Short report / *Kısa rapor*

The efficacy of flupenthixol decanoate in bipolar disorder patients who have no sufficient remission with existing treatments

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ABSTRACT

Objective: *It is aimed to evaluate the prophylactic effect of flupenthixol decanoate in remitted BD patients.* ***Methods:*** *Remitted patients with bipolar disorder (BD), who had at least one mood episode each year in the last five years in spite of adequate pharmacotherapy, were included. Flupenthixol decanoate 20 mg/ml was administered in every two weeks. Hamilton Depression Rating Scale (HDRS), Young Mania Rating Scale (YMRS), Bipolar Disorder Functioning Questionnaire (BDFQ), General Assessment of Functionality (GAF) and Side Effect Rating Scale (UKU) were applied. Patients were followed up for 12 months.* ***Results:*** *Eight patients with a mean age of 34.7±7.5 were enrolled to the study. None of the patients were under monotherapy before the study enrollment. Three (37.5%) of the three patients were dropped out. The data of remaining 5 patients' were evaluated. At the end of the study mean number of mood episodes declined to 0.2±0.4 per year indicating a statistical significance and the mean score of BDFQ declined to 119.6±2.7.* ***Conclusions:*** *Flupenthixol decanoate significantly improved functionality and decreased the number of mood episodes allowing an alternative treatment even in remitted BD patients.* ***(Anatolian Journal of Psychiatry 2015; 16(5):364-367)***

Key words: *bipolar disorder, depot neuroleptics, prophylaxis, flupenthixol decanoate*

Kullanılan tedavilere karşın yeterli remisyona giremeyen bipolar bozukluk hastalarında flupentiksol dekonoatın etkinliği

ÖZET

Amaç: *Bu çalışmada flupentiksol dekanoatın remisyondaki bipolar bozukluk hastalarındaki koruyucu etkilerinin incelenmesi amaçlanmıştır.* ***Yöntem:*** *Yeterli farmakoterapiye karşın son beş sene içinde her yıl en az bir duygudurum atağı geçiren remisyondaki hastalar alınmıştır. Hastalara iki haftada bir flupentiksol dekonoat 20 mg/ml uygulanmıştır. Hamilton Depresyon Derecelendirme (HDRS), Young Mani Derecelendirme Ölçeği (YMRS), Bipolar Bozukluk İşlevsellik Ölçeği (BDFQ), İşlevselliğin Genel Değerlendirilmesi (GAF) ve Yan Etki Derecelendirme Ölçeği (UKU) uygulandı. Hastalar 12 ay boyunca izlendi.* ***Bulgular:*** *Hastaların ortalama yaşı 34.7±7.5 yıl idi. Çalışma öncesi hastaların hiç birisi tekli farmakoterapi kullanmıyordu. Çalışmaya alınan sekiz hastanın üçü (%37.5) çalışma dışı kaldı. Kalan beş hastanın verileri değerlendirildi. Çalışma sonunda ortalama duygudurum atağı sayısı 0.2±0.4/yıla ve ortalama BDFQ puanı 119.6±2.7'ye düştü.* ***Sonuç:*** *Flupentiksol dekonoat işlevselliği belirgin ölçüde arttırırken ortalama duygudurum sayısını da düşürmüştür. Flupentiksol dekonoat remisyondaki hastalar için bile iyi bir seçenek oluşturmaktadır.* ***(Anadolu Psikiyatri Derg 2015; 16(5):364-367)***

Anahtar sözcükler: *Bipolar bozukluk, depo nöroleptikler, profilaksi, flupentiksol dekanoat*

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INTRODUCTION

Bipolar disorder (BD) is a chronic mental illness associated with marked psychosocial disability, diminished academic and occupational success and accelerated cycling in patients when undertreated.[1,2] High nonadherence rates (33%) are considered as one of the most common causes of poor prognosis and recurrence of mood episodes.[3,4] Today, the treatment of BD is aiming not only the acute treatment of the episodes, but also to prevent new episodes and preserve psychosocial functioning of the patients.[5-7]

Although monotherapy is the main intention in the maintenance treatment of BD, longitudinal studies demonstrated that 40-72% of all patients are treated with antipsychotic agents either with monotherapy or in combination with mood stabilizers.[8,9] Both first and second generation antipsychotic agents have been demonstrated to prevent relapses in long-term studies.[10,11]

To date, no randomized, controlled trials of depot antipsychotics in the maintenance treatment of BD have been performed. In the present study it is aimed to investigate the prophylactic effect of flupenthixol decanoate in remitted BD patients.

METHODS

Patient population

Remitted BD patients aged 18-65 years, diagnosed with BD according to Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Text Revision (DSM-IV TR),[12] were eligible for the study. Patients, who had at least one mood episode each year in the last five years in spite of adequate pharmacotherapy, were included. Patients had been required to have under a score of 8 at baseline on the 17-item Hamilton Depression Rating Scale (HDRS)[13] and 9 at baseline on the 11-item Young Mania Rating Scale (YMRS)[14] Laboratory tests were carried out and vital signs and weight were measured at the screening visit and at the end of study. Patients with any medical condition, substance abuse or Axis II disorder were excluded. The study protocol was approved by the relevant ethics committee and conducted in accordance with Declaration of Helsinki as revised in 1989. All subjects gave written informed consent to participate.

Drug administration and assessment instruments

Flupenthixol decanoate 20 mg/ml were injected in the gluteal muscle in every two weeks. All oral medications were discontinued within 7-10 days following the first flupenthixol decanoate injection. Every month YMRS, HDRS, Bipolar Disorder Functioning Questionnaire (BDFQ),[15] General Assessment of Functionality (GAF)[12] and Side Effect Rating Scale (UKU)[16] were applied. Patients were followed up for 12 months.

Data analysis

Statistical analyses were performed using SPSS for Windows 13 (SPSS Inc., IL, USA). For categorical variables frequency and descriptive statistics were calculated. To determine the degree and the level association between variables correlation analysis was performed. Repetitive which is a nonparametric test Wilcoxon Signed Ranks Test and variance analysis were performed for repetitive measurements. A p value of less than 0.05 was regarded as statistically significant difference.

RESULTS

Eight patients (five women, three men) with a mean age of 34.7±7.5 were enrolled to the study. None of the patients were under monotherapy before the study enrollment. All patients were under SGA (second generation antipsychotic) + MS (mood stabilizer) treatment prior to the study enrollment. All medications were at their effective doses. Recurrence of episodes (50%), nonadherence to the previous medication (37.5%) and side-effects of the previous medication (12.5%) were the reasons for switching to flupenthixol decanoate.

Three (37.5%) of the eight patients were dropped out. One patient was dropped out due to extrapyramidal side effects at the fourth month of the study. One patient withdrew his informed consent. One patient dropped out due to lack of efficacy at the seventh month of the study. The data of remaining five patients' were evaluated.

Mean number of mood episode was 1.3±0.4 per year in the last five years before the study took place. At the end of the study mean number of mood episodes declined to 0.2±0.4 per year indicating a statistical significance (p=0.02).

The mean score of BDFQ significantly (p=0.042) declined to 119.6±2.7 at the end of the trail compared to the screening visit which was 114.50±7.57. No significant changes were detected regarding metabolic, cardiovascular and biochemical parameters. No significant side effects were reported or detected in patients who completed the trial.

CONCLUSION

The major findings of the present study are; i) number of mood episodes significantly decreased; ii) functionality of the patients significantly improved with flupenthixol decanoate in remitted BD patients.

Though, BD patients are often nonadherent to psychotropic medications, studies demonstrate that even at effective doses, psychotropic drugs cannot prevent further episodes. Subsyndromal symptoms are blamed for recurrences as well as nonadherence.[17] Some small sample sized studies demonstrated that depot antipsychotics are effective in preventing relapses. In Lowe and Batchelor study,[18] 12 patients suffering from BD who were receiving both lithium and antipsychotic medication had their antipsychotic changed to depot haloperidol decanoate, with their lithium medication remaining unchanged. Successful transfer to haloperidol decanoate was achieved with 100% compliance in eight patients who all remained free of hypomanic relapse, including four patients with rapid-cycling disorder. By comparison, in the three years before switching to haloperidol decanoate these four patients had required 16 admissions for hypomanic relapses resulting in 34 months in-patient treatment. White et al.[19] demonstrated that depot antipsychotics are effective in reducing relapses without any depressive episodes in their studies which are in line with our findings. Esparon et al.[20] demonstrated in a two year longitudinal study that flupenthixol decanoate significantly reduced hospitalization duration. Likewise, Littlejohn et al.[21] demonstrated that depot antipsychotics reduce the number of relapses and hospitalization duration in their retrospective study.

Abovementioned studies indicate that depot antipsychotic agents may be an effective alternative for certain BD patients in terms preventing relapses and reducing hospitalization duration. These studies comprised of subjects while they are at their mood episodes. However, the present study, which is unique at its field, included remitted BD patients. Thus, the present study's data should be interpreted from this point of view. Nevertheless, present study indicates that flupenthixol decanoate can be considered an effective alternative for certain BD patients. Also flupenthixol decanoate may also help improving functionality of BD patients.

Small sample size is the major limitation of the study. This may cause a type-1 or 2 errors in statistical evaluation. On the other hand, providing a large amount of subjects for such a study is only possible by multicenter trials. Second, bias could have affected the study results due to its open-label design. Despite to its limitations, this study represents the clinical implementations for real world of clinical practice. Though it might be a small sample sized study, the results could help the physicians to rethink the possible efficiency of old but effective drugs.

BD is a real challenge for clinicians in terms of diagnosis and treatment. Each patient has its unique course of the disorder. Thus, clinicians often provide patient based treatment strategies in the treatment of BD. All treatment options should be regarded in the maintenance treatment of noncompliant BD patients. Though, flupenthixol decanoate is known as an effective and safe in the treatment of BD for several decades, prophylactic effect of flupenthixol decanoate BD patients had not been studied. In this regard, despite to its limitations, the present study has a valuable contribution to the field.

Adequate and effective maintenance treatment in BD patients is crucial since it is known that every mood episode deteriorates brain neuroplasticity which leads to poor prognosis, more frequent episodes, treatment resistance, and loss of social and occupational functionality.[22] Therefore, of the conventional depot antipsychotics which are proved to be effective in maintenance treatment of BD, flupenthixol decanoate may serve as an effective alternative option in maintenance treatment of BD. The findings of the present preliminary study should be replicated with further studies regarding cost-effectiveness and adherence. Multicenter studies including larger sample sizes and longer duration of follow-up are needed for better understanding the effectiveness of depot antipsychotics in terms of preventing mood episodes in certain BD patients.

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