Lithium Treatment of Conduct Disorders in Adolescents

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Objective: The authors examined the efficacy of lithium carbonate for treating conduct disorder in adolescents. Method: The subjects were 33 inpatients aged 12–17 years. Lithium or placebo was administered in a double-blind fashion for 2 weeks. Results: On several measures of clinical change the groups showed no significant differences. Of the patients who completed the study, 8.3% of those receiving placebo (one of 12) versus 21.4% (three of 14) of those receiving lithium were considered responders. Conclusions: Lithium does not appear beneficial for this indication.

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Conduct disorder in adolescents is a serious and common mental disorder. No psychosocial treatment has been proven effective. To our knowledge, there has been only one double-blind, controlled study of drug treatment for adolescents with conduct disorder (1). That study used methylphenidate, which was superior to placebo. Other controlled drug trials for adolescents included children with attention deficit hyperactivity disorder (ADHD); one study involved bupropion, which showed no benefit for conduct disorder (2), and the other study used methylphenidate, which did provide benefit (unpublished 1994 study of R. Klein et al.).

METHOD

The subjects were boys and girls aged 12 through 17 years who had been admitted to the psychiatric inpatient service of Elmhurst Hospital Center, a municipal hospital in Queens, N.Y., and had a diagnosis of conduct disorder. A subject was excluded if he or she had 1) an IQ of less than 70; 2) a concomitant diagnosis of stereotyped movement disorder, pervasive developmental disorder, organic mental disorder, schizophrenia, or mood disorder; or 3) a major physical disorder that might account for the behavior or make treatment with lithium undesirable.

Diagnoses were made by the ward attending physicians and were confirmed by the director of child and adolescent psychiatry and by the principal investigator (A.R.), who interviewed each subject with a structured interview, the Diagnostic Interview Schedule for Children (3), using DSM-III criteria.

Potentially eligible subjects were rated after 1 week of hospitalization on the Overt Aggression Scale (4). This scale measures four areas of aggression: verbal aggression, physical aggression against self, physical aggression against objects, and physical aggression against other people. To be eligible for the study each subject must have had at least three episodes of overt aggression as rated on the Overt Aggression Scale.

These ratings were done by a clinical research rater after consultation with the ward staff. Subjects who met the criteria after the first week in the hospital and who, with a parent or guardian, gave written informed consent received placebo in a single-blind manner. The subjects who continued to meet the eligibility criteria, i.e., the same threshold rating on the Overt Aggression Scale, after 1 week of placebo administration were randomly assigned to capsules of lithium carbonate or matching placebo for 2 weeks. The dose of lithium was adjusted in a nonblind manner by a psychiatrist to maintain a blood level of 0.6 to 1.0 mmol/liter. We determined the lithium dose by the lithium level 24 hours after administration of 600 mg of lithium carbonate (5). To maintain the blind, any change in the dose of lithium was matched by a change in another subject's dose of placebo. Follow-up blood levels were measured weekly. Blood was also drawn from subjects taking placebo to maintain the blind.

The Overt Aggression Scale (4) was completed three times weekly by a clinical rater on the basis of discussion with all team members on the subject's ward. The weekly score used in the data analysis was the mean of these three ratings. The Behavior Rating Scale (6) was completed weekly by a clinical rater from interviews with the ward staff. The Hamilton Rating Scale for Depression (7), the 21-item version, was completed weekly by the clinical rater on the basis of direct interview of the subject. The Treatment Emergent Side Effects Scale (8), amended to include items for polyuria and polydipsia, was completed weekly by the subject's treating attending psychiatrist. The Conners Teacher Rating Scale (9) was completed weekly by the subject's hospital teacher. The ADD/H Adolescent Self-Report Scale (10) was completed weekly by each subject.

An analysis of a preliminary data sample indicated good reliability for these scales.

RESULTS

Thirty-three subjects entered the study. They ranged in age from 12 to 17 years (mean=15.15, SD=1.48). Fourteen were boys, and 19 were girls. Seven subjects dropped out. The completers comprised 14 subjects treated with lithium and 12 given placebo.

Analysis of variance (ANOVA) of the interaction of treatment group and time, using total scores and all fac-

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tors, showed no significant effects for scores on the Overt Aggression Scale, Behavior Rating Scale, Conners Teacher Rating Scale, or Hamilton Rating Scale for Depression.

There were more side effects in the lithium-treated subjects. This difference reached statistical significance in ANOVAs comparing the two treatments over 2 weeks for "autonomic side effects" (although no subject taking lithium had more than mild symptoms) and for "distress attributable to symptoms" (for which the highest value was for the first week of lithium treatment, and the distress was only present to a mild degree). No subjects were removed from the study because of side effects, and the side effects were few. The blind raters, staff, and subjects were unable to guess, at a rate better than that achieved by chance, which treatment was given.

We defined remission as the absence of the threshold rating for admission to the study. One (8.3%) of the 12 subjects taking placebo and three (21.4%) of the 14 taking lithium reached remission at the conclusion of the study. This difference is not statistically significant (χ^2=0.14, df=1, p=0.71). If the placebo remission rate was 10%, there would be an 80% chance of detecting a lithium response rate of at least 48%. For the observed difference of 13 percentage points, the 95% confidence interval is –15% to 41%.

The combined treatment groups and the separate treatment groups showed only low, nonsignificant correlations between age and change in Overt Aggression Scale score, with two exceptions in the placebo group: for aggression against objects (r=–0.65, df=14, p=0.01) and aggression against others (r=–0.54, df=14, p=0.05) the younger subjects showed more aggression in the second week.

Seven subjects did not complete the study: four receiving placebo and three receiving lithium. Five refused to stay in the study, and two left for administrative reasons. No one left because of clinical worsening or side effects. An intent-to-treat analysis using all 33 subjects showed no important difference from the analysis of the completers. There was no trend in the second (final) week for lithium to show a more favorable response at the end of the week than at the start.

There was no correlation between lithium level (mean= 0.79 mmol/liter, median=0.84, range=0.60–1.25) and change in score on the Overt Aggression Scale.

Although all subjects had some degree of inattentiveness, distractibility, episodic overactivity, and poor impulse control, interviews of the subjects and their parents did not disclose any clear diagnosis of ADHD in either adolescence or childhood.

DISCUSSION

Our results fail to support a difference between lithium and placebo in the treatment of conduct disorder in adolescents. Both treatments appeared ineffective.

The major limitation of this study was the short duration of lithium treatment: 2 weeks. It is possible that longer treatment might have produced a drug effect, since Campbell et al. (11, 12) demonstrated lithium's efficacy for hospitalized children with conduct disorder. Alternatively, the response of adolescents may be different from that of children.

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