Predictors of Effect of Atypical Antipsychotics on Speech

Preeti Sinha, Vallya Parambath Vandana¹, Nikita V Lewis¹, Mannaralukrishnaiah Jayaram¹, Pamela Enderby²

ABSTRACT

Background: Most of the studies have looked into the effect of typical antipsychotics on speech secondary to tardive dyskinesia. Aims: This study was aimed to explore the factors predicting the effect of atypical antipsychotic medications on the production of speech. Materials and Methods: One hundred and forty patients on stable regimen of three or more months on risperidone (92), olanzapine (28), aripiprazole (14), and clozapine (6) were recruited for the study. Speech was assessed by maximum phonation duration task, s/z ratio, diadochokinetic task, acoustic analysis and Frenchay Dysarthria Assessment (FDA). Extrapyramidal symptoms (EPS) were assessed by Simpson Angus scale. Statistical Analysis: Spearman correlation analysis was carried out to find the association between speech parameters and continuous variables. Effect of EPS, duration and dose of antipsychotic treatment on speech parameters was compared using Mann–Whitney test. Results: The risperidone group differ from other antipsychotics groups significantly in s/z ratio (0.07), FDA-total (0.23) and FDA-reflex (0.25). People who took antipsychotic for more than 2 years had lower score of FDA-palate (P = 0.042), and FDA-respiratory (P = 0.04) and higher values in noise-harmonic ratio (P = 0.011) and maximum fundamental frequency (MFF) for males (P = 0.02). Effect of EPS was seen on MFF for males (spearman correlation coefficient = 0.34) and on almost all sections of FDA (spearman correlation coefficients = –0.2 to –0.33). Conclusion: Both duration of use and propensity of atypical antipsychotics to cause EPS can influence the speech performance of the patients. This information can be useful, particularly in people with the requirement of high quality speech.

Key words: Atypical antipsychotics, dysarthria, extrapyramidal symptoms, maximum fundamental frequency, noise-harmonic ratio, s/z ratio, speech

INTRODUCTION

Antipsychotic drugs can influence the neuromuscular system, and hence have the potential to affect speech production mechanism. Speech problems particularly acquired type can have a negative impact on communication and life-experiences.¹ So far, most studies have focused on typical antipsychotics which again, is limited to cases who had tardive dyskinesia...
Speech is affected in Parkinson’s disease (PD) in all its stages across the various dimensions of speech production. It includes voice quality, breathing, articulation and prosody of speech. Parkinsonism symptom or extrapyramidal symptoms (EPS) is an adverse effect of antipsychotics including atypical ones and may influence speech production of patients on atypical antipsychotics. Besides, the effect of other characteristics of antipsychotic treatment on speech production needs to be determined.

This study was planned with the aim to examine the pattern of speech production in patients who are stabilized on atypical antipsychotics and find the associated treatment variables as predictors of associated speech problems if any.

MATERIALS AND METHODS

Subjects
A total of 140 patients in the age range of 20-60 years (mean age = 35.9 years, standard deviation [SD] = 10.9 years) were recruited. Eighty-one (57.9%) were males and 59 (42.1%) were females. They were diagnosed as either schizophrenia (67 patients, 47.9%), persistent delusional disorder (17 patients, 12.1%), or acute and transient psychotic disorder (56 patients, 40%) as per the International Classification of Diseases-10 classification of mental and behavioral disorders and were on the stable regimen of one of the following antipsychotics for a minimum duration of 3 months-risperidone/olanzapine/clozapine/aripiprazole. For the convenience of nomenclature, the dose of antipsychotic was considered low if it was ≤4 mg/day for risperidone, ≤10 mg/day for olanzapine, ≤15 mg/day for aripiprazole, and ≤200 mg/day for clozapine. Doses greater than this were considered to be high. The only psychotropic medications allowed concurrently were benzodiazepine and trihexyphenidyl.

Patients having TD as mild or more degrees of movements in any area according to abnormal involuntary movement scale were excluded. The presence of tardive dystonia was also an exclusion criteria. Those having co-morbid illnesses, which are likely to cause speech difficulties were also not recruited. None of them had a history of speech difficulty before the starting of an antipsychotic drug. They were either Kannada, Hindi or English speaking and gave written informed consent for their participation in the study. The study was approved by the Institute’s Ethics Committee. The investigator examining the speech performance was fluent in Kannada, Hindi and English languages.

Procedure
The assessments were done in a single visit. The respiratory and laryngeal (glottal sufficiency) subsystems were assessed by maximum phonation duration (MPD) task and s/z ratio. The MPD task measures the time till the individual sustains a vowel sound (here /a/) produced in one deep breath at a relatively comfortable pitch and loudness. s/z ratio takes the ratio of time for consonant /s/ to that of consonant /z/. In both tests, the best of three attempts at sustaining the vowel was considered. Diadochokinesia (DDK) represents the ability of repeating a simple segment of speech at maximum speed. The iterations per second was noted for rapid repetition of a single syllable (/pa/, /ta/, or /ka/) and a syllable sequence (/pataka/). The former is called alternate motion rate, and the latter is called sequential motion rate.

The objective acoustic analysis of voice was done by multidimensional voice profile in the computerized speech laboratory- 4300 (Kay Elemetrics) software. We assessed the sustained vowel phonation (/a/) in the middle phase of 3 s discarding at least the first 25 ms of phonation, as well as the terminal phase of phonation. In this study, voice parameters analyzed were maximum fundamental frequency (MFF) (in Hertz), jitter (%), shimmer (%), and noise to harmonic ratio (NHR), which represent the fundamental frequency, frequency perturbation, amplitude perturbation and noise related aspects of voice, respectively. The average of two attempts was measured.

We administered the Frenchay Dysarthria Assessment (FDA), FDA-2nd Edition to assess oromotor involvement and dysarthria. FDA includes seven sections that comprise of subsections of reflex, respiration, lips, palate, laryngeal, tongue, and intelligibility. Assessments were carried out for each of these sections by observing the person at rest and while various actions were carried out (such as the swallow, cough, movements of lips and tongue, and variations in speech). Each item within the section was rated on the 10-point rating scale (0-9), and total score for each section, as well as the final score was calculated by averaging them. A detailed evaluation was planned for those speech production or related aspects (like
The presence of EPS, if any, and its degree was assessed using the Simpson Angus scale (SAS).\textsuperscript{11,14} It has 10 items, which includes tremors, rigidity, bradykinesia (slowness in activity) and postural instability. Each item is rated using a 5-point scale (0–4). The mean score is obtained by averaging the score of all items. The cut-off for antipsychotic-induced EPS was kept as the mean score of 0.65.\textsuperscript{13}

Statistical analysis
Descriptive analysis was done for demographic, clinical and speech-related variables. Spearman correlation analysis was done to find the association between speech parameters and continuous variables (age, duration of treatment with antipsychotic in months and SAS EPS scores). The groups based on the presence of EPS, duration of treatment with antipsychotic medication for more or less than 2 years, and high or low dose of antipsychotic medications were compared separately for various speech parameters using Mann–Whitney test. For MFF, data of males and females were analyzed separately parameters were considered to be significant at $P < 0.05$ level.

RESULTS

Medication details
Ninety-two patients (65.7%) were on treatment with risperidone, 28 patients (20%) on olanzapine, 14 (10%) on aripiprazole, and six (4.3%) on clozapine. The average duration of treatment with antipsychotic was 22.9 months (SD = 33.7 months). Among them, 22 patients (15.7%) were taking the antipsychotic drug for more than 2 years and rest 118 (84.3%) had antipsychotic for two or less than two years. The dose of antipsychotic was high in 51 patients (36.4%) and low in 89 (63.6%) patients. The concurrent medication to antipsychotic was trihexyphenidyl alone in 87 patients (62.1%), and both trihexyphenidyl and clonazepam in 15 patients (10.7%). Thirty- eight patients (27.2%) patients were receiving antipsychotic alone.

Speech parameters
Table 1 shows the mean scores with SDs of speech assessments for 140 patients. On comparing the groups of risperidone and other antipsychotics in t-test, the significant difference was noted in s/z ratio, FDA-total score and FDA-reflex [Table 2].

Findings of spearman correlation analysis are presented in Table 3. The values were correlating with SAS mean score for all sections of FDA except palate. The duration of treatment correlated with MFF (for males), FDA-lips and FDA-reflex. MPD, s/z ratio, DDK, and the acoustic parameters (besides MFF) did not correlate with SAS score or duration of treatment with antipsychotic.

The results of Mann–Whitney test [Table 4], indicates that the group with antipsychotic-induced EPS ($n = 20$) had significantly lower scores for larynx, tongue, intelligibility sections, and total score of FDA and higher values for MFF (in males only) and total score of FDA and higher values for MFF (in males only) and NHR compared to that in the group without antipsychotic-induced EPS ($n = 120$). Besides, the scores of the palate and respiratory sections of FDA were lower, and MFF (in males only) and NHR had higher values in those who took antipsychotic for longer than 2 years [Table 4].
Sinha, et al.: Effect of atypical antipsychotics on speech

There was no significant difference in performance in various speech assessments in groups with high and low doses of antipsychotics.

DISCUSSION

This study looked into aspects related to speech performance of patients on atypical antipsychotics. This is the first study of its kind addressing this issue. We assessed various subsystems of speech production, which included respiratory, laryngeal, and articulatory subsystems. In addition, the presence or absences of any other associated speech problems were identified through detailed history.

Patients on different atypical antipsychotic drugs showed similar performance in tests assessing speech production subsystems, albeit few exceptions. Individuals who were on risperidone had increased s/z ratio, and total score and reflex section of FDA, compared to those who were on olanzapine, clozapine or aripiprazole, which may be indicative of the possible effect of risperidone on speech subsystems. In fact, there are case reports of risperidone related dysphagia.[4,16-18] However, it is noticeable there were additional factors in these cases such as tardive dystonia, concurrent medication (lithium), intellectual disability, or old age, which would have had a confounding effect in addition to medication.

EPS associated with the use of atypical antipsychotic drugs can indirectly affect speech production. SAS was used to assess the severity of EPS, and it was found to correlate with the total score, as well as various subsections of FDA which includes the laryngeal, respiratory, articulation, reflex, and intelligibility aspects of speech. Among them, those who had EPS differed in objective analysis of voice from those who do not have EPS. Patients who had EPS symptoms had higher NHR. MFF was higher in men with increased EPS alone. In fact, literature has reported that in PD, where EPS is the hallmark, the person may have breathy voice quality, reduced pitch, and loudness variation, slurred speech and speech rate problems.[5,19,20]

Besides EPS, the duration for which the person used the antipsychotic also had an effect on speech parameters, including subsections of FDA, which assessed swallowing, respiration, and articulation. Those who had antipsychotic for more than 2 years had harsh voice and increased fundamental frequency, particularly in men. The mechanisms involved in the long-term effect of atypical antipsychotic on speech require further exploration. The results of this study indicate that it may be beyond the influence of TD and dystonia.

We found statistical significance mostly in parameters of voice. However, these were not clinically or perceptually evident. These parameters may be early markers of speech involvement and needs to be further explored. Another factor to be considered while interpreting the results is that there was an unequal distribution of various atypical antipsychotic drugs in different groups, and hence generalization is difficult. Furthermore, the duration of antipsychotic drug use was variable in the patients recruited in this study. It was a cross-sectional study and hence absence of deficits in the speech production before the start of antipsychotics could be ascertained through history only. The assessor was not blind to the medication status.

CONCLUSION

Atypical antipsychotics can have an impact on speech production independent of TD and dystonia. Some of these effects may be related to the duration of antipsychotics, and some may be linked to the degree of EPS. A prospective study addressing the premedication speech status, as well as follow-up speech evaluation at regular intervals may throw more light in this regard.

REFERENCES

1. Walshe M, Miller N. Living with acquired dysarthria: The speaker’s perspective. Disabil Rehabil 2011;33:195-203.
2. Gabbert G, Schwade N, Tobey E. A tutorial on speech production sequelae associated with psychotropic and

| Treatment factor | Speech parameter | P    |
|------------------|------------------|------|
| Antipsychotic induced EPS | NHR             | 0.046|
|          | FDA-total       | 0.027|
|          | FDA-larynx      | 0.006|
|          | FDA-tongue      | 0.025|
|          | FDA-intelligibility | 0.012|
|          | MFF-(males)     | 0.007|
| Antipsychotic duration with grouping at 2 years | FDA-palate | 0.042|
|          | FDA-respiratory | 0.040|
|          | NHR             | 0.011|
|          | MFF-(males)     | 0.020|

*FDA – Frenchay dysarthria assessment; MFF – Maximum fundamental frequency; EPS – Extrapyramidal symptoms; NHR – Noise to harmonic ratio
Sinha, et al.: Effect of atypical antipsychotics on speech

3. Bär KJ, Häger F, Sauer H. Olanzapine- and clozapine-induced stuttering. A case series. Pharmacopsychiatry 2004;37:131-4.

4. Duggal HS, Mendhekar DN. Risperidone-induced tardive pharyngeal dystonia presenting with persistent Dysphagia: A case report. Prim Care Companion J Clin Psychiatry 2008;10:161-2.

5. Ho AK, Iansek R, Marigliani C, Bradshaw JL, Gates S. Speech impairment in a large sample of patients with Parkinson's disease. Behav Neurol 1998;11:131-37.

6. Haddad PM, Sharma SG. Adverse effects of atypical antipsychotics: Differential risk and clinical implications. CNS Drugs 2007;21:911-36.

7. World Health Organization. In the ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva, Switzerland: World Health Organization; 1993.

8. Lane RD, Glazer WM, Hansen TE, Berman WH, Kramer SI. Assessment of tardive dyskinesia using the Abnormal Involuntary Movement Scale. J Nerv Ment Dis 1985;173:353-7.

9. Aronson AE, Bless DM. Clinical Voice Disorders. 4th ed. New York: Thieme Medical Publishers, Inc.; 2009.

10. Lundeen DJ. The relationship of diadochokinesis to various speech sounds. J Speech Hear Disord 1950;15:54-9.

11. Kent RD, Weismer G, Kent JF, Vorperian HK, Duffy JR. Acoustic studies of dysarthric speech: Methods, progress, and potential. J Commun Disord 1999;32:141-80, 183.

12. Kent RD, Vorperian HK, Kent JF, Duffy JR. Voice dysfunction in dysarthria: Application of the Multi-Dimensional Voice Program. J Commun Disord 2003;36:281-306.

13. Enderby P, Palmer R. Frenchay Dysarthria Assessment. 2nd ed. Austin, Texas: PBO-ED, Inc.; 2008.

14. Simpson GM, Angus JW. A rating scale for extrapyramidal side effects. Acta Psychiatr Scand Suppl 1970;212:11-9.

15. Janno S, Holli MM, Tuisku K, Wahlbeck K. Validity of Simpson-Angus Scale (SAS) in a naturalistic schizophrenia population. BMC Neurol 2005;5:5.

16. Varghese ST, Balhara YP, George SA, Sagar R. Risperidone and dysphagia. J Postgrad Med 2006;52:327-8.

17. Brahm NC, Fast GA, Brown RC. Risperidone and dysphagia in a developmentally disabled woman. Prim Care Companion J Clin Psychiatry 2007;9:315-6.

18. Stewart JT. Dysphagia associated with risperidone therapy. Dysphagia 2003;18:274-5.

19. Logemann JA, Fisher HB, Boshes B, Blonsky ER. Frequency and cooccurrence of vocal tract dysfunctions in the speech of a large sample of Parkinson patients. J Speech Hear Disord 1978;43:47-57.

20. Zwirner P, Barnes GJ. Vocal tract steadiness: A measure of phonatory and upper airway motor control during phonation in dysarthria. J Speech Hear Res 1992;35:761-8.