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Letter to the Editor

Extrapyramidal side-effects and clinical response during acute neuroleptic treatment of schizophrenia

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For most cases of acute schizophrenia, the optimal dose of haloperidol is around 10 mg/day. Higher doses have been claimed to be no more effective and to cause more extrapyramidal side-effects (EPS) and more drop-outs. The relationship between improvement in positive symptoms and EPS is not clear (Levinson *et al*, 1990; Van Putten *et al*, 1990; Rifkin *et al*, 1991).

Twenty consecutive inpatients with acute schizophrenia (DSM III-R) were treated with neuroleptics and the relationship between improvement in positive symptoms and EPS was studied.

The study comprised 11 males and 9 females, mean (SD) age 33.2 (9.7) years, range 18-53 y. At baseline and weekly thereafter they were evaluated by the Brief psychiatric rating scale, BPRS (Overall and Gorham, 1962), the positive and negative syndrome scale, PANSS (Kay *et al*, 1989), and the Simpson-Angus scale for EPS (Simpson and Angus, 1970). Endpoint examinations were carried out at the end of the 4th week or before, if the patients were discharged. Most patients were taking oral neuroleptic medication when they relapsed and were hospitalized. In hospital, mean (SD) haloperidol equivalent dose was 10.9 (4.7) mg/day, range 5-20. The dose was adjusted according to clinical response. Haloperidol was the most widely used neuroleptic. Benzodiazepines were associated in 85% of cases, and anticholinergics prophylactically in 15%.

A negative correlation ($r = -0.65$, $P < 0.01$) was found between endpoint percent improvement in positive symptoms and endpoint EPS severity.

The group was divided into two subgroups: those with less than 40% endpoint improvement in positive symptoms and those with 40% or greater improvement (table I).

Mean EPS severity in the less than 40% improvers was significantly higher than in the other subgroup.

There were no significant baseline differences in mean PANSS+ score (positive symptoms), mean BPRS score, mean age and mean duration of treatment of current episode. Mean doses of neuroleptics and benzodiazepines were not significantly different.

The group was split into two endpoint subgroups, according to the presence or absence of akinesia (table II).

Endpoint mean percent improvement in positive symptoms was significantly higher in the akinesia- subgroup.

There were no significant baseline differences in mean PANSS+ score, mean BPRS score, mean age and mean duration of treatment of current episode. Mean doses of neuroleptics and benzodiazepines were not significantly different.

The akinesia+ subgroup did not have more dysphoria (a possible cause of reduced improvement). Different degrees of rigidity at endpoint were not associated with improvement in positive symptoms.

In conclusion, improvement in positive symptoms was associated with fewer EPS and lack of akinesia.

This study has several limitations, apart from the small sample size. It was an uncontrolled, non-blind

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Table I. EPS severity at endpoint according to different degrees of improvement in positive symptoms.

	Less 40% *(n = 12)*	*40% or greater* *(n = 8)*
Endpoint mean Simpson score (EPS severity)	6.9	1.5 $t = 3.14$, $P < 0.01$

Table II. Improvement in positive symptoms according to the presence or absence of akinesia.

	Akinesia	
	Present *(n = 9)*	*Absent* *(n = 11)*
Endpoint mean percent improvement in positive symptoms	17.4	43.8 $t = 2.98$, $P < 0.01$

study, where doses were flexible and determined by clinical response. Several neuroleptics were used. In such a situation, patients who are less responsive tend to receive higher doses than patients who are highly responsive. Therefore, the negative correlation found between EPS and positive symptoms could be the result of partially refractory patients receiving higher doses and consequently developing more EPS. However, the mean dose of neuroleptics was not higher in the subgroup with less improvement than in the subgroup which improved substantially.

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