

Ketogenic therapy: The experience of 14 adult brain tumour patients supported by Matthew's Friends.



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WHAT IS A KETOGENIC DIET

- A ketogenic diet (KD) is low in carbohydrate, adequate in protein and high in fat.
- The reduced availability of carbohydrate (glucose) leads to increased fatty acid oxidation in the liver, ketones circulating in the bloodstream and adaptive changes in many metabolic pathways.

Why is there increasing interest in ketogenic diet as an adjuvant therapy for brain tumours and associated symptom management? (1).

- Healthy cells readily use ketones as a fuel source but tumour cells are considered less adaptive and may be disadvantaged by the KD fuel shift.
- KD may provide a means to exploit the metabolic dysregulation and associated pathway changes known to feature in most tumour cells.
- KD is an effective anticonvulsant therapy with a low side effect profile (2).

Table 1:

Summary: The 14 brain tumour cases returning questionnaires	
TUMOUR TYPES	<ul style="list-style-type: none"> 5 Glioblastoma Multiforme (GBM) 3 Oligodendroglioma [2 with seizures] 5 Astrocytoma [3 with seizures] 1 Medulloblastoma
8 MALE, 6 FEMALE [AGE 30-64]	<ul style="list-style-type: none"> Starting KD between 2011- 2015
TIME ON KD	<ul style="list-style-type: none"> 8-57 months - mean 19.7 months at June 2016
MEDICAL THERAPY WHILE ON KD	<ul style="list-style-type: none"> Chemo-radiation [4] None [4] Chemotherapy [2] Surgery [5] Radiotherapy [2]
OUTCOMES JUNE 2016	<ul style="list-style-type: none"> 8 alive & well (3 GBM, 4 Astrocytoma , 1 Oligodendroglioma) 4 died (2 GBM , 1 Medulloblastoma , 1 Astrocytoma) 2 progression of disease (2 Oligodendroglioma)

What KD support is available for UK brain tumour patients?

- Between 2011 and 2016, Matthew's Friends provided charitably funded* specialist dietetic support to over 50 adults from across the UK and Ireland, requesting help to explore KD therapy as a component of their brain tumour management. There are no NHS ketogenic therapy services for these patients. A KD requires individualised prescribing, monitoring and adjustment to optimise outcomes.

*All patients expressed gratitude to Matthew's Friends and the Astro Brain Tumour Fund for charitably funding their specialist ketogenic therapy support.

Learning from the patients experience of KD...

- A questionnaire was devised to gather information on the experiences, thoughts and feelings in relation to pursuit of KD.
- It was sent to 23 patients (n=10 in Sep. 2014, n=13 in Nov. 2015) receiving charitable support.

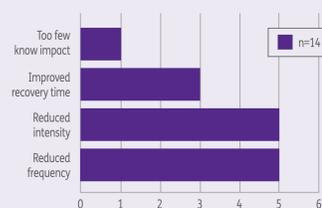
The questionnaire response:

- 14 (60%) completed and returned**
- 9 (40%) no response**

See Table 1 for a summary of the 14 glioma cases returning their questionnaires.

SUMMARY OF RESPONSES

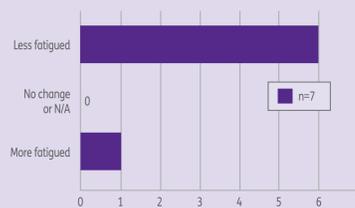
SEIZURES: any changes?



Seizure symptoms improved in all five cases reporting regular or frequent seizures with reduced frequency, reduced intensity being cited by all.

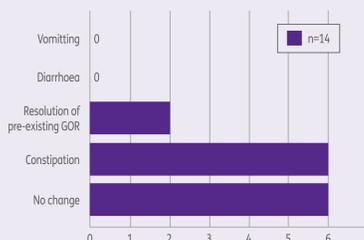
- One experienced too few seizures to comment.
- Changes in anticonvulsant therapy (AED's)?
- No change (4).
- Reduced number of AED's (1).
- Small increase in AED dose (2).

FATIGUE: any changes?



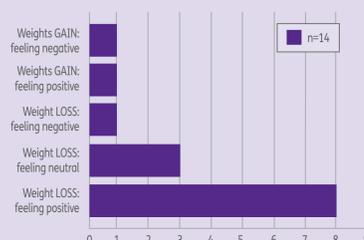
The majority felt less fatigue on ketogenic therapy; not requiring naps as before, having energy to join in more with family etc.

GI SYMPTOMS: any changes?



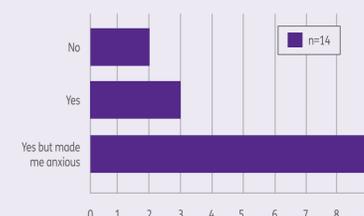
- Six reported a problem with constipation;
- Two reported this to be 'mild'.
- One reported an existing problem with constipation prior to starting their diet.
- Two reported a past history of chronic reflux that resolved completely on KD.
- Six reported no effect on gastrointestinal function.

BODY WEIGHT: any changes?



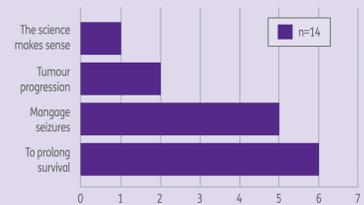
- Twelve lost weight (mainly in the early weeks) and most felt positive about this.
- One increased weight back to a 'normal' level and felt positive about this.
- One increased in weight and felt negative about this.

BLOOD MONITORING: was it useful?



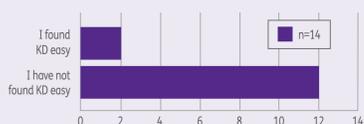
Blood glucose and ketone monitoring was found to be useful in all but one patient, although all reported anxiety associated with seeing results outside the target range for ketones (2-5mmol/l).

What was your primary reason for starting ketogenic therapy?



- Prolonging survival was the reason stated by most, with seizure control, management of tumour progression and management of fatigue also of relevance.
- Two indicated that family pressure played a part in starting ketogenic therapy.

Have you found ketogenic therapy easy?



Despite 12/14 not finding KD 'easy'; all had been on KD for 8-57 months.

DISCUSSION

Seizure and fatigue management:

- Those experiencing seizures prior to KD gained evident benefits from their KD in terms of reduced frequency, reduced intensity and shorter recovery time.
- Those experiencing fatigue prior to KD reported a significant improvement in energy levels with less reliance on daytime naps.

The potential of KD to deliver benefits to brain tumour patients experiencing seizures and fatigue is significant. Neuro-oncology teams should be more aware of KD as an optional support strategy for UK brain tumour cases struggling to manage seizures and fatigue.

Impact on the tumour:

- Most stated that their reason for starting a KD was to prolong survival.

To date, the relatively small amount of preclinical and clinical evidence has focussed on the impact of KD on malignant tumours (3). Any potential to influence the growth and progression of low grade brain tumours has yet to be explored.

Tumour/ KD related monitoring:

- The most accurate method available for glioma patients to track the metabolic shift associated with KD is blood glucose and ketone monitoring. A ratio 1:1 - 2:1 of blood glucose: ketones is recommended eg. glucose 4mmol/l coinciding with ketones 2-4mmol/l (4). Adults can find these levels challenging to achieve.

There is a need for tumour-specific markers of KD effect so that the therapy can be initiated, adjusted and weaned in accordance with these.

Ease of KD lifestyle:

- Most patients did not find ketogenic therapy easy to initiate but gained knowledge and confidence over time; continuing KD for 8-57 months.
- Matthew's friends have developed a new practical guide for adults starting out on dietetically supervised KD but this cannot replace individually tailored therapy and ongoing access to specialist support throughout

Glioma patients require experienced clinical support to accompany them throughout their KD therapy journey, where priorities readily shift along the way; initiation, learning new skills and integrating KD into daily life, symptom management, optimising ketone levels, coping with hospital admission etc.

CONCLUSION

- Neuro-oncology teams need to be made aware of the potential for KD to deliver improvements in seizures and fatigue where medications have failed.
- KD is an option for those keen to play an active part in their glioma therapy.
- Clinical trials are required (UK trial in the planning stages) to explore KD delivery, monitoring and outcomes in a range of tumour types.

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ADDITIONAL COMMENTS ABOUT THEIR KD EXPERIENCE:

"Being on the diet at least made me feel as though I'm doing my bit to keep this thing at bay... I do have the odd cheat but don't see the harm in that now and again, especially when I am feeling as great as I am now."

"Since starting the diet I feel that I have more energy because I am not up all night with heartburn. My mood & irritability is much improved... my family has noticed."

"My mood is generally better as the diet gives me hope. I am less anxious about focal seizures and am therefore more inclined to see friends which is important to me. I do get frustrated as there (are) lots of extra things for me to do such as writing & monitoring what I am doing, but understand that it is necessary if I want things to improve."

"Before the ketogenic therapy, I had no control of my brain tumour, but now I am trying to control it. Just by doing that, whether it is successful or not, makes me feel good. Empowering."