Current Controversies in Nutrition

Fermented Wheat Germ Extract—An Adjunct Treatment for Cancer?

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Over the years, I have read about dozens of alternative treatments that have been promoted for controlling or reversing cancer, including, but by no means limited to, laetrile, macrobiotics, Hoxsey, Gerson, and Krebiozen. While conventional treatments (surgery, chemotherapy, and radiation) are often brutal—and serious questions remain about their long-term effectiveness—a certain skepticism is warranted when it comes to claims of alternative therapies for cancer. In the late 1960s, I was convinced that laetrile had real merit—until a study funded by the drug's advocates found that vitamin A was more effective.

I do believe that some alternative therapies for cancer have been of exceptional value, such as a 1950s-era immune-enhancing therapy known as Krebiozen (and a later variation known as Carcalon), although it faded into history with the death of its chief researcher and clinician, Andrew Ivy, MD, in 1978. Likewise, considerable research now supports the use of high-dose intravenous vitamin C as an adjunct treatment for cancer.[1,2]

Many alternative therapies have grown out of personal or anecdotal reports—that is, by sharing the knowledge of an unexpected benefit. I am always mindful of an observation by the late Emanuel Cheraskin, MD, DMD, who noted that such reports are called "case histories" if a physician wants to give them credence and "anecdotal" if he/she wants to dismiss them. Still, I have no doubt that many alternative therapies benefit at least *some* people. However, cancer is an insidious disease, driven by adaptive mutations, and few conventional or alternative therapies provide sustained benefits for the majority of patients. The reason for this is probably continuous gene mutations and chromosomal aneuploidy.[3]

Unfortunately, few alternative anticancer therapies have been subjected to scientific studies. One of the notable exceptions is fermented wheat germ extract (FWGE). More than 100 studies—including clinical trials—have been conducted on this nutrient-based substance, although not all of these studies have been published.

The origins of FWGE as a cancer treatment date back to the 1930s. Albert Szent-Györgyi, MD, PhD—who was awarded a Nobel Prize for his work on bioenergetics (what would eventually become known as the Krebs cycle) and discovering vitamin C—believed that compounds called benzoquinones might inhibit the uptake of glucose by cancer cells, in effect, starving cancer cells of their metabolic fuel. Born in Hungary, where he is still revered, Szent-Györgyi was one of the most brilliant physicians and biochemists of the twentieth century; he knew that wheat germ contained high concentrations of benzoquinones.

Toward the end of his life, when he was conducting research at the Woods Hole Research Center, in Falmouth, Massachusetts, Szent-Györgyi received some funding for cancer research. He hypothesized that a new class of anticancer drugs might be based on benzoquinones.* After he died in 1986, Szent-Györgyi's files and scientific notebooks were being readied for disposal, but they were saved at the last minute and shipped to Mate Hidvegi, PhD, a Hungarian biochemist. There was an interesting coincidence in this event—Dr. Hidvegi's grandfather had been a friend and professional colleague of Szent-Györgyi decades before. Dr. Hidvegi started working on the chemistry of wheat, believing that fermentation might increase the bioavailability of benzoquinones.* He developed a process that utilized baker's yeast (*Saccharomyces cerevisiae*) to increase benzoquinones, specifically 2,6-dimethoxy-benzoquinone (DMBQ) and 2-methoxy-benzoquinone.[4]

By 1996, Dr. Hidvegi and his colleagues had conducted animal experiments and found that the main effect of FWGE was to inhibit the growth of metastases from different types of cancer. This effect could be related to blocking glucose uptake by cancer cells, or it could be related to other mechanisms, including cell signaling and oncogene suppression. Dr. Hidvegi and his colleagues started clinical trials in Hungary and Russia in 1999, and later on in Italy, focusing on the use of FWGE as an adjunct treatment for colorectal cancer, head and neck cancer, breast cancer, and stage-3 melanoma. Later on, Dr. Hidvegi obtained government approval to identify FWGE as a "dietary food for [a] special medical purpose for cancer patients." This was the first such category for a dietary supplement in Europe, according to Dr. Hidvegi.* Today, FWGE is sold in packets for mixing with ~ 4 oz of cold water and then shaken vigorously to dissolve the powder.

*Personal communications in an interview with Mate Hidvegi, PhD, via Skype, February 29, 2012.

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Clinical Research in Patients with Cancer

Animal and cell studies suggest that FWGE might be beneficial for patients with leukemia, breast cancer, and many other types of cancer.[5] A combination of fermented wheat germ extract and vitamin C might help prevent metastases.[6] However, the most impressive findings on FWGE have come out of clinical trials, some of which have been published in top-tier journals. The following sections are summaries of six of these clinical studies.

Colorectal Cancer

In an open-label trial, doctors treated 170 patients who had undergone conventional treatments for colorectal cancer. Sixty-six patients took a preparation containing 5.5 g of pure FWGE daily for 6 months, and these patients were compared with 104 control subjects. Only 7.6% of the patients in the treatment group developed new metastases. In contrast, 23% of the patients who received only conventional treatment developed metastases. The findings were statistically significant, with a *P*-value of 0.0184 for progression-free survival and a *P*-value of 0.0278 for overall survival.[7]

Head and Neck Cancer

Oxidative stress is strongly associated with cachexia in patients who have cancer. Because some research suggests that FWGE has potential antioxidant properties, doctors treated 60 patients with either conventional therapies or conventional therapies plus FWGE for head and neck cancers (stages IIIa, IIIb, IV) in an open-label trial. After 2 months, 55 patients were still alive, with no statistical difference between the treatment and control groups. However, markers of oxidative stress decreased significantly, and quality-of-life (QoL) scores were improved significantly in the group taking FWGE.[8]

Oral Cancer

In an article and position paper, the Hungarian Association of Oral and Maxillofacial Surgeons reviewed research on FWGE in oral cancers and recommended its use as a "supportive treatment." The Association described a study in which 50 patients with tumors of the larynx and pharynx, as well as patients with soft-tissue tumors of the oral cavity received FWGE daily for 3 years. Eighty percent of the patients had squamous-cell carcinoma. Using FWGE as an adjunct therapy, the 5-year survival rate increased considerably, and the patients' QoL improved. The researchers wrote:

> At the end of the three-year-long study it was established that the majority of patients taking Avemar [FWGE] experienced no tumor recurrences or metastasis after surgery and radiation, and/or chemotherapy. In some of the patients even the existing recurrences and metastasis regressed. Avemar increased the therapeutic effects of both chemo- and radio-therapy, while significantly reducing the side effects. The appetite of patients taking Avemar improved, and the body weight of cachectic patients increased.[9]

Melanoma

Researchers treated 52 postoperative patients who were at high risk of recurrent melanoma. The patients received either conventional treatment or conventional treatment plus FWGE for 1 year in a randomized, pilot, phase-2 clinical trial. After 7 years of follow-up, patients who had taken FWGE had significantly better progression-free and overall survival rates. The mean progression-free survival was 55.8 months for the FWGE group, compared with 29.9 months for the control group. The mean overall survival of the FWGE group was 66.2 months versus 44.7 months in the control group.[10]

Chemotherapy-Related Infection

FWGE appears to enhance immunity and resistance to infection in children undergoing cancer treatment. In an open-label, matched-pair, pilot clinical trial, doctors treated 22 patients with chemotherapy or chemotherapy plus daily FWGE. The types of solid tumors varied, and included sarcomas and hepatoblastomas. During treatment and follow-up, no progression of the cancers was evident in either group (follow-up periods varied). However, 30 instances (24.8%) of febrile neutropenia were noted in the FWGE group, compared with 46 (43.4 percent) in the control group.[11]

Rheumatoid Arthritis

Some chemotherapeutic drugs, such as methotrexate and rituximab, are also used to treat rheumatoid arthritis (RA). Interestingly, one clinical trial has found FWGE helpful for treating RA. In a year-long, open-label trial, doctors treated 15 women with severe RA. All of the patients had tried and had failure of a response to two disease-modifying antirheumatic drug (DMARD) treatments. After taking FWGE for 6 and 12 months, a health-assessment questionnaire and assessment of morning stiffness showed improvements.[12]

Apparent Mechanisms

Studies have shown that FWGE may exert its anticancer effects through multiple mechanisms, many of which inhibit or slow the uptake of glucose by cancer cells. In addition, the benzoquinones may be only some of the active ingredients in FWGE. A research article noted that FWGE induces apoptosis through the poly (ADP-ribose) polymerase (PARP) pathway.[13] FWGE also reduces several promoters of inflammation, including cyclo-oxygenase-1 (COX-1), cyclo-oxygenase-2 (COX-2), and tumor necrosis factor–α (TNF-α).[14,15]

FWGE might also work via a mechanism similar to that of conventional cancer treatments and high-dose vitamin C. Radiation treatments and most chemotherapeutic drugs work by increasing hydrogen peroxide levels in cancer cells, enabling this potent oxidant to destroy cancer cells.

Cancer cells are weak producers of catalase, so they are not well-equipped to defend the body against hydrogen peroxide. Interest-

ingly, researchers at the U.S. National Institutes of Health found that high-dose intravenous vitamin C exploits this low-catalase weakness of cancer cells; at high concentrations, vitamin C generates large amounts of hydrogen peroxide in cancer cells.[1]

A similar oxidative stress therapy for cancer has been hypothesized by doctors of a Tijuana-area cancer clinic.[16] According to their theory, the key players of the anticancer regimen among others could be vitamin C and a quinone for producing oxidants, and a glucose-uptake inhibitor to undercut cancer's antioxidant defenses. Because FWGE is a nontoxic source of benzoquinones, and this extract has been shown to selectively inhibit glucose uptake and metabolism in cancer cells,[17] it is very possible that FWGE also disarms cancer cells' defenses against hydrogen peroxide, according to Dr. Hidvegi.*

Dr. Hidvegi pointed out that patients with cancer should suspend taking fermented wheat germ extract at least 1 week before undergoing a positron emission tomography (PET) scan. The scan uses a glucose solution with a radioactive isotope to identify areas of rapid glucose uptake, such as cancer cells. Because fermented wheat germ extract reduces glucose uptake in cancer cells but not in healthy cells, positron-emission tomography scans may yield a "false negative," leading a patient to believe that he/she is cancer free.*

Conclusion

Because of the insidious nature of cancer, I would never suggest that a person put his/her life on the line for just one therapy, regardless of whether it is conventional or alternative. The best approach is to me the most rational one: to use both conventional and alternative treatments. In my own personal experience, I have found that people undergoing conventional cancer treatments (surgery, chemotherapy, and radiation) tend to wait too long before adopting alternative treatments, and then these patients end up doing too little. I favor pursuing the aggressive use of nutritional and alternative therapies in conjunction with conventional treatments.

Finally, it is also important to remember that cancer is a disease of mutations and a microcosm of the evolutionary process. Any treatment selects for the survival of cells resistant to that treatment. Therefore, I believe it is important *not* to use all potential alternative treatments at once. In a personal conversation, the late Robert C. Atkins, MD, once told me that he treated patients who had cancer with as many as fifty different regimens. As the cancer adapted to one treatment, Dr. Atkins would shift the patient to a different regimen, in effect, to stay ahead of the mutation curve. Again, it is crucial that both clinician and patient be vigilant and aggressive in treating cancer in a wholistic fashion.

Disclosure Statement

The author has received product samples but no financial compensation from American Biosciences, the U.S. maker of fermented wheat germ extract. ■

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