



A Comparison of Heart Rate Variability Measures Between Risperidone and Olanzapine Treated Schizophrenia Patients

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INTRODUCTION

- Schizophrenia (SCZ) patients have a 15–20-year lower life expectancy than the general population (1)
- It is largely attributed to the almost threefold increased risk of cardiovascular disease (CVD) in this population (2)
- Antipsychotic use has been reported to increase mortality by affecting metabolic parameters and increasing risk of sudden cardiac death risk (3)
- Antipsychotic mechanism like anticholinergic and antiadrenergic actions can lead to impaired cardiac autonomic regulation
- Healthy autonomic functioning of the heart is characterized by a high degree of variability in heart rate and higher parasympathetic activity
- Heart rate variability (HRV) analysis is a simple and non-invasive method that can be used to assess autonomic activity of the heart
- It is defined as the variation in time intervals between heart beats (R-R interval in continuous ECG sampling)
- Lower HRV has been independently associated with individual CVD risk factors

AIM

To examine the differential effect of RSPN and OLZ on HRV parameters in SCZ patients

METHOD

Subjects and setting 70 patients with DDSM-1V diagnosis of SCZ aged between 18-50 years on stable doses of risperidone (RSPN) and olanzapine (OLZ) were recruited from outpatient services of psychiatry department of St. John's Medical College Hospital, Bangalore

Patients with co-morbid psychiatric disorders, multiple psychotropics, pre-existing cardiac diseases and acute medical illness were excluded

Assessments:

- Clinical measures: BPRS & CGI-S
- Anthropometric measures: height, weight, BMI, waist circumference

Procedure: 30 minute ECG recording. Analog lead II ECG signal obtained was digitized using analog to digital converter (CIO-AD16r A/D card) and RR interval determined. HRV analysis was performed using the fast fourier transform (FFT) and power spectral density (PSD) obtained.

Frequency domain measures

- LF- low frequency band – reflects sympathetic and parasympathetic activity
- HF-high frequency-reflects parasympathetic activity
- LH/HF ratio- indicates sympathovagal balance towards sympathetic activity

METHOD

HRV parameters:

Time domain measures

SDNN- standard deviation of normal interbeat intervals
RMSSD-Root mean square successive difference between adjacent normal interbeat intervals
pNN50-Percentage of adjacent intervals that vary by 450 ms
RMSSD & pNN50- reflect parasympathetic activity
Decrease in HRV parameters are indicative of autonomic imbalance

RESULTS

Comparison of clinical and anthropometric variables between RSPN and OLZ treated groups

Variables	Risperidone (N=43)	Olanzapine (N=27)	Test statistics (t/χ ²)	P-value
Gender (M:F)	28:15	10:17	5.27	0.02
Age [Mean (SD)]	32.91(9.18)	34.59(8.14)	-0.781	0.44
BMI(kg/m ²)	26.44(5.08)	25.86(4.59)	0.48	0.63
Waist circumference (cm)	91.26(16.15)	91.20(12.46)	0.018	0.99
BPRS	20.74(3.63)	20.41(3.28)	0.39	0.70
CGI-S	1.58(0.91)	1.48(0.85)	0.46	0.65
Illness duration (months)	99.16(110.83)	65.17(52.67)	1.73	0.09
Chlorpromazine equivalents	248.83(105.50)	281.48(115.32)	-1.22	0.23
Drug use duration(months)	8.20(8.70)	12.91(12.77)	-1.69	0.10
Trihexyphenidyl dose (mg)	1.58(1.20)	0.81(1.27)	2.54	0.01
FBS (mg%)	95.93(25.44)	97(25.02)	-0.171	0.87

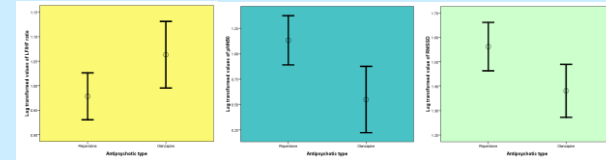
Comparison of HRV parameters between RSPN and OLZ treated patients

HRV parameter	RSPN	OLZ	F	P value
LF	2.56(0.56)	2.44(0.35)	0.54	0.46
HF	2.65(0.60)	2.36(0.57)	3.24	0.08
LF/HF ratio	0.98 (0.16)	1.06(0.17)	5.06	0.03
pNN50	1.13(0.72)	0.55(0.75)	5.64	0.02
RMSSD	1.56(0.32)	1.38(0.27)	4.57	0.04
SDNN	1.65(0.25)	1.57(0.18)	1.19	0.28

Univariate Analysis of Variance performed on log transformed values with sex and trihexyphenidyl dose as covariates

RESULTS

Comparison of the key HRV measures



There was no significant correlation between the anthropometric measures and HRV parameters in both RSPN and OLZ treated groups

Relationship between anthropometric measures and HRV parameters:

CONCLUSIONS

- HRV parameters reflecting the parasympathetic activity of the heart like RMSSD and pNN50 are specifically decreased in the OLZ group
- Increased LF/HF ratio is also indicative of sympathovagal imbalance due to reduced parasympathetic activity mediated by vagus nerve
- Thus decreased HRV was observed in OLZ treated in comparison to the RSPN group
- This is independent of anthropometric and metabolic measures
- Symphovagal imbalance due to impaired parasympathetic activity is a known risk factor for development of arrhythmias and sudden cardiac death (4)
- There is existing evidence for decreased HRV in schizophrenia both in pre and post antipsychotic use study populations(5,6).
- There is limited evidence comparing the HRV parameters in patients on stable doses of two commonly prescribed antipsychotic medications with differences in anticholinergic and antiadrenergic properties which can effect cardiac functioning.
- This study highlights the need for periodic cardiac monitoring for patients on antipsychotics like olanzapine irrespective of age and metabolic profile for early detection of cardiovascular diseases to reduce mortality.

REFERENCES

- Brown S, Kim M, Mitchell C, et al. Twenty-five year mortality of a community cohort with schizophrenia. British Journal of Psychiatry. 2010;196:116–121.
- Hennekens, C. H., Hennekens, A. R., Hollar, D. & Casey, D. E. Schizophrenia and increased risks of cardiovascular disease. Am. Heart J. 150, 1115–1121 (2005).
- Ray WA, Chung CP, Murray KT et al. Atypical antipsychotic drugs and the risk of sudden cardiac death. New England Journal of Medicine. 2009;360:225–235.
- Kalla M, Herring N, Paterson DJ. Cardiac sympatho-vagal balance and ventricular arrhythmia. 2016;199:29-37.
- Chung M, Yang AC, Lin Y et al. Association of altered cardiac autonomic function with psychopathology and metabolic profiles in schizophrenia. Psychiatry Research. 2013; 210:710-715.
- Wang J, Liu Y, Zhu W et al. Olanzapine-induced weight gain plays a key role in the potential cardiovascular risk: evidence from heart rate variability analysis. Scientific Reports. 2014;4:7394

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