

Comment on the *JAMA* article “Efficacy and Safety of Echinacea in Treating Upper Respiratory Tract Infections in Children”

One of the most highly regarded immune-supporting herbs available, echinacea has been used for decades to help prevent, shorten the duration of, and relieve symptoms of upper respiratory infections (URIs). Research suggests it may activate phagocytic function, relieve symptoms when used at the first sign of a URI, and reduce the recurrence of infectious symptoms. Additionally, it has been shown to be well tolerated in both adults and children.

In support of previous findings that echinacea may reduce the recurrence of upper respiratory infections, a recent study published in the *Journal of the American Medical Association (JAMA)* (290, 21:2824-30, 2003) conducted on 524 children ages 2 to 11 showed that echinacea was significantly more effective than placebo in preventing second and third infections ($P = .015$). However, this finding was not part of the study's primary outcomes, and echinacea did not significantly reduce the severity of infections. There are several possible explanations for this demonstrated lack of efficacy.

1. Timing of Supplementation

As stated by the authors of the study, "It is thought that echinacea therapy should be initiated at the first signs of a URI to be effective....It is conceivable that if the medication were started even earlier in the course of the illness, we may have found benefit." In this study, the researchers instructed the parents to begin echinacea supplementation as soon as their child developed at least 2 URI symptoms—such as sneezing, coughing, nasal congestion, runny nose, or temperature greater than 100.4° F (38.0° C). In previous trials demonstrating positive outcomes with echinacea use, patients began supplementation when they first had a subjective feeling of a cold, and were not required to wait until they had two or more symptoms. "It is conceivable that echinacea stimulated an immune response in study children that was too late to modify the URI for which it was given but provided a window of protection against another URI in the child," the study's authors stated. They followed with referencing a study in which a similar echinacea preparation was effective in preventing URIs in patients 13 to 84 years of age.

2. Children's Symptomatic Assessment

Compounding the issue of when supplementation was begun is the potential inaccuracy of assessing symptomatic relief in children. As stated by the study's authors, "Not only is the assessment secondhand (i.e., made by the parent instead of the child), fewer symptoms can be evaluated than in trials of adults. In addition, although the scoring system we used for assessing symptoms was based on criteria developed and validated in adults, there are, to our knowledge, no scoring systems that have been validated in children." The researchers postulated these inherent problems may also explain the results in similarly designed trials of zinc gluconate, in which supplementation was

shown to be efficacious when adults were studied, but negative results were seen in children.

3. Source of *Echinacea*

According to the study's authors, "In 2 trials using products similar to that used in our study, patients receiving echinacea had significantly shorter and less severe URIs than placebo recipients." The echinacea preparation used in the study was the dried and pressed *E. purpurea* juice, consisting of only the above-ground herb (aerial parts) and not the root, which was said to be similar to an extract that has been studied extensively in clinical and in vitro research. Unfortunately, the source used in this study was not standardized for the active constituents, making it difficult to determine whether an optimal dosage was used. The study's authors acknowledged that "we may have had different results in our study if we had used a different species of echinacea or different preparation of *E. purpurea*..." They further explained that "other investigators have used *E. pallida* root, mixtures of *E. purpurea* root and herb, and mixtures of *E. purpurea* root, herb, and *E. angustifolia* herb; in each of these studies the active medication was found to be more effective than placebo in decreasing duration and/or severity of URIs."

The fact that the preparation was a dried, pressed juice from aerial parts may also be the reason that the echinacea group had a higher incidence of mild adverse reactions (i.e., rashes) compared to the placebo group, 7.1% to 2.7%, respectively. As stated by the study's authors, "...placebo-controlled studies in adults have not documented any increase in rash or allergic reactions among echinacea recipients." Since rashes are not normally associated with most echinacea preparations, it is conceivable they may have been caused by allergic reactions to pollen in the echinacea juice, reported Mark Blumenthal, founder and executive director of the American Botanical Council, in the Natural Products Insider. Many echinacea products on the U.S. market incorporate an extract of the root, which usually has no pollens.

Conclusion

A recent study published in *JAMA* has brought speculation on echinacea's efficacy and safety for children with URIs. The possible reasons for the lack of demonstrated efficacy involve issues in the study design, including the time of supplementation, children's symptomatic assessment, and source of echinacea used. Furthermore, incidence of rashes were reported to be more common in children given echinacea than the placebo group, which may be attributed to pollens in the aerial parts used to make the dried, pressed echinacea juice. Rashes are not typically associated with echinacea use, possibly because many echinacea products on the U.S. market utilize an extract of the root.

A significant, positive outcome was also reported. Although not a primary focus of the study, supplementation with echinacea was associated with a significant reduction in preventing second and third infections when compared to placebo. The study's authors conclude that "further studies using different echinacea formulations, doses, and dosing frequencies are needed to delineate any possible role for this herb in treating colds in young patients. Our finding that echinacea may be effective in preventing URIs also deserves additional study."