

# A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy

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# A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy

Response to Letter-to-the-Editor

We would like to thank Dr. Almomen and Dr. Burton for their interest in our article.<sup>1</sup>

We fully agree that the distribution of the etiologic category genetic and structural is uneven between the ketogenic diet (KD) group and the care as usual group (CAU; the control group). The program used for randomization was not stratified by etiology of the epilepsy nor for the syndrome classification. Patients were stratified according to age (1-6 years, 7-12 years, and 13-18 years), having a percutaneous gastrostomy tube or not, and whether the child is living at a residential center or attends the epilepsy center as an outpatient while he/she lives at home. The study was designed as an RCT-based economic evaluation among children and adolescents referred to our tertiary referral center for epileptology. The study did not intend to focus on a particular type of refractory epilepsy and both the MCT ketogenic diet as the classical ketogenic diet was accepted.

At the time the study protocol was written, there was substantially less information on syndrome specific effectiveness of the KD. Furthermore, currently it is still not possible to predict good responders, except for the glut-1 deficiency syndrome and pyruvate dehydrogenase complex deficiency.

Taking into account the syndromes, of which there is most information of cohort studies at present, the difference in number of included patients in both groups is not extremely different (West syndrome: N=3 in KD group and N=2 in CAU, Dravet syndrome: N=1 in KD group and N=0 in control group, Lennox-Gastaut syndrome: N=1 in KD group and N=0 in CAU, and finally, Doose syndrome: N=3 in KD group and N=2 in CAU group).

We did perform a logistic regression analysis. There was no variable (including etiology of the epilepsy and syndrome classification or age at ketogenic diet initiation) with a statistically significantly influence on being a responder or not.


Patients aged between one and eighteen years old were included, which is a wide age range. In our opinion, this has not caused any major problem in terms of dietary compliance or seizure documentation. Ketosis, which is an indicator for compliance, was measured frequently. Ketosis was checked daily by the parents in urine or three times a week in blood via a finger puncture. The largest challenge with compliance can be expected in teenagers, which was the smallest group in our cohort; 27% was younger than 5 years and another 50% was younger than 10 years. Parents and caregivers were responsible for good seizure documentation. This was necessary because of the age distribution of the cohort and the fact that half of the children had an IQ <70. The reliability of the use of seizure diaries in clinical

research is a shared concern, although it is accepted and as yet no alternative is available, especially for long-term follow-up.

Given the nature of the intervention, it is not possible to reach the golden standard of a placebo-controlled double-blinded trial. But in our opinion, this has not biased the adjustments in antiepileptic drug (AED) dose. The percentages mentioned in the table with demographic and clinical characteristics are the percentage of patients with no changes in AED dose. The adjustment of AED dose occurred more frequently in the CAU group. At 4 months, two children in the KD group had an increase and one child a decrease in the dose of one AED. In the CAU group, three children had a dose increase in one AED and two children a dose increase in one AED combined with a dose decrease in another AED.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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## REFERENCE

1. Lambrechts DA, de Kinderen RJ, Vles JS, de Louw AJ, Aldenkamp AP, Majoie HJ. *Acta Neurol Scand.* 2017;135:231-239.