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FYI: Issues regarding Curcumin Therapy in Niemann-Pick Disease, Type C Patients

Use of various supplements in NPD patients is routinely discussed by families and is a challenging issue. There is often little data on use of the supplements in children and teens, or even in adults, for that matter. There is also limited data on reasonable dosing and on potential side effects. One such supplement, curcumin, has been discussed over the last few months on the NNPFD list serv.

There have also been concerns raised in the scientific community that higher doses of this compound are not as effective as lower doses, and in fact, may be toxic rather than being helpful to patients (see data from Dr. Erickson below).

The following is a summary of the limited data on use of curcumin, although there is no current data on use in NPC patients. This information is not intended to be a medical directive or endorsement of the use of any product, but rather is for use by families as they consider the issue of curcumin supplementation for their affected family member.

At a scientific meeting in May 2009 sponsored by the Ara Parseghian Medical Research Foundation, Dr Robert Erickson of the University of Arizona reported the following: based on previously-reported work of Drs. Lloyd-Evans and Platt which showed an increase in median survival of NPC mice from approximately 70 days to approximately 90 days using 150 mg/kg/day curcumin, Dr. Erickson and colleagues tested higher doses of curcumin and different preparations as compared to what was used by Lloyd-Evans and Platt.

A diet with 2% curcumin extended median survival from 71 to 88 days. The first of two formulations produced by Verdure Sciences resulted in an 11-times higher level in the blood and a 4-times higher level in the brain than with equal doses of powdered curcumin, while the second Verdure preparation resulted in even higher levels.

However, **these did not increase survival as well as the plain curcumin did**, thus more curcumin does not seem to be better. The challenge with this data is that it does not necessarily correspond to a dose in humans, i.e. the 150mg/kg/day – that would be a fair amount (gram amounts) of powdered curcumin for a larger child.

One very good review of clinical trials and several newly published articles in reputable journals were also reviewed and provided the following information. The list of attributes for curcumin is impressive, and includes use as an anti-inflammatory, anti-oxidant, anti-viral, and anti-fungal as well as being a chemo-preventive agent, and neuro-protective, promoting cell survival. This

extensive claim of benefit may make one wonder why those who consume significant curcumin in the diet, such as those in the East Indian culture, don't live longer, healthier lives.

The review paper looked at safety and anti-inflammatory activity of curcumin in papers published from 1966 to 2002. It cited one adult human clinical trial where curcumin was given in graduated doses up to 8000mg (8 grams - that's a lot of curcumin) each day for 3 months without toxicity. They had planned to go to 12 grams, but the volume of powder was deemed too great and unpalatable for routine use. Five additional human trials with doses ranging from 1125 mg to 2500 mg all showed safety of use and demonstrated anti-inflammatory activity.

A paper from Korea published in the Journal of Biological Chemistry (a very highly regarded journal) indicated that curcumin has been reported to be capable of preventing the death of neurons in animal models of neurodegenerative disease (Parkinson's, Alzheimer, etc).

They studied the effect of curcumin on cultured neural progenitor cells (like stem cells) and found that curcumin exhibits a biphasic effect: at low concentration (0.1 to 0.5 microMolar) it stimulates cell growth and proliferation while at high concentration (>10 microMolar) it is cytotoxic (kills cells).

At the low concentrations, curcumin enhanced neurogenesis (nerve cell growth) in mouse hippocampus and increased neural plasticity (like adaptability) and repair. A concentration of 500 nM (nanomolar) was most effective. The conversions to human doses are difficult, but the paper mentioned doses of less than 0.2mg/kg/day led to an increase in growth of neural stem cells in adult mouse hippocampus.

An additional study indicated that curcumin is not toxic at lower doses but in a tumor cell system, was toxic at higher doses.

Much of this addresses the safety of use of curcumin, with apparent concerns for toxicity at higher doses. There is little data on potential effectiveness. We do not know how much curcumin is absorbed into the blood stream. In addition, if it is absorbed, it is not known how much of that makes it to the brain where it is needed to impact the neurological aspects of NPC.

Dr. Fran Platt's studies also suggest that there may be a window of opportunity for anti-inflammatory agents to help the NPC mouse, and that there may be some risk associated with use outside that timeframe.

According to Dr. Marc Patterson, who we consulted on this issue, the only way to answer these questions about curcumin use in NPC would be in a controlled clinical trial, with phase I dose finding and safety, and phase II proof of principle studies.

A NOTE OF CAUTION: according to a recent publication *, curcumin was studied in mice to assess its effect on iron stores in the body. The studies showed that curcumin affected general iron balance in the body, and can affect system-wide iron metabolism, especially in individuals who already have iron deficiency.

This could be of significance to NPD patients on curcumin because chronic disease can lead to anemia and reduced stores of iron, which could be further compromised by use of curcumin. Careful monitoring of hematocrit, hemoglobin, serum iron and transferrin saturation in individuals using curcumin is indicated.

Blood. 2009 Jan 8;113(2):462-9. Epub 2008 Sep 24. Curcumin, a cancer chemopreventive and chemotherapeutic agent, is a biologically active iron chelator.

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