Eating Well: Nutritional & Supplemental Support for Brain Tumor Patients

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UCLA
• Lifestyle risk factors for brain tumors
• Exercise
• Diet during treatment
  – Antioxidants
  – Ketogenic diet
• Diet during recovery/remission
• Selected supplements
Lifestyle Risk Factors for Brain Tumors

**HARMFUL**
- Exposure to ionizing radiation
- Low physical activity in adolescence
- High BMI in adolescence

**HELPFUL**
- Caffeine containing beverages
- Soy
- High antioxidant food

If lifestyle choices don’t directly affect risk, how are they useful?
Physical Activity

• Physical activity improves quality of life in patients with brain metastases
• Study* following 31 adults with brain metastases
  – Stood for 1.6 hours or more per day better quality of life
  – Sat or were supine for 20.7 hours or more had more depression & anxiety
• Be as physically active as you are able to be

Lowe SS et al. J Pain Symptom Manage 2014. E pub ahead of print
Let Food Be Your First Medicine
NUTRITION DURING TREATMENT
Nutritional Challenges for Brain Tumor Patients

• Severe protein catabolism follows elective craniotomy*
  • Uncomplicated surgery
  • Significant decreases in total protein, albumin, transferrin & lymphocytes
  • Significant increases in nitrogen loss
• Nausea
• Medications
• Taste Changes

*Krylov K et al. Zh Vopr Neirokhir Im N N Burdenko 2012 76: 32-6;
Nutritional Antioxidant: Help or Harm?

• Definition: an enzyme or other organic substance, as vitamin E or beta carotene, that is capable of counteracting the damaging effects of oxidation in animal tissues. [Generally considered protective]

• Foods high in “antioxidants”: often brightly colored, especially for the brain the dark blue, purple, red fruits but can also include some spices and beverages like tea

• Research on protection from antioxidant rich foods suggests an inverse relationship for primary prevention.
• No evidence of harm during treatment.
## Table 2: Association between total antioxidant index (TAI) and survival in population-based glioblastoma multiforme patients from the San Francisco Bay Area, 1991–2004

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1: TAI (Trolox equivalent)</td>
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<tr>
<td>TAI &lt; 1,500</td>
<td>0.98 (0.94, 1.02)</td>
<td>1.07 (0.98, 1.16)</td>
<td>1.01 (0.95, 1.07)</td>
<td>0.88 (0.82, 0.94)</td>
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<tr>
<td>1,500 ≤ TAI ≤ 2,999</td>
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<tr>
<td>3,000 ≤ TAI ≤ 4,499</td>
<td></td>
<td>1.06 (0.84, 1.33)</td>
<td>1.29 (0.93, 1.79)</td>
<td>1.07 (0.63, 1.81)</td>
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<tr>
<td>TAI ≥ 4,500</td>
<td></td>
<td>1.13 (0.87, 1.45)</td>
<td>1.51 (1.00, 2.27)</td>
<td>1.32 (0.76, 2.27)</td>
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<td>4: TAI and vitamin/supplement intake:</td>
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<tr>
<td>Low TAI (no regular vitamin/supplements)</td>
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<tr>
<td>Low TAI + regular vitamin/supplements</td>
<td>0.90 (0.673, 1.10)</td>
<td>0.97 (0.70, 1.34)</td>
<td>0.64 (0.42, 0.99)</td>
<td>0.94 (0.63, 1.39)</td>
</tr>
<tr>
<td>High TAI (no regular vitamin/supplements)</td>
<td>0.99 (0.79, 1.24)</td>
<td>1.20 (0.77, 1.86)</td>
<td>1.07 (0.71, 1.60)</td>
<td>0.70 (0.47, 1.04)</td>
</tr>
<tr>
<td>High TAI + regular vitamin/supplement</td>
<td>0.94 (0.77, 1.16)</td>
<td>1.10 (0.76, 1.59)</td>
<td>0.94 (0.64, 1.37)</td>
<td>0.66 (0.46, 0.96)</td>
</tr>
</tbody>
</table>

- **TAI** scaled such that HR represents a 1,000 unit change. In Models 1–3—covariates included age, gender, ethnicity, series, proxy-reporting, treatment (resection, radiation, temodar, and other chemotherapy), total calorie intake, and regular vitamin/supplement use (yes/no); In Model 4—covariates included all the covariates used in Models 1–3 except regular vitamin/supplement use (yes/no), which was part of the main exposure.

- 1,500 TAI units correspond approximately to one cup of green (~800) or black (~900) tea plus one serving of Brussels sprouts (~500) plus one serving of carrots (~150).

- High TAI is above median, low TAI is equal or below median.
Ketogenic Diet & Management of GBM

- Not standard of care
- Initial observations
  - 1995 Nebling first attempted KD for refractory seizures in 2 previously treated BT patients
  - Long term management & even survival seen in these pts
- Biological principle
  - Under caloric stress, ketosis develops
  - Normal brain cells can metabolized ketones, cancer can’t
- Ketogenic diet: Very low carbohydrate, calorie restricted, higher fat
- Animal models successful
- Cautions- not appropriate for diabetic patients or very cachexic patients

Ketogenic Diet & Management of GBM

Fig. 8. Relationship of circulating glucose and ketone body levels to brain tumor management. These values are within normal physiological ranges of glucose and ketones under fasting conditions in mice and produce anti-angiogenic and proapoptotic effects causing metabolic isolation of tumor cells and delayed tumor growth. We refer to this state as the zone of metabolic management. The glucose and ketone levels predicted for brain tumor management in human patients are 3.1–3.8 mM and 2.5–7.0 mM, respectively [19]. (Reprinted with permission from Epilepsia, 49(Suppl. 8):114–116, 2008).
Ketogenic Diet & Brain Tumor

• Case report 63 y/o woman
• Glioblastoma multiforme poorly differentiated expressing hypermethylation of MGMT gene promoter
• Surgery incomplete resection
• Standard therapy + ketogenic diet (4:1 fat: carbohydrate) 600 cal diet
• Patient lost 20% of her body weight
• Complete remission of tumor
• Recurred 10 weeks after stopping diet

Zuccoli G et al. Nutrition & Metabolism 2010. 7:33-40
Webinar on Ketogenic Diet

- Presented by American Brain Tumor Association
- Free educational series
- Wednesday 10/8/2014 live at 11-12 AM PST
- More information at www.abta.org
Symptom Management

• Decreased Appetite
• Weight loss
• Nausea
• Pain
• Fatigue
• Skin changes
Quality of Life & Survival in GBM

- In 220 GBM patients: Lower quality of life and increase fatigue were independently associated with worse prognosis. Improving QOL should have benefits*

- Survival in depressed low grade glioma patients was 1/3 to 1/2 shorter than non-depressed patients**

How to Eat if Nauseated

• Small frequent meals
• Don’t overfill your stomach, including with liquids
• Eat more at your best time of day (usually AM)
• Increase easily digestible protein
• Decrease fat, especially saturated fat
• Adjust spices for taste
• Use ginger- as candy, as tea, added to food or smoothies
• Be sure to stay hydrated
Eating to Combat Fatigue

• Eat consistently throughout the day
• Smaller meals good
• Avoid low glycemic foods (“white”, no fiber, too much sugar)
• High fiber carbohydrates help support blood sugar and energy
• Add protein to each meal
• Add a good fat to most meals
NUTRITION DURING RECOVERY/ REMISSION
Healthy Diet - The New Plate

Anticancer Plate

**Animal proteins (optional)**
- fish, organic meat, omega-3 eggs, organic dairy products

**Grains**
- multigrain bread, whole-grain rice, quinoa, bulgur...

**Fats**
- olive, canola, or flaxseed oil, omega-3 butter

**Herbs and spices**
- turmeric, mint, thyme, rosemary, garlic...

**Vegetables and fruits**
- lentils, peas, beans, tofu...

**Vegetable and fruit proteins**
- lentils, peas, beans, tofu...

Recommended Diet

• 7 servings of fruits + vegetables
  – Half of your plate at every meal should be fruits & veggies
• Limit or eliminate red meat, especially preserved meats
• Eat a mostly plant based diet with some fish. Chicken used moderately is ok
• Use whole grains and other foods high in fiber
• Add good fats such as avocado, olive oil, nuts
## Phytochemicals in Food

<table>
<thead>
<tr>
<th>COLOR</th>
<th>PHYTOCHEMICAL</th>
<th>FRUITS &amp; VEGETABLES</th>
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<tbody>
<tr>
<td>Red</td>
<td>Lycopene</td>
<td>Tomatoes &amp; tomato products: juices, soups, sauces</td>
</tr>
<tr>
<td>Red-Purple</td>
<td>Anthocyanins &amp; Polyphenols</td>
<td>Blackberries, raspberries, grapes, blueberries</td>
</tr>
<tr>
<td>Orange</td>
<td>α-Carotene &amp; β-Carotene</td>
<td>Carrots, mangos, pumpkins</td>
</tr>
<tr>
<td>Orange-Yellow</td>
<td>β-Cryptoxanthin &amp; Flavonoids</td>
<td>Cantaloupe, peaches, papaya, tangerines, oranges</td>
</tr>
<tr>
<td>Yellow-Green</td>
<td>Lutein &amp; Zeaxanthin</td>
<td>Spinach, avocado, honeydew</td>
</tr>
<tr>
<td>Green</td>
<td>Glucosinolates &amp; Indoles</td>
<td>Broccoli, bok choi, kale</td>
</tr>
<tr>
<td>White-Green</td>
<td>Allyl Sulfides</td>
<td>Leeks, garlic, onion, chives</td>
</tr>
</tbody>
</table>

SUPPLEMENTS
Some Potentially Useful Supplements/ Foods

- Green tea extract
- Flaxseed lignans
- Medicinal mushrooms
- Ginger
- Calcium
- Vitamin D
- Melatonin
- Ginkgo
- Curcumin

- Herbs of special interest to brain tumor patients: *Boswellia*
- Herbs with interesting preliminary information: Ginseng; *Scutelleria baicalensis*; *Angelica sinensis*; Berberine containing herbs
Safety of DS & Herbs

• Herbs & Dietary supplements
  – Most adverse events related to poor manufacturing or poor patient selection
  – Nausea or GI upset common early symptoms
• Potential for interactions- may be more of an issue with newer chemotherapy
• Generally, if what’s on the label is in the bottle, supplements are safe
• Choosing a good supplement
  – Know good brands by understanding quality control
  – Using the label (Good label doesn’t always guarantee good quality inside, but a bad label is a definite red flag)
  – New GMP regulations should even out quality
• Disclose use to medical team
Carnitine: Radiation-induced fatigue

- Open-label, dose-finding study
- Results:
  - 83% of these patients (15/18) had carnitine deficiency
  - Preliminary data analysis of 13 patients showed that total carnitine increased from 30.0 +/- 6.9 to 41.0 +/- 12.1 (mean +/- SD) after 1 week of supplementation (P = 0.01)
  - Free carnitine increased from 24.3 +/- 6.1 to 33.8 +/- 9.8 (P = 0.004)
- Carnitine oxidizes free fatty acids contributing to overall energy production

Cerebral Edema: Corticosteroid Concerns

• Prolonged use has significant side effects
  – Mental changes
  – Immunosuppression
  – Cushing syndrome
  – Osteoporosis

• Corticosteroids effect on tumor cells and cancer treatment
  – Stabilize blood-brain and blood-tumor barriers
  – Reduce tumor perfusion
  – Inhibit apoptosis in human malignant glioma cells

• These corticosteroid induced changes may interfere with efficacy of adjuvant chemotherapy for malignant gliomas

Edema in Brain Tumors

Study Design/Demographics

• Small, open-label study of BSE (H15) (N=12)
• Group A: Patients with tumor progression-related edema (n=7)
• Group B: Patients with prior radiotherapy or radiochemotherapy-related edema with leukoencephalopathy (n=5)
• H15 1200 mg TID

Results

• H15 reduced edema in
  – 2/7 patients in Group A
  – 3/5 patients in Group B
• H15 allowed steroid discontinuation in 3/5 patients in Group B
• H15 more effective in controlling treatment-related edema than tumor progression-related edema
• H15 was well tolerated

BSE, *Boswellia serrata* extract; TID, 3 x’s/day.
Primary outcome: cerebral edema volume on MRI
Secondary outcomes: dexamethasone medication (mg/wk), toxicity (RTOG/EORTC-CTC score), QOL (EORTC-QLQ 30), cognitive functioning (mini-mental exam), and PFS

Eligibility Criteria
- Primary brain tumor or brain metastases
- Whole brain or partial brain XRT to > 60% of brain volume
- No prior brain XRT
- Dexamethasone ≤ 24 mg/d

Randomization
(N=44)

BSE (H15) (n=22)
1400 mg TID

Placebo (n=22)

CTC, Common Toxicity Criteria; EORTC, European Organisation for Research and Treatment of Cancer; MRI, magnetic resonance imaging; PFS, progression-free survival; QOL, quality of life; QLQ, quality of life questionnaire; RTOG, Radiation Therapy Oncology Group; TID, thrice daily; XRT, radiotherapy.

BSE (H15): Effect on Edema in Brain Tumors

Kirste et al

RESULTS

• MRI measurements (end of XRT)
  – BSE: 60% of patients had <25% of baseline values or no edema at the end of treatment
  – Placebo: 26% of patients reached similar outcome
  – Effect from tumor response cannot be ruled out
    • BSE: 13% CR, 25% PR, 62% SD
    • Placebo: 10% CR, 36% PR, 36% SD

• No significant difference between groups for
  – Dexamethasone use
  – QOL
  – Mental functioning
  – PFS

• Adverse effects
  – Common XRT AEs were same in both groups
  – 6 patients in BSE group reported grade 1/2 diarrhea; no patients in placebo group reported diarrhea

AE, adverse event; BSE, *Boswellia serrata* extract; CR, complete response; MRI, magnetic resonance imaging; PFS, progression-free survival; PR, partial response; QOL, quality of life; SD, stable disease; XRT, radiotherapy.

Ginkgo & Brain Irradiation

- Open Phase II crossover trial*
- Symptomatic irradiated brain tumor patients (n=34)
- Ginkgo 40mg TID (product not adequately characterized) for 24 weeks
- Results: 56% completed 24 weeks of treatment
  - Cognitive Function improved
    - Executive function (p=0.007)
    - Attention/concentration (p=0.002)
    - Non-verbal memory (p=0.001)
  - Mood improved (p=0.002)
  - QOL improved: physical function (p=0.003)
- CAUTION with ginkgo- higher risk of bleeding unless terpenoids removed from the extract

Vitamin D & Malignant Brain Tumor

Fig. 3. Dose-response relationship between modeled serum 25(OH)D and incidence rates of brain cancer per 100,000 population in 175 countries, 2002. Source: data from GLOBOCAN [1]. Three outliers are labeled.
Higher you go away from the equator the higher the rate of malignant brain tumor.

Mohr SB et al. Neuroepi 2010 35: 281-90
Calendula & Dermatitis with Radiation

- Phase III Randomized trial 254 breast cancer patients
- *Calendula officinalis* homeopathic ointment vs Trolamine
- BMI greater than 25 and prior chemotherapy predicted greater likelihood to develop dermatitis
- Grade 2 dermatitis
  - Calendula vs Tolamine (41% vs 63%; p<.001)
  - Calendula less likely to interrupt treatment (1 vs 15); Attributed to XRT 0 in calendula, 12 in placebo; avg length of interruption 10 days
  - Calendula group had less pain (1.54 vs 2.10 p=.03)
  - Calendula harder to apply but greater satisfaction

Curcumin & Brain Tumor

- Preliminary data only- Very little human clinical data in brain tumor
- Some interesting early work:
  - Anti-proliferative; anti-migratory; anti-invasive properties in GBM cell lines*
  - Induces apoptosis & decreased proliferation in MB cells**
  - Potentiates the effects of etoposide & temozolomide in cell lines***
- Tumeric may have effect on platelets- no adverse event reports but caution should be taken in patients on Avastin or with active bleeding

Making a Personal Plan

• Pick a reasonable goal
• Change diet & lifestyle first
• Discuss options with oncologist & other skilled professional
• Consider risks as well as benefits
• Integrate natural therapies into your conventional care
• Find high quality products
• Use the appropriate dose
• Monitor for effectiveness & safety
• Don’t lose sight of the larger context of healing

CHOOSE WELL & BE WELL!!
Please Join Me at My Website
www.DrMaryHardy.com

Dr. MARY Hardy 🍓 Wellness Works

JOIN DR HARDY AS SHE HIGHLIGHTS:
* Important research papers
* Practical tips
* Expert information

TO HELP YOU:
* Reduce your risk of cancer
* Minimize treatment effects
* Generally keep yourself well

Because WELLNESS WORKS!
Summary & Questions

Thank you for your attention!