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■ CLINICAL COMMENTARY:

Respect the accepted inclusion and exclusion criteria for using thrombolytics

Acute ischemic stroke has always posed the dilemma of giving treatment that may be either beneficial or harmful. Now the stakes of success or failure are dramatically higher. Family physicians must be knowledgeable about treatment options, as the 3-hour window for using rtPA after symptom onset is a diagnostic and logistic challenge for physicians and staff.

Our radiology colleagues help by using the unenhanced head CT to exclude lesions that mimic ischemic infarct and to confirm that true stroke victims do not have identifiable infarction greater than one third of the middle cerebral artery territory. Clinicians involved in the rtPA decision must know and respect fully and without deviation the accepted inclusion and exclusion criteria for using thrombolytics for acute ischemic stroke, to promote recovery and minimize death and disability due to intracranial hemorrhage.

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Is methylphenidate useful for treating adolescents with ADHD?

■ EVIDENCE-BASED ANSWER

Methylphenidate (Ritalin) is effective in the short-term treatment of attention deficit/hyperactivity disorder (ADHD) (strength of recommendation [SOR]: **A**, multiple randomized control trials).

Though the immediate-release preparation is the best studied of methylphenidate formulations, extended-release methylphenidate (Concerta) has similar benefits, with a dosing regimen that may better suit an adolescent lifestyle (SOR: **B**, based on extrapolation of 1 randomized controlled trial and expert opinion).

■ EVIDENCE SUMMARY

The subjects of most ADHD medication studies have been school-age children. Most children with ADHD will have symptoms persisting into teenage years, and methylphenidate has been increasingly prescribed for them.[1,2] Various systematic reviews and meta-analyses have demonstrated the effectiveness of short-term methylphenidate in the treatment of adolescents with ADHD.[3–5] Most participants in these studies are males aged <13 years. Therefore, any conclusions about the effectiveness of methylphenidate in older adolescents must be inferred.

The most comprehensive systematic review found 8 well-controlled crossover trials with an average sample size of 24.8 (range, 9–48).[6] The average duration of the studies was 6 weeks. The majority of the participants were white males with a mean age of 13 years. Each study showed statistically significant improvement from treatment with methylphenidate. Average effect sizes were calculated for 3 domains: ADHD symptoms (0.94), social behavior (1.06), and academic performance (1.25). Effect sizes were calculated using a modified Cohen's d, which is the difference between the treated and

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untreated means divided by the standard deviation in the untreated condition. It is difficult to translate these changes in effect size into clinically meaningful outcome measures, although one rule of thumb estimates an effect size of 0.8 is moderate to large.

Of the 3 studies that reported the proportion of subjects with clinically significant improvement, the modal result was about one half showings improvement with methylphenidate. Of trials assessing dosing levels, <50% found significant differences between "low" and "high" doses. However, the researchers did not give their definition of low and high doses. Also, diminishing clinical improvement was noted with higher methylphenidate doses.

A single study on the once-daily stimulant preparation, extended-release methylphenidate, shows statistically significant improvement in adolescent ADHD.[7] In this multicenter, randomized, double-blind, placebo-controlled trial of 177 adolescents, subjects were given placebo (n=87) or extended-release methylphenidate (n=90) at titrated doses from 18 mg/d to 72 mg/d. Following a subsequent 2-week randomization phase, clinical investigators found extended-release methylphenidate significantly superior to placebo (P=.001) on the ADHD scale. Subjects also rated it significantly superior to placebo (P=.001) on the Conners-Wells' Self-Report Scale. Mean dose and average age were not reported. This study has been presented as an abstract and is not yet published.

RECOMMENDATIONS FROM OTHERS

The American Academy of Child and Adolescent Psychiatry (AACAP) supports the prescribing of methylphenidate in adolescents with ADHD.[8] Given the unique psychosocial, environmental, and scheduling challenges of adolescence, the AACAP mentions extended-release methyl-phenidate as "well-suited for treatment of adolescents."

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CLINICAL COMMENTARY: Patients with childhood ADHD usually benefit from continuing their medication

Adolescents must face the challenge of becoming more organized and independent to be successful in middle school and high school. Those with childhood ADHD may have a particularly difficult transition, and will usually benefit from continuing to take their stimulants. Some adolescents, who were not previously identified as having ADHD, may declare themselves at this age due to school performance issues. Careful evaluation and treatment of these patients will contribute to their success.

Physicians should use the lowest effective dose of methylphenidate, as the studies seem to indicate that higher dosages do not improve performance in adolescents. Teens often prefer long-acting preparations, which obviate the need to take medication at school. The studies reviewed do not define long-term academic or vocational success, which is a more important outcome than symptom control for adolescents.

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EVIDENCE SUMMARY

No studies of inhaled beta-agonists have been conducted with patients who have an explicit diagnosis of acute cough due to URI. While some clinicians feel a distinction between URI and acute bronchitis should be made, there is significant overlap between these diagnoses in clinical practice, as well as in the available studies.

A systematic review looking at beta-agonists for acute bronchitis included the clinical diagnoses of both acute bronchitis and acute cough because a standard definition of bronchitis is lacking.[1] Only two trials in this review examined inhaled beta-agonists. When results from these trials were combined for the outcome of productive cough at 7 days, inhaled beta-agonists showed no benefit. However, the authors note that details of the individual trials may help to clarify the effect of inhaled beta-agonists.

One trial, a randomized controlled trial of adult patients with acute bronchitis in 2 community-based family practices, compared 23 patients receiving albuterolin a multidose inhaler (MDI) with 23 patients receiving placebo inhaler.[2] Patients were also randomized to receive erythromycin or placebo tablets. Patients with pneumonia or a history of asthma or chronic obstructive pulmonary disease (COPD) were excluded. At 7 days, 61% of patients in the albuterol group reported cough compared with 91% in the control group (P=.02, NNT=3). No statistically significant difference was seen in productive cough or night cough. Smokers responded to inhaled albuterol similarly to nonsmokers. Erythromycin had no effect on cough and side effects were similar among all groups.

The other trial was a randomized controlled trial of 80 adults with cough due to acute respiratory infection; it compared fenoterol aerosol 4 times daily with placebo.[3] Inhaled fenoterol is not available in the US but is similar to albuterol. This study showed no difference in cough at 7 days (relative risk [RR]=0.83; 95% confidence interval [CI], 0.52–1.30). In a subgroup analysis, however, smokers and those wheezing on initial exam had lower overall symptom scores when treated with fenoterol.

With beta-agonists, outcomes such as need for OTC medications and return to work do not improve

RECOMMENDATIONS FROM OTHERS

We were unable to find any guidelines on the use of albuterol via MDI for cough from bronchitis or URIs.

CLINICAL COMMENTARY:

Inhaled beta-agonists may aid symptoms; other outcomes may not be improved

Even without a history of lung disease, patients presenting with cough due to acute respiratory illness and with evidence of airflow obstruction (wheezing) appear to receive symptom relief from inhaled beta-agonists. Smokers may be another subgroup who benefit from treatment. However, important patient-oriented outcomes (such as reduced need for over-the-counter medicines, general well being, and return to work) do not improve. If using inhaled albuterol to treat acute cough in practice, one must also consider the financial costs and adverse effects associated with treatment.

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