

# Ketogenic diet for epilepsy



## Findings by SBU Alert

The ketogenic diet has been used for intractable epilepsy in children, and is a method that has been used sporadically for years. However, only recently has the ketogenic diet been used more systematically in Sweden. Although the treatment has been available for many years, there is little evidence about active mechanisms of diet. Several uncontrolled studies show markedly good effects in terms of seizure reduction. Known, and perhaps yet unidentified, side effects should be weighed against opportunities for improvement in a group of patients with intractable disease. Since the method requires special competence and experience, and since it is very demanding on the families, until further notice it should be used only within the framework of research projects that include systematic followup.

According to the judgment of the SBU Alert, there is currently poor\* evidence about the benefits of the method for patients. Hence, it is essential to continue assessing the medical effects, side effects, and costs.

\*This assessment by SBU Alert uses a 4-point scale to grade the quality and evidence of the scientific documentation. The grades indicate: (1) good, (2) moderate, (3) poor, or (4) no scientific evidence on the subject. For further information please see "Grading of evidence".

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## Technology

In the early 1900s, it was observed that starvation could alleviate seizures in individuals with epilepsy. In an attempt to maintain the secretion of ketones that results from starvation, researchers found that this could be achieved using a diet containing 80% fat and approximately 1-gram protein/kilogram body weight, with the remaining content being carbohydrates. This knowledge was used to develop the treatment method now available in its classical form and several modified variations.

The method was never widely adopted, partly because of the practical problems involved. During the 1940s, 1970s, and particularly the 1990s several new antiepileptic drugs have been introduced that reduced the interest in dietary treatment. Unfortunately, despite the development of new drugs, there continues to be a smaller group of children who do not receive sufficient help by these drugs or surgical treatment. Therefore there continues to be a need for treatment alternatives, of which ketogenic diet is one. In recent years, the method has received a renaissance primarily in the United States [1,2] where dietary treatment is available at many centers for severe epilepsy.

Generally, treatment is based on monitoring the effects of the diet on patients by continually testing and adjusting the diet for at least 3 months. The patients who have shown to benefit from treatment are offered continued treatment for 2 years, whereafter the therapy is successively discontinued during 6 to 12 months. As a rule, dietary treatment seldom extends longer than 2 years.

## Target group

Treatment is mainly used in younger children (1 to 12 years) with epilepsy, but in the United States, older children and adults are also being treated in trials. In Sweden, approximately 10 000 children under the age of 17 years have epilepsy. Within this group there are children with seizure disorders that are particularly difficult to treat. These disorders are often combined with other neurological disabilities such as autism, cerebral palsy, and mental retardation. It has been shown that dietary therapy is somewhat more effective with certain types of seizures, particularly in younger children. Given this background, it can be estimated that approximately 200 children would be likely candidates for dietary treatment. This implies a maximum of 15 to 20 new cases per year in Sweden.

## Relation to other technology

The ketogenic diet is a complement to other treatment methods for intractable epilepsy. Primarily drugs are used. Patients where the ketogenic diet can be considered should also be evaluated for the possibility of surgical treatment. Assessment and the choice of treatment should be the responsibility of a treatment team that particularly deals with intractable epilepsy in children.

## Patient benefits

The medical effects of the ketogenic diet have been studied in several uncontrolled studies. The most common outcome measure is seizure reduction, sometimes related to different seizure types or epileptic syndrome. Furthermore, there is information about increased general well being and improved cognitive ability, which is not always related to the rate of seizures.

A problem in interpreting the study results is that the definitions regarding seizure types and epilepsy syndrome have changed several times, hence the results from older studies are difficult to compare with newer studies. As with other types of treatment, the effects may be good initially, but later are less positive. The results in terms of seizure reduction are at least equally good or better than the results reported for new drugs. The results reported generally address the situation after 6 months. Newer studies report that 48% to 67% of the patients achieve more than 50% reduction in seizures [1,2,4].

The largest modern study [1] involving 150 children provides additional information, eg, the younger the child the better the effects. After 1 year of treatment 55% of the children are still receiving treatment. That percentage corresponds well to the number of patients who are seizure-free (7%), experience more than 90% seizure reduction (20%), and experience 50% to 90% seizure reduction (23%). Hence, the

conclusion can be drawn that the children who continue treatment are those who achieve good results early.

## **Complications and side effects**

A reported side effect is that treatment affects a child's growth. However, reliable data on monitored patients are lacking. Some patients also discontinue treatment because of the limitations which the diet places on daily life, or because of other diseases where an association with dietary therapy could not be confirmed.

## **Costs and cost-effectiveness**

The ketogenic diet always requires the services of a dietitian for approximately 2 weeks, full time. Furthermore it requires a nurse for approximately 1 week and a physician for 10 to 15 hours. Learning this treatment also requires considerable time on the part of the family. The treatment demands that the family spend considerably more time preparing food and it involves considerable extra costs. Both the direct and the indirect costs of therapy are currently being studied.

If a child with severe epilepsy achieves substantial or complete reduction in seizures, this would result in lower nursing costs and lower consumption of health services in addition to increased well being for both the patient and the family. The cost effectiveness of treatment cannot be determined at this time.

## **Structure and organization of health services**

The ketogenic diet as a means to treat severe epilepsy requires a special organization and staff with relevant skills and good knowledge about the method. Even in the long term, only a small group of children are candidates for this type of treatment, which necessitates continued consolidation of these activities. Centralization of resources, however, is inconsistent with good accessibility to treatment in all areas of the country.

## **Ethical aspects**

Treatment decisions must nearly always be made by the attending physician in consultation with guardians since children, because of age and developmental level, are unable to participate in such a decision. Side effects and long-term effects are not documented, but certain risks are acceptable in this group of patients since successful therapy may have a very positive effect on the child's long-term health and the family's situation. Because of uncertainties regarding active mechanisms, side effects, selection criteria, etc, patients on dietary treatment should, for the present, always be included in a systematic followup program.

## **Diffusion in Sweden**

Dietary therapy has been offered sporadically for many years. In the past 2 years, a small group of children have been treated, mainly at the Astrid Lindgren Pediatric Hospital in Stockholm. It is estimated that approximately 15 children are being treated in Sweden. The method used in Sweden basically follows the model developed at Johns Hopkins Hospital in Baltimore [1,2].

## **Current evaluation research**

Open studies are underway at several centers in the United States. Patients in Sweden are also being followed up in a standardized way. An attempt at a controlled study of short-term effects is under way at the Johns Hopkins Hospital. Studies addressing active mechanisms and metabolic changes are under way in several places, including The Karolinska Hospital.

## **Expert**

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## References

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