THE HIGH INCIDENCE ILLUSION: AKATHISIA WITH ARIPIPRAZOLE

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ABSTRACT

Background: Clinicians have voiced concerns over the possibly high frequency of akathesia that occur with aripiprazole use, however, the existing literature is not consistent with these observations.

Aim: To compare the frequency of akathesia occuring with aripiprazole and risperidone.

Method: A total of 60 patients were included in the study. Patients fulfilling the inclusion criteria were then randomly assigned into 2 groups of 30 patients each. One group is given Aripiprazole (10 mg) and the other is prescribed Risperidone (2mg). Patients of both groups were re-called on the 7th day after the start of the medication and were screened and calibrated for Akathisia using the Barnes Akathisia Rating Scale (BARS) with a cut off value of 2 or more on global assessment indicating the presence of Akathisia. The patients not having akathesia of the 7th day were put in a sub-group and were re-assessed for presence of akathesia on the 21st day following start of anti-psychotic.

Results: The akathesia assessment done on the 7th day revealed the presence of akathesia in two (6.67%) patients getting Aripiprazole 10 mg. One patient (3.34%) in the group receiving Risperidone 2 mg presented with akathesia of the 7th post treatment day. Furthermore, no patients in either of the sub-groups had akathisia when assessed on 21st post treatment day. One way ANOVA analysis gave p=0.895.

Conclusion: The frequency of akathesia occuring with Aripiprazole is comparable to that with Risperidone and is considered low.

Keywords: Akathisia, Aripiprazole, BARS, Risperidone

INTRODUCTION

Risperidone (1993) and Aripiprazole (2002) are second generation of anti-psychotics, Risperidone with a mean dose of 3.9mg/day was established as a well-tolerated drug In Clinical Anti psychotic Trials of Intervention Effectiveness CATIE 1998[6]. Risperidone and aripiprazole, have been chosen as a monotherapies for first episode of psychosis in schizophreniform and schizophrenia treatment of in this clinical trial[7]. Risperidone and aripiprazole's are best choices in oral form in acute psychotic episodes in which rapid titration is required[5].

Risperidone is administered both in the form of oral tablets or in solution from. It is a dopamine antagonist possessing anti-serotonergic, anti-adrenergic and anti-histaminergic properties, Adverse effects of risperidone include significant weight gain and metabolic problems such as diabetes mellitus type 2 as well as Extra-pyramidal symptoms and neuroleptic malignant syndrome[5].

Aripiprazole has partial D2 and 5HT1A agonistic rather than antagonist, it also has affinity for presynaptic D2 auto receptor agonist as well, so it is believed to have lesser neurological side effects but its impact on effectiveness is unclear as it was not tested in CATIE trial[8]. Weight gain and metabolic disturbances are not associated with aripiprazole, it is believed to cause less EPS but akathisia has been reported from this drug[1]. Intra muscular Second generation Anti-psychotics are associated with akathisia in patients who are clearly at risk of Dystonia or Parkinsonism[5].

Anti-psychotics can cause 'unpleasant sensation of motor restlessness' in lower extremities known as akathisia causing non adherence to drugs with other problems including self-harm behaviors and worsening of psychosis[2]. Propranolol and low dose mirtazapine have been found useful in treatment of akathisia[3,4].

Concerns regarding aripiprazole having greater tendencies to cause akathisia has come to surface but there's lack of substantial evidence[5]. Agitation and akathisia being noted in patients on aripiprazole[5] by clincians has moved authors to run a clinical trial in Lahore General Hospital , to primarily establish the incidence of akathisia in aripiprazole in comparison to risperidone.

AIM OF STUDY

This is a comparative study which is aimed at determining that whether Aripiprazole does or does not has a higher incidence of akathisia than that of Risperidone, so that, the raised concern of clinicians regarding Aripiprazole induced akathisia could have a more scientific (evidence based) ground, which is somewhat challenged because of the lack of existing literature on the subject.

Hypothesis:

"Aripiprazole induced akathisia has a lower incidence than Risperidone induced Akathisia"

METHOD

A total of 60 patients were included in the study. The patients fulfilled the DSM-V criteria for Acute Psychotic Episode, Schizophreniform disorder or Schizophrenia with the illness being a first episode in all the cases and the patients were either anti-psychotic naive or had taken any antipsychotic in the past three months. There was no demarcation of age, sex or duration of illness in the inclusion criteria. Patients fulfilling the inclusion criteria were then randomly assigned into 2 groups of 30 patients each. One group is given Aripiprazole (10 mg) and the other is prescribed Risperidone (2mg). Both groups were directed to take the medicine in tablet form and at night time. Both groups were not receiving any other medication for their psychiatric disorder except clonzepam 2mg or less. Patients of both groups were re-called on the 7th day after the start of the medication and were screened and calibrated for Akathisia using the Barnes Akathisia Rating Scale (BARS) with a cut off value of 2 or more on global assessment indicating the presence of Akathisia. The patients not having akathesia of the 7th day were put in a sub-group and were re-assessed for presence of akathesia on the 21st day following start of anti-psychotic.

RESULTS

The akathesia assessment done on the 7th day revealed the presence of akathesia in two (6.67%) patients getting Aripiprazole 10 mg. The score of both patients as caliberated on Barnes Akathisia Rating Scale (BARS) global assessment was 3 and 4 which correspond to moderate to marked level of akathesia respectively. One patient (3.34%) in the group receiving Risperidone 2 mg presented with akathesia of the 7th post treatment day having a score of 3 on BARS corresponding to moderate level akathesia. Furthermore, no patients in either of the sub-groups had akathesia when assessed on 21st post treatment day. One way ANOVA analysis gave a p=0.895 which means that there was no statistically significant difference between the akathisia scores in two groups.

DISCUSSION/CONCLUSION

The results of the study depict a nearly comparable frequency of akathesia between Aripiprazole and Risperidone when seen in context of the relatively small sample size. The frequency of akathesia with Aripiprazole found in this study is 6.67% which is consistent with results of previous studies on the subject which have found the incidence to be equal or greater than 5%[9] . In a 12-week, placebo-controlled, fixed-dose schizophrenia trial, 2 out of 415 patients discontinued Aripiprazole due to akathesia[9]. The incidence of akathesia with aripiprazole is not found to be dose related[9] . The frequency of akathesia with Risperidone (3.34%) in less than the incidence found in the plethora of previous studies on the subject. Some studies have found the incidence of akathesia with risperidone to be as high as 10%. The smaller frequency in our study could be a result of small sample size and/or the low dosage of 2mg of risperidone used.

Despite the nearly comparable frequency of akathesia with both drug, the question remains that why clinicians' suspicion or fear index for aripiprazole is much higher for aripiprazole than risperidone. We hypothesized that one explanation for this dilemma could be the presence of numerous case reports on severe akathesia being reported with aripiprazole. Many of these reports came around the time of launch of aripiprazole in the market which may have put a bias in the heads of doctors who were still just familiarizing themselves with the drug.

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