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Early interventions for schizophrenia look promising, but evidence is inconclusive

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Schizophrenia is a chronic illness that most often comes on in late adolescence or young adulthood and can devastate patients' lives. Many physicians and researchers believe that early intervention can increase the chances for recovery, reduce recurrences and even prevent the warning signs of psychosis from progressing to the actual disease.

Yet, a systematic review of clinical trials using a variety of treatments toward these ends found "insufficient data to draw any definitive conclusions" as to the effectiveness of any one approach.

Taken together, however, the studies add up to "a growing body of evidence that there are some special things we can do for people in the early stage of the illness," said Max Marshall, M.D., professor of community psychiatry at University of Manchester in the UK and lead review author.

Early intervention is a critical issue in schizophrenia. "If we could get people at an earlier stage, they would be less ill," and the disease would not yet have wreaked the damage to social, vocational and family life that often accumulates, said Oliver Freudenreich, M.D., director of the First Episode and Early Psychosis Program at Massachusetts General Hospital. He has no affiliation with the review.

"The illness strikes in the developmental years; once someone drops out of school it changes his or her life trajectory… the more episodes occur, the harder it is to sustain a job or get a job back," Freudenreich said.

The review appears in the latest issue of *The Cochrane Library*, a publication of the Cochrane Collaboration, an international organization that evaluates medical research. Systematic reviews draw evidence-based conclusions about medical practice after considering both the content and quality of existing medical trials on a topic.

The reviewers analyzed data from 18 randomized controlled trials that included 1,808 patients. Because patient groups, types of treatment and outcome measures varied so widely, it was only possible to pool data from two studies.

Six of the studies involved individuals with "prodromal" symptoms — that is, symptoms that might indicate that a disease is coming on — such as social withdrawal, anxiety and confused thinking. About 10 percent to 20 percent of these people will ordinarily go on to develop full-blown schizophrenia. The aim of treatment was to keep this from happening.

Approaches varied in these studies: some involved antipsychotic medication, some specialized psychotherapy, some a combination of both. In one, patients received omega-3 fatty acids, a nutritional supplement.

"All these studies were quite interesting, but there isn't any one you would single out," Marshall said. "Even though the trials were quite small, there is some evidence to suggest that we can intervene in the prodrome, but we have to treat these findings with great caution."

For example, one of the included randomized controlled trials found that patients who received the drug risperidone combined with cognitive behavioral therapy were significantly less likely to develop psychosis after six months, but not after one year.

A study that aroused particular interest found a significant reduction in

psychosis among patients who received omega-3 fatty acids. “But it was only a single trial, it was small, and it has not yet been replicated,” Freudenreich said.

The remaining studies involved people in their first episode of schizophrenia. The interventions included diverse “phase specific” treatments—social or psychological therapies specifically developed for use early in the disease; attempts to detect psychosis and begin treatment earlier; programs to reduce marijuana use; and specialized teams as opposed to conventional clinics. Patients, for the most part, received medication according to standard guidelines.

In the largest study, which enrolled 547 patients, those in an intensive integrated treatment program that included several types of psychosocial therapy in addition to medication did better than those who received usual care during the first year. A year later, however, the difference had largely disappeared.

Among the interventions under study, “there seems to be pretty good evidence that family therapy and individual placement and support for employment are useful in early psychosis,” Marshall said. “We know that they work in schizophrenia generally, and it makes a lot of sense [for them] to be helping young people in the early stages of the disease.”

The review, overall, was “somewhat depressing,” Freudenreich said. “It concluded that we can’t conclude much, because studies were too small, not enough work has been done, and what has been done has not been very convincing.”

One lesson that seemed to emerge was the necessity of an integrated approach that combines different kinds of treatment. Freudenreich drew an analogy with other areas of medicine: “In orthopedics, you don’t just have knee surgery, you also have physical therapy.” Similarly,

medication alone is not enough for schizophrenia.

“[Medication] can go a long way to reduce psychosis, but you still have to figure out how to live with subtle psychosis and other symptoms. That’s where [a treatment like] cognitive behavioral therapy can be tremendously helpful.”

Future studies should strive to include more patients and follow them longer than those reviewed, nearly all of which involved fewer than 100 participants and lasted no more than two years, Freudenreich said. “There’s no substitute for large multisite trials.”

More information: Marshall M, Rathbone J. Early intervention for psychosis. *Cochrane Database of Systematic Reviews* 2011, Issue 6.

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