



The long-term efficacy and safety of fluphenazine in patients with Tourette syndrome

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INTRODUCTION

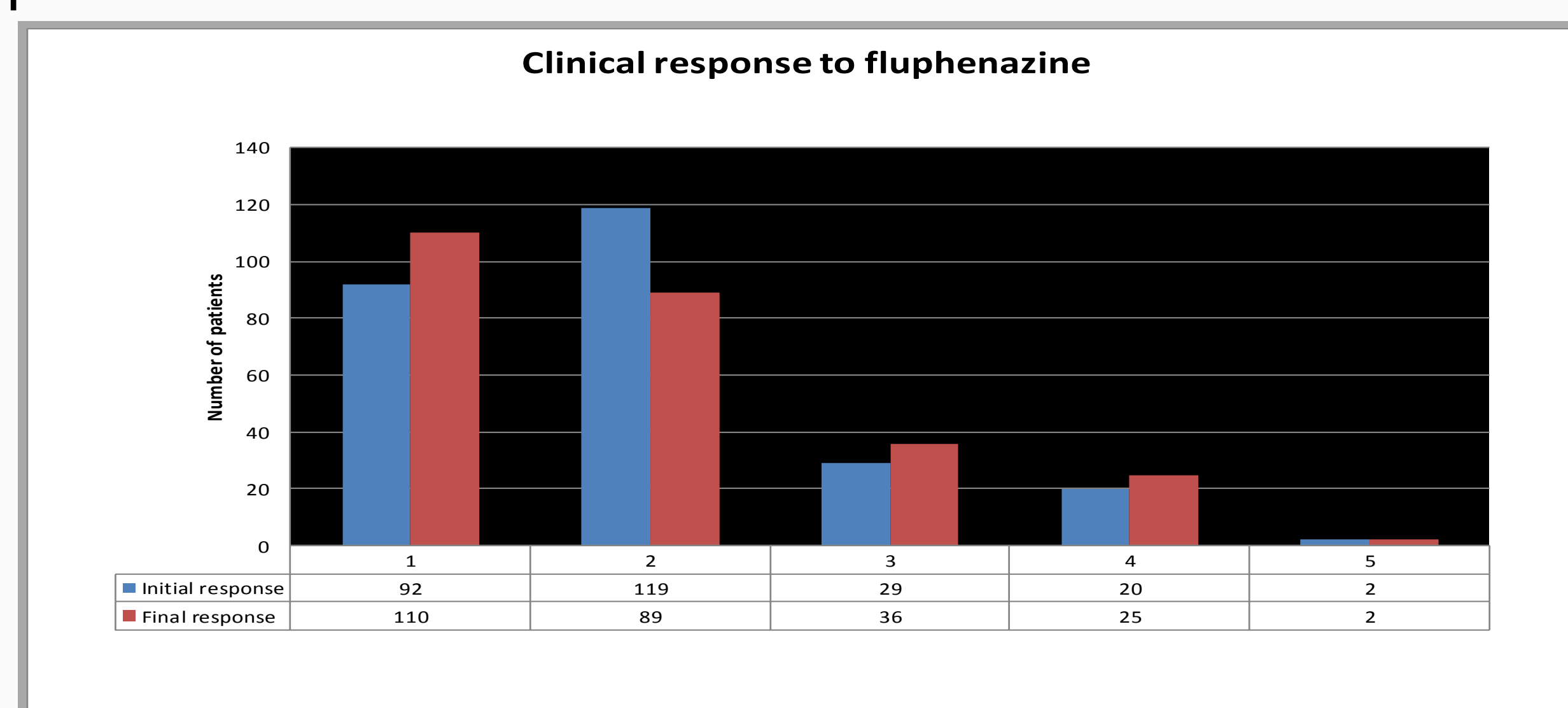
- Tourette syndrome (TS) is a complex neurobehavioral and genetic disorder of childhood onset characterized by the presence of motor and phonic tics, often associated with attention deficit hyperactivity disorder, obsessive compulsive disorder, and other behavioral abnormalities, including impulse control problem.
- Haloperidol and pimozide, both classic antipsychotics with high D2 receptor antagonism, are the only medications currently approved by the Food and Drug Administration for the treatment of TS.
- Although studies have demonstrated the effectiveness of these two medications in controlling tics, their side effect profile is a major limitation to their use.
- Fluphenazine is a phenothiazine derivative with D1 and D2 receptor blockade. Although fluphenazine has been used in clinical practice for a long time, there are no studies systematically examining the long term efficacy and side effect profile in patients with TS.
- We conducted a retrospective chart analysis of a large cohort of patients with TS, who have been treated with fluphenazine to assess the efficacy and side effect profile of fluphenazine in patients with TS.

METHODS

- A retrospective chart analysis, approved by the Baylor College of Medicine Institutional Review Board for Human Research was performed in patients with a primary diagnosis of TS, who were treated with fluphenazine to control motor tics at Baylor's Movement Disorders Clinic from October 1985 through December 2011.
- The response to treatment was rated 1 through 5 (1=marked reduction in tics, 5=worsening of tics)

RESULTS

Figure 1



RESULTS

Table 1

Number of study patients	n=268
Sex (M/F)	223/45
Mean age at symptom onset (year)	6.8±3.23
Number of patients where fluphenazine was the first agent used in our clinic	187(69.77%)
Mean age at which fluphenazine was first started (years)	15.8 ±10.67(range: 4.09-70.2)
Number of patient below age 10 years when fluphenazine was first started	62
Number of patient above age 20 years when fluphenazine was first started	50
Number of patient above age 40 years when fluphenazine was first started	13
Duration of fluphenazine treatment (years)	2.6±3.21(range 0.01-16.8)
Number of patients on fluphenazine for over 5 years duration	40
Number of patients on fluphenazine for over 10 years duration	13
Mean dose at initial treatment visit (mg/day)	2.6±1.56
Mean dose at last follow up (mg/day)	3.24±2.27 (range 0.5-12.5)

Table 2

Adverse effect	n=268
Drowsiness	70 (26.1%)
Weight gain	31 (11.56%)
Akathisia	23 (8.5%)
Acute dystonic reaction	19 (7.0%)
Depression	17 (6.3%)
Nausea	8 (2.9%)
Tremor	8 (2.9%)
Nervousness/Anxiety	6 (2.2%)
Dizziness	3 (1.1%)
parkinsonism	2 (<1%)
Increased liver enzyme	3 (1.1%)
Myoclonus	2 (<1%)
Elevated prolactin	1 (<1%)
Classic tardive dyskinesia	0

Table 3

Total discontinued	n=122(%)
Side effects alone	51 (41.8%)
Lack of efficacy alone	28 (22.9%)
Combined side effects and lack of efficacy	8(6.5%)
Better results with botulinum toxin	7(5.7%)
Other (included those tics resolved)	28(22.95%)

Table 4

Adverse effect	Total no discontinued due to side effects n=59
Drowsiness	24 (40%)
Weight gain	14 (23.7%)
Acute Dystonic reaction	13 (22%)
Akathisia	10 (16.9%)
Depression	6 (10.1%)
Nausea	4 (6.7%)
Tremor	4 (6.7%)
Nervousness/Anxiety	4 (6.7%)
Dizziness	2 (3.3%)
Myoclonus	2 (3.3%)
parkinsonism	1(1.6%)
Increased liver enzyme	1(1.6%)
Elevated prolactin	1(1.6%)
Salivation	1(1.6%)

Table 1: Demographic data of patients with Tourette syndrome receiving fluphenazine
Table 2: Adverse effect profile among patients with Tourette syndrome receiving fluphenazine Treatment
Table 3: Reasons for discontinuation of fluphenazine treatment
Table 4: Adverse effects that led to discontinuation of fluphenazine.
Figure 1: Clinical response to fluphenazine

DISCUSSION

- In this retrospective, longitudinal study of a large cohort (n=268) of patients with TS, 211 (81%) showed a marked to moderate initial response to fluphenazine (Rating 1 or 2).
- Fluphenazine continued to be effective after a mean duration of 2.6±3.21years in 199 (74.2%) patients.
- The average initial dose used in our study was 2.6±1.56 mg per day in divided doses and the average doses used at the time of the last review was 3.24±2.27 mg per day (range 0.5-12.5 mg) per day in divided doses.
- The commonest side effects noted during the course of our study was drowsiness 70 (26.1%), weight gain 31(11.56%), akathisia 23 (8.5%), acute dystonic reactions 19 (7.0%) and depression 17 (6.3%).
- There were no cases of classic tardive dyskinesia
- Fifty one (41.8%) patients discontinued fluphenazine due to side effects alone and 28 (22.9%) discontinued treatment due to lack of efficacy alone.
- The main limitation of our study is the retrospective study design.
- Our study shows that fluphenazine is safe and effective in patients with TS, and tardive dyskinesia was not seen in this large cohort of patients treated with fluphenazine.
- In our practice we continue to recommend fluphenazine as a first line agent in children with TS¹, but use tetrabenazine, a monoamine depletor², in adults with TS as they may be at a higher risk for development of tardive dyskinesia³.

REFERENCES

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