Hydrazine Sulfate: anti-cancer treatment agent

Cachexia is the result of a complex array of metabolic abnormalities which results in loss of appetite, tissue wasting, muscle and visceral organ atrophy, weakness, and loss of fat stores. It may be accompanied by energy, anemia, lowered serum albumin, lowered immune function, lactic acidosis, hyperlipidemia, glucose intolerance and increased gluconeogenesis. These abnormalities alert clinicians to the possibility of an underlying disease.

Cachexia is defined as physical wasting with loss of weight and muscle mass caused by disease. Patients with advanced cancer, AIDS, and some other major chronic progressive diseases may appear cachectic. Anorexia (lack of appetite) and cachexia often occur together. Cachexia can occur in people who are eating enough, but who cannot absorb the nutrients. Cachexia is not the same as starvation. A healthy person's body can adjust to starvation by slowing down its use of nutrients, but in cachectic patients, the body does not make this adjustment.

The relationship between cachexia and cancer has been known for some time. Although cachexia is not a universal feature in cancer, it occurs frequently in lung, pancreatic, and gastric cancer. As a consequence it has been suggested that cachexia may contribute to death.

The awareness among oncologists of demonstrable differences between cachexia and starvation prompted many researchers to investigate the mechanisms underlying cachexia in the hope of reversing it. Cachexia is the result of a complex interaction between the growing tumor and the host; when the entire tumor is removed, normal metabolism and weight gain resume.

Gluconeogenesis is the production of glucose from molecules which may not be sugars. This synthesis of new glucose takes place in tissues like liver and kidney when a high-energy compound named phosphoenolpyruvate (PEP) is synthesized by the enzyme PEPCK present in mitochondria.

Enter Hydrazine Sulfate

Hydrazine sulfate (HS) is an inexpensive common chemical which is commercially available for about 11 cents per gram. HS is used in the refining of rare metals, in analytical blood tests, and as an antioxidant in soldering flux. HS is carcinogenic. It induces a range of in vitro genotoxic effects including DNA and gene damage in mammalian cells and bacteria, and chromosomal aberrations in mammalian cells. In 1968, HS was shown to induce lung adenomas, adenocarcinomas and liver cell carcinomas in male rats. HS is either genotoxic or a non-genotoxic carcinogen, i.e., it acts as a tumor promoter for preexisting initiated cells.

HS produces hypoglycemia in dogs and rabbits. In 1966, Brown et al reported that HS caused genetic mutations in normal cells and cautioned that if it was used in animals over the long term, HS should he considered potentially carcinogenic.

Joseph Gold, MD, is a general practitioner and the director of the Syracuse Cancer Research Institute. Gold postulated that a metabolic circuit existed in cancer patients that allow energy needed for tumor growth to be drawn from normal metabolic pathways. According to Gold, lactic acid from tumor glycolysis, amino acids from protein breakdown and glycerol from fat mobilization drive gluconeogenic activity which drains away the energy which normal anabolic processes need to produce and maintain tissue integrity. This alleged 'energy short circuit' causes cachexia in cancer. If the circuit could be broken, cachexia would be overcome and the cancer would he deprived of the energy needed to grow.

In 1966 P. D. Ray first published the results of his studies on the effect of L-tryptophane and HS on the formation of phosphoenolpyruvate in the gluconeogenesis in rat liver. Later he reported effects of various hypoglycemia-inducing agents on carbohydrate metabolism in rats. While HS did not react directly with PEP, it did inhibit the conversion of oxaloacetate to PEP, the high-energy compound considered essential for the synthesis of glucose by gluconeogenesis in liver and kidney

tissue. He found that the enzyme phosphoenolpyruvate carboxykinase (PEPCK) which controlled new glucose formation in liver and kidney tissues was inhibited by HS.

When Gold learned of these results, he concluded HS was the means to reverse cachexia. He suggested that by feeding HS to cancer patients one could block gluconeogenesis without blocking normal energy metabolism, thus overcoming cachexia and reversing cachexia-dependent tumor progression.

Dosing

Adults (over 18 years old)

Various clinical trials have used 60 milligrams of hydrazine sulfate taken by mouth one to three times daily for 30 days in patients with cancer and or cachexia. Injections have also been given by a healthcare provider.

Children (under 18 years old)

Because of insufficient available information the discretion of the healthcare provider is required. The loading rate may range any where below the adult dosage and also the frequency of administration is to be determined on a case by case basis.

Safety

Many complementary techniques are practiced by healthcare professionals with formal training, in accordance with the standards of national organizations. However, this is not universally the case, and adverse effects are possible. Due to limited research, in some cases only limited safety information is available.

Warnings

Hydrazine Sulfate is a MAOI (Momoamine Oxidase Inhibitor). What it does is inhibit an enzyme that breaks down monoamines (serotonin,

norepinephrine, and dopamine), those brain chemicals that make us happy. MAO inhibitors have been used as antidepressants. MAOI is a class of compounds that can have potentially deadly interactions with other drugs. For over three decades it has been known that central nervous system depressants—such as barbiturates, tranquilizers and alcohol—are incompatible with MAO inhibitors and use of the two together could result in extremely dangerous effects.

However, MAOIs have another job in the body: they metabolize tyramine, an amino acid. When taking a MAO inhibitor, tyramine is not broken down, and *eating foods with tyramine can raise your blood pressure and heart beat dramatically and causes the worst headache you have ever experienced.* This is a very dangerous condition, especially for someone already battling cancer. Most of the foods containing tyramine are not on the cancer diet plan, and you should be avoiding them anyway. In addition to all of these things, foods high in glucose should be avoided.

Foods containing tyramine are (mainly) aged, fermented, or pickled, such as most cheeses (except cottage cheese, cream cheese, and fresh Mozzarella), lunch meats, hot dogs, yogurt, wines and beers. Here is a pretty good list of foods that contain tyramine:

- Barley grass (perhaps the highest percentage of all according to Dr. Duke, but he doesn't list other grasses), which would exclude all barley supplements,
- Dry and fermented sausage (bologna, salami, pepperoni, corned beef, and liver),
- pickled herring and salted dried fish,
- broad beans and pods (lima, fava beans, lentils, snow peas, and soya beans),
- meat extracts,
- yeast extracts/brewer's yeast, beer and ale, red wine (chianti, burgundy, sherry, vermouth),
- sauerkraut,

- Fruits listed (oranges, tangerines, lemon, grapefruit), and overripe fruits.
- some fruits (bananas, avacados, canned figs, raisins, red plums, raspberries, pineapples),
- raisins, figs, dates and dried fruit in general
- cultured dairy products (buttermilk, yogurt, and sour cream),
- chocolate,
- caffeine (coffee, tea, and cola drinks),
- white wine, port wines, distilled spirits,
- soy sauce, miso, peanuts, almonds,
- beef or chicken liver, herring,
- meat tenderizer, MSG,
- pickles,
- Pumpkin seeds.
- most cheeses
- cured meats or fish
- yoghurt,
- tofu and tempeh
- sour cream

Tranquillizers or sedatives in doses greater than 100 mg per day, especially benzodiazepines and phenothiazines should be avoided, also antihistamines, alcohol and other agents that depress the central nervous system such as morphine. Also vitamin C and B6 should not be taken; Natural vitamin C from fruits is OK.

In general, any high protein food that has undergone aging should be avoided. Also, any over-the-counter cold or allergy remedy should also be avoided.

Note: there is absolutely no accurate list of what foods have tyramine. One site says raspberries and grapes do have them, and another site says they do not. The bottom line is if the cancer patient gets headaches,

then it is highly likely they are eating something with tyramine in it. Start eliminating foods *in the same food categories* as in this list.

If the cancer patient is in a lot of pain, the cesium chloride with DMSO treatment and the Aloe Immune may be able to stop the pain within 2 or 3 days. The patient may be able to get off of morphine, or a similar drug. However, *wait until the morphine, or other drug, is out of the system before beginning hydrazine sulfate.*

Finally, hydrazine sulphate should be taken in exact doses. Overdosing can do more harm than good.

Dr. Joseph Gold, the pioneer in hydrazine use in cancer patients, has conducted several studies on the effects of hydrazine sulfate; he suggested that patients using hydrazine sulfate refrain from using benzodiazepines and barbiturates.

Hydrazine sulfate used with bleomycin, a chemotherapy drug, may lead to an additive effect of both agents. Hydrazine sulfate used with cyclophosphamide, a chemotherapy drug, may lead to enhanced antitumor effects of cyclophosphamide.

Hydrazine sulfate may induce hypoglycemia (low blood sugar) or hyperglycemia (high blood sugar). Use of hydrazine sulfate with diabetes medications/oral hypoglycemic agents may result in either additive or negative effects.

Hydrazine sulfate used along with isoniazid may lead to enhanced effects of hydrazine.

Hydrazine may increase the length of time that levodopa works.

Hydrazine sulfate used with methotrexate may lead to an additive effect of both agents.

Hydrazine sulfate used with mitomycin C may lead to enhanced antitumor effects of mitomycin C when these agents are *administered six hours apart* from each other. The study found that if hydrazine sulfate

and mitomycin C are mixed in the same syringe, they inactivate each other.

Hydrazine sulfate is typically suggested as a cancer treatment, and thus hydrazine sulfate may interact with herbs or supplements also used for cancer. As extensive data is not available, caution is advised.

Pregnancy and Breastfeeding

Not recommended due to lack of sufficient data.

History

Hydrazine sulfate is a common industrial chemical, which was used as a component of rocket fuel during World War II. It was first proposed as a cancer treatment in the early 1970s by Joseph Gold, MD, of the Syracuse Cancer Research Institute, Syracuse, NY. Gold drew on the work of Nobel laureate Otto Warburg, who in the 1930s theorized that cancer derived its energy from anaerobic glycolysis (i.e., fermenting sugar) rather than respiring in the normal way. In 1968, Gold proposed using chemicals to control cancer's growth by exploiting this 'Warburg effect.'

In the early 1970s, Gold indicated that hydrazine sulfate could inhibit the growth of leukemia, lymphoma, melanoma and other cancers in rats. He suggested that by cutting off a tumor¹s supply of 'new glucose' in the liver, the drug could help starve the tumor. This, in turn, would stop cancer from preferentially depleting the body¹s energy pools and put an end to cachexia, the terrible wasting process that appears in the final stages of the disease.

In fact, it is this wasting process that often kills the cancer patient. Some doctors believe that the answer to the weight loss in advanced cancer is to inject patients with all the nutrients they need through an intravenous drip. This is called total parenteral nutrition (TPN).

However, carefully controlled studies have shown "no significant improvement in either response or survival" associated with TPN for most kinds of cancer. In fact, in two instances, TPN was associated with decreased survival.

Gold also showed that hydrazine sulfate could enhance the effect of such conventional drugs as Cytoxan, Mitomycin C, methotrexate and bleomycin in rats. He proposed that a combination chemotherapy with hydrazine sulfate and a cytotoxic agent may be useful in the treatment of human cancer.

Gold analyzed 84 terminally ill cancer patients who had been treated with hydrazine sulfate under a drug company[1]s investigational new drug (IND) license. He found that 59 out of the 84, or 70 percent, improved subjectively while 14 out of the 84, or 17 percent, improved objectively. Subjective responses included increased appetite, weight gain or stoppage of weight loss, increased strength, improved performance status and decreased pain.

Objective responses included measurable tumor regression, disappearance of cancer-related medical problems and more than one year of stabilized condition. About half of the people who responded had no other cancer therapy while they were receiving hydrazine sulfate. Some patients relapsed quickly; other remissions were long-term.

In Gold[1]s 1975 study, the side effects were mild, consisting for the most part of a few incidents of tingling in the fingers and toes, nausea, itching and drowsiness. There was no indication of bone marrow depression.

Hydrazine sulfate could be used alone or in combination with other drugs. In 1981, Gold showed that hydrazine sulfate treatment resulted in marked appetite improvement. In those patients receiving hydrazine sulfate alone, appetite improvement occurred in over 86 percent. In those who were also receiving conventional chemotherapy, it was almost 70 percent. Average weight gain for people receiving hydrazine sulfate alone was about 4 kilos, while for those with other therapies it was only 250 grams.

In the 1980s, Rowan Chlebowski, MD, PhD and colleagues at Harbor Hospital UCLA studied 38 patients with advanced cancer and weight loss. Patients were placed in a carefully-controlled study to evaluate the influence of hydrazine sulfate on carbohydrate metabolism. They were given a standard dose of 60 milligram capsules three times a day for 30 days. Glucose tolerance was much better in patients who received hydrazine sulfate than in those who received a placebo ('sugar pill').

Side effects of hydrazine sulfate were minimal. In one study, over 70 percent of the patients reported no toxic effects. The UCLA team concluded that hydrazine sulfate can influence the abnormal carbohydrate metabolism associated with weight loss in patients with cancer.

Hydrazine sulfate was also evaluated in 101 heavily pretreated cancer patients who were suffering from weight loss. After one month, 83 percent of the hydrazine sulfate-treated patients, but only 53 percent of the controls, were able to maintain or increase their weight. In addition, UCLA scientists reported appetite improvement was more than twice as frequent in the hydrazine group. The hydrazine sulfate patients did not simply consume more calories, but utilized calories better than did the control patients.

Writing in the Lancet, UCLA researchers reported on 12 malnourished patients with lung cancer. They too received 60 milligrams three times a day for a month. There was less loss of the amino acid lysine in the hydrazine sulfate group than in those receiving the placebo. These too concluded that hydrazine sulfate reduced the 'flux' of amino acids and could therefore favorably influence abnormalities in digestion among late-stage cancer patients.

In a larger study of lung cancer patients, the UCLA researchers reported on 65 patients with non-small-cell lung cancer which could not be operated on. All the patients received the same combination of standard chemotherapy (cisplatin, vinblastine and bleomycin) and the same dietary counseling. But patients who received hydrazine sulfate showed

much greater intake of calories. Survival was somewhat greater in the hydrazine sulfate-treated group, especially those with less advanced cancers. A team of 11 scientists at the N.N. Petrov Research Institute of Oncology, Leningrad (St. Petersburg) have been working on hydrazine sulfate since the 1970s. The Russians have had the greatest single clinical experience with hydrazine sulfate, having treated and evaluated over 740 patients.

The patients were of many kinds, including 200 with lung cancer, 138 with stomach cancer, 66 with breast, 63 with Hodgkin's disease and 31 with melanoma. Patients were treated for one month at a time. If their disease became stabilized, there was an interruption of two to six weeks. Then they were treated again for a month. Nearly half the patients had less cachexia while on the treatment: 14 percent had pronounced and 33 percent had moderate benefits. In addition, 10 percent showed tumor regression. All had disease stabilization.

Thus, in the Russian, as in the Syracuse and UCLA studies, hydrazine sulfate did something few other treatments could do: it inhibited the wasting process. The best results were seen with desmosarcoma, neuroblastoma, laryngeal cancer, Hodgkin's disease and breast cancer.

Later studies showed: hydrazine sulfate increased appetite, decreased pain, diminished anorexia, stabilized tumor growth and promoted survival; and it had few side effects.

Hydrazine sulfate is inexpensive and accessible. In most studies, the treatment regimen was three 60 milligram tablets each day for a month. Then patients stop for two to six weeks, and take another course as needed.

In the Russian studies, such courses were repeated two or three times. In some cases (especially neuroblastoma) there were 10, 20 or even 40 repeated courses. For cancer of the esophagus or larynx, the drug was administered as a 0.4 percent solution (in which 15 milliliters equaled one 60 milligram tablet). Barbiturates and alcohol are strictly prohibited during the administration of hydrazine sulfate. Hydrazine sulfate's use in

cancer has always been controversial. After years of denigrating its use, NCI finally agreed to sponsor a phase III clinical trial at three medical centers. They are now under way.