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Positive Results from Randomized Trial of Surgery for Pediatric Epilepsy Underscores Need for Earlier Referrals

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1. Dwivedi R, Ramanujam B, Chandra PS, Savita Sapra S, Sheffali Gulati S, Kalaivani M, Garg A, Bal CS, Tripathi M, Dwivedi SN, Sagar R, Sarkar C, & **Tripathi M. Surgery for Drug-Resistant Epilepsy in Children. N Engl J Med** 2017; 377:1639-1647.
2. **Chandra PS, Ramanujam B, Tripathi M. Surgery for Drug-Resistant Epilepsy in Children. N Engl J Med. 2018 Jan 25;378(4):399.**

Children with medication-resistant epilepsy who were randomly assigned to undergo surgery were far likelier to be seizure-free afterward compared to those assigned to continued medical management, according to the first randomized trial of surgery in this pediatric population.

During the 12 months following surgery, 21 of 57 patients assigned to surgery (37%) were entirely seizure-free, compared to zero of 59 patients assigned to continued medication management. Most of the seizures occurred in the first six months following surgery; in the second six-month period, 77% of the patients assigned to surgery were seizure-free, compared to 7% of those assigned to medical management.

The study, published in the New England Journal of Medicine and carried out at the All India Institute of Medical Sciences in New Delhi, under my guidance placed half of the 116 patients in the trial on a wait list to have surgery after completion of the trial.

Along with modest improvements in cognition and behavior favoring surgery over continued medical management, the findings underscore the need for physicians to follow AAN guidelines by promptly referring such patients to comprehensive epilepsy care centers, neurologists and others specializing in epilepsy said.

It really does show that epilepsy surgery is better than continued medications for epilepsy that doesn't respond to the first two lines of therapy in children,We didn't have anything like this for pediatrics. This gives us great information to give to parents who have children who don't respond to medication to say, we really need to think about surgical options early on.

Two randomized trials of surgery for adults with medication-resistant epilepsy were previously published, but both involved only patients with temporal-lobe epilepsy. The trial in children included not only 14 who required temporal lobe resections, but also 12 who required resection in a lobe other than temporal, 15 who required hemispherectomy, 10 who required corpus callosotomy, and six who underwent disconnection or resection of hypothalamic hamartoma.

Study Details

At the 12-month follow-up visit, all 14 of the children who had undergone a temporal lobectomy, and all six who had undergone hypothalamic hamartoma surgery, were seizure-free. Eleven of the 12 children (92%) who had undergone extratemporal resection, and 13 of 15 (87%) who had undergone a hemispherectomy, were likewise free of seizures at the 12-month mark. As expected, however, none of the 10 children who had undergone a corpus callosotomy were seizure-free.

Secondary outcomes favored surgery. Significant between-group differences were seen in the change from baseline to 12 months in favor of surgery on the Hague Seizure Severity scale (difference, 19.4; 95% confidence interval [CI], 15.8 to 23.1; $P<0.001$), on the Child Behavior Checklist (difference, 13.1; 95% CI, 10.7 to 15.6; $P<0.001$), on the Pediatric Quality of Life Inventory (difference, 21.9; 95% CI, 16.4 to 27.6; $P<0.001$), and on the Vineland Social Maturity Scale (difference, 4.7; 95% CI, 0.4 to 9.1; $P = 0.03$).

To check for changes in IQ, the Binet–Kamat test was administered to 63 patients (30 in the surgery group and 33 in the medical-therapy group). The reduction from baseline in the mean (±SD) intelligence quotient was not significant in the surgery group (-1.3 ± 6.5, $P = 0.29$) but was significant in the medical therapy group (-3.8 ± 3.6, $P<0.001$). Even so, the between-group difference in change from baseline to 12 months was not significant (difference, 2.5; 95% CI, −0.1 to 5.1; $P = 0.06$).

No deaths were observed in either group, but 19 of the children assigned to surgery (33%) experienced serious adverse events, including hemiparesis in 15 (26%). Those events included monoparesis in just two patients who had undergone resection of mesial parietal focal cortical dysplasia (monoparesis of lower limb-power 3/5) and temporal lobectomy (monoparesis of upper limb-power 3/5) . By contrast, hemiparesis occurred in 15 patients who had undergone hemispherotomy, and generalized hypotonia and language deficits in one patient each who had undergone frontal lobectomy.

Of the 17 patients with monoparesis or hemiparesis,, “15 (with the exclusion of 2 of those with hemiparesis) were able to move all major joints against gravity or better at 12 months. In the child with generalized hypotonia and the one with language deficits after surgery, both reached baseline levels of motor and language functions, respectively, at 12 months.”

Of note to parents and clinicians who remain fearful of surgery, the study found that adverse outcomes were also seen in the medical-therapy group. Ten of those 59 children, in fact, experienced physical injuries associated with seizures, including cuts, burns, and fractures. One had an adverse event associated with an antiepileptic drug, and another developed features of autism.

The adverse events associated with surgery are mostly those which are expected to happen for surgery being performed in a particular area, Even when there are adverse events most of these eventually improve, providing a significant benefit in favor of surgery Moreover it is only after surgery can medicines be scaled down one by one.

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