family history of psychiatric illness	4.6(4.66%)	33(13.98%)	12(5.08%)	0.19	0.91	
Duration of use of 1 st Antipsychotic (in months)	5.51(6.79)	17.09 (16.11)	60.68 (42.45)	83.94	<0.01	E<M<L
Duration of use of 2 nd Antipsychotic (in months)	4.31(2.83)	14.72(11.07)	62.97(123.42)	15.81	<0.01	E<M<L
Number of antipsychotic trials prior to Clozapine	4.0(1.24)	3.86(1.34)	3.9(1.33)	0.19	0.82	
Interval between illness onset and Clozapine initiation (in months)	85.19(95.53)	89.60(56.93)	158.27(78.78)	19.06	<0.01	E,M<L

Results:

- Duration of untreated psychosis (DUP) had a trend towards significance, where proportion of longer DUP (>6months) was more in late-onset resistance, reflecting the severe course hence early intervention in early resistance cases.
- The time course to TRS and time course to initiate Clozapine was different in the three groups.
- An average of 4 antipsychotics were administered before initiating Clozapine in all three groups.
- The time course to TRS did not predict outcome or response to Clozapine.

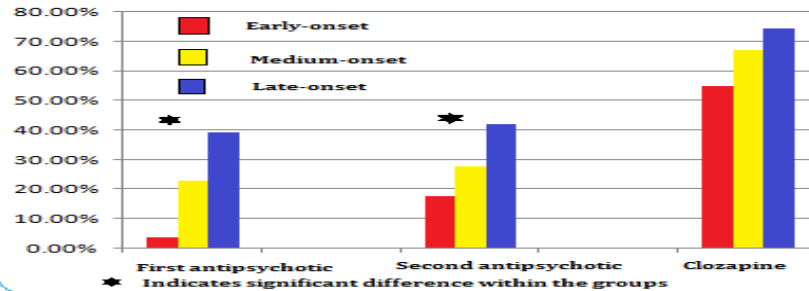
Conclusion

- Response to initial antipsychotic could predict the time course to treatment resistance.
- Delay in Clozapine initiation does not seem to be influenced by time-course to TRS.
- Time course to TRS was not associated with response to Clozapine.

References

Smart et al. Predictors of treatment resistant schizophrenia: A systematic review of prospective observational studies. *Psychological Medicine*, 51(1), 44–53.

Responders to antipsychotics across duration of treatment resistance



- Response rates to initial antipsychotics were lower and briefer in early compared to medium and late onset resistance groups.
- The antipsychotics were continued for a longer period even after resistance to an antipsychotic was noted, usually in combination with other oral or depot antipsychotics before discontinuing.