Micronutrients: Molybdenum

Transcript

Hello and welcome to our micronutrients module on molybdenum. Molybdenum is one of those difficult to say nutrients but it's got a lot of interesting functions and history behind it so we'll be taking a look at that. Let's just jump in and begin and before we begin make sure you understand and when you're working with patients on this and clients that this information is not intended to replace a one-on-one relationship with a qualified health professional. It is not medical advice, it is just a sharing for me to view of things that I have researched and I encourage you to encourage her clients that if they are under the care of a doctor before they start specific nutrient intervention that they get checked out and they make sure it's okay with their doctor.

Good old molybdenum. Molybdenum is an essential trace element and it is needed in microgram amounts, just little teeny tiny amounts. We looked at other nutrients which you need much larger milligram amounts and those are called more macro nutrients, macro minerals. This is a micro mineral. It's needed is a cofactor for a lot of different things and you're going to recognize some of these enzymes when I say them and maybe didn't know that molybdenum was actually important for these functions. In the body and in where comes in a nature is usually bounce to sulfur or to oxygen. It's a very big in the sulfur metabolism pathways.

It's important in chemical transformation, think carbon, nitrogen, and sulfur cycles, so different cycles in the body, chemical transformations meaning moving from one chemical to another. The molybdenum content of our food is very dependent on supply of molybdenum in the soils and many minerals are like that. One of the things that esophageal cancer has been linked to is the molybdenum content and soils and food so that's kind of an unusual little correlation they have found there.

Let's take a look at the digestion and absorption of molybdenum. Molybdenum like most minerals is bound to amino acids in the food. What's required to cleave that away, to separate the molybdenum from the amino acid is HCl, hydrochloric acid, and pepsin and that is in the stomach. The HCl activates the pepsin to pepsinogen which then starts the breakdown of the bonds that are connecting the amino acids in a protein. It is also breaking down the bonds that connect the amino acid to a mineral. Then proteolytic enzymes in the small intestine further break these down to release the bombs and allow the molybdenum to be observed.

Passive diffusion is the main mechanism of absorption but in some animals they have found carrier proteins that carry it in. For the most part passive diffusion is the way it's going to go. The way that molybdenum is transported in the blood is thought to be molybdenum, which is MB, 4 oxygens, and the -2 means that there is 2 extra electrons. The highest concentration of molybdenum is in the liver, the kidneys, and the bones. There is also other tissues that have been found to have molybdenum but not in such high amounts are thyroid, lungs, spleen, brain, muscle, and adrenals.

When we're looking at building up people in their thyroid or the adrenals, one of the minerals is not often talked about which could indeed be low would be molybdenum. Usually anywhere between 50 and 90% is absorbed in the amount that's absorbed depends on the gradients between the bloodstream and the intestine and how much is being put in the system at any given time. What are the functions of molybdenum? Well, there is an organic molecule known as the molybdenum cofactor and the molybdenum cofactor is listed on the left-hand side of the diagram, that's what it looks like, and the way that molybdenum does its thing, that's one of the ways. Also, there's something else called the molybdoenzymes so the molybdoenzymes actually is where the molybdenum becomes part of this other chemical property for chemical structure and then does its thing. You recall enzymes catalyze reactions.

Here's some of the molybdenum containing enzyme, some molybdoenzymes if you will, that are important in the body and we will go through each one of these in detail. Xanthinoxidase, you might have heard of that one; sulfide oxidase which is involved in sulfur metabolism; aldehyde oxidase, which is involved in alcohol breakdown; and then mitochondrial amidoxime reducing component, MARC is what it's known as. That's important in the mitochondria and the functioning to make energy. Let's look at each of these.

Sulfide oxidase is an enzyme found in the membranes of the mitochondria, so it's a mitochondrial outer membrane enzyme namely found in liver, heart, and kidney. There's these two what's called molybdopterin and 2 cytochrome residue to visit the pieces that put this together to make sulfide oxidase. What it does in reality is an important job because in the pathways in the body where sulfite needs to be converted to sulfate and then be eliminated. When we have sulfur containing amino acids like methionine and cystine we need this enzyme to transform, to pull off the sulfur containing pieces and transform the sulfite to sulfate. Why is that important? Well, if that gets backed up we're going to get a backup of sulfur compounds and that could put a kink in the system.

Now we are moving over to Xanthinoxidase. It's an iron dependent enzyme so in addition to needing molybdenum it also requires iron and it's found mainly in the thyroid in the intestine. It causes a breakdown of nucleotides. You know what the nucleotides are, like adenine, guanine, cytosine. Those are precursors to DNA and RNA, that's what makes up and forms the DNA and RNA.

Because of the breakdown of those nucleotides to form uric acid and in the uric acid needs to be excreted, usually is excreted by the kidneys. It's pulled apart in the liver and it's one of the enzymes that actually helps with the antioxidants capacity in the blood. It's one of the antioxidants that are important in the bloodstream.

The next and we're going to look at is aldehyde oxidase. Aldehyde oxidase is found mostly in the liver. It uses oxygen of the electron receptor. I just want to take a pause to just remind you what redox is. Oxidation and reduction. It's basically a chemical reaction oxidation is when we are adding electrons onto a particular chemical and that becomes oxidized. We have molecules that would run around in our bloodstream that are called antioxidants and what they basically need is that they are an electron acceptor. They are able to take on an electron, they basically commit Harry Carey for something else. You think about vitamin C, you think about Xanthinoxidase, you think about aldehyde oxidase, you can think about super oxide dismutates, vitamin A. They are antioxidants so they basically commit suicide or they become unstable so to speak and help other things to become stable again. They pull in electrons to allow these other molecules to become stable.

The way that this happens is that there are hydroxylation reactions that involve a number of different molecules that have similar structures and Xanthinoxidase and aldehyde oxidase also play a role in the metabolism of drugs and toxins so they are in the liver and one of the things that aldehyde oxidase is involved in is the breakdown of alcohol. One of the breakdown products of alcohol is acid aldehyde and acid aldehyde can be eliminated and reduced by aldehyde oxidase so that it doesn't cause so much damage. Acid aldehyde is also produced in the gut when you have a Candida overgrowth or when your clients have a Candida overgrowth. He produces acid aldehyde. If you ever have people say I don't drink but when I eat certain foods sometimes when I eat fruit or eat sugar I feel drunk it has to do with the acid aldehyde. Aldehyde oxidase is what breaks it down.

Then we have mitochondrial amidoxime reducing compound. Some of these words are hard to say, MARC. Basically it forms a three component enzyme system with cytochrome B5, NADH cytochrome B5 reductase so it causes a detoxification of mutagenic, meaning they're not quite carcinogenic that they are able to produce mutations, and hydroxylated bases. These are any number of toxic compounds that this particular mitochondrial molybdenum dependent enzyme helps to reduce. The one that's been found to be crucial for human health is the sulfite oxidase so remember that takes the sulfide to the sulfate and allows that to be broken down.

If you know if people who say they are sensitive to sulfates, set oh I can't eat garlic or onion, I am really sensitive to sulfates, one of the problems is they have a problem with this enzyme because they can't break it down and eliminate it. It could be a molybdenum deficiency.

When people look at some of the genetic pathways and people are looking at the sulfur and reducing sulfur and they find out that they have some sulfur metabolism snips, that molybdenum is one of the nutrients that is given to help overcome this.

Let's look at the nutrient interactions. We know that our nutrients come in and sometimes the nutrients work well together, sometimes they antagonize each other and I get a lot of questions from people asking me about can I take this mineral with that mineral and there are charts out there that will tell you which minerals go well with each other and I'm going to look for one and we will post it but the truth of the matter is that there are some major antagonists and then there are some minor antagonist so we really have to look at not driving our clients and patients nuts with rules that they may not be able to follow just because we're trying to get a little slightly increased uptake of a certain nutrients. When we look at something like tungsten which is not an essential nutrient really, it's a major antagonist so if somebody gets too much tungsten in their bodies that's going to antagonize the molybdenum stores.

With copper, it seems that when you get excessive molybdenum, if you get in takes between 500 and 1500 mcg a day of molybdenum it can increase the excretion of copper so that can lead to a copper deficiency. There are others that have been proposed, the mechanisms aren't all that clear. Manganese, think, iron, lead, ascorbic acid which is vitamin C, methionine, cystine, protein, and silicone. Lots more to be explored here but the major nutrient interactions happen to be the tungsten and copper.

A molybdenum-dependent chemical in the body is called tetrathiomolybdate and this particular chemical is used to create compounds that contain both sulfur and molybdenum. They are called thiomolybdates. What has been found is that this tetrathiomolybdate molecule can prevent the absorption of copper and can cause fatal copper dependent disorders. That doesn't sound too good, does it? We don't want to have a complete disruption in the absorption of copper. However, there are certain conditions in which this has been found to be helpful and there is some experimental research being done to try to help people who have something called Wilson's syndrome, Wilson's disease, which is a copper toxicity disease.

They've been using this tetrathiomolybdate molecule to latch onto the copper and pull it out. Wilson's disease can cause severe neurologic complications so this is a good thing that they could find something that would work. The TM, we're just going to call it for short, controls free copper. It basically takes any copper that's not bound to the carrier molecule for copper, which is ceruloplasmin, it can take that and it can bind it up and then it can just chaperone it around and take it out of the body but not good in excess if somebody is on the brink of a deficiency.

There's a couple of other studies that have been done with tetrathiomolybdate as a therapy for copper toxicity. It's been used for kidney cancer, colorectal cancer, and breast cancer.

The TM stabilized the disease and prevented relapse in correlation with the depletion of copper, so this is a good thing. It's also been used for a variety of different inflammatory and immune related diseases. It helps to stabilize and improves survival in those with biliary cirrhosis. There is some good stuff on there. Biliary cirrhosis, pulling copper out of the body in Wilson's condition, some use in therapies for kidney and colorectal and breast cancers so it's not shabby what it can do. It helps with the conversion of the sulfates and getting rid of extra sulfur compounds in the body, and while we need sulfur compounds desperately in the body for detoxifications, sulfation is one of the phase 2 liver pathways, we also can be damaged by excess copper.

There are things called inborn errors of metabolism and many different nutrients are subject to these inborn errors of metabolism. When you have an inherited copper and molybdenum cofactor deficiency there's certain things that can happen. There's certain genes that can create this so if you were to do, I'm not sure if these are on the 23ME, I haven't actually looked for them, but you can certainly look up a person's genetics and see if the person has these genes, MOCS1, 2, and 3 and then GPHN. This is how this moco, this molybdenum protein, is synthesized. If you've got a snip in these areas and you're not synthesizing that well then a lot of those enzymes which have this moco as a part of it the molybdenum cofactor, you're not going to have those functions working well. We saw that those are pretty potent antioxidants.

There have been identified more than 60 mutations affecting mostly the MOCS1 and 2. That's a lot of different mutations. Then we have acquired molybdenum deficiency. It's really rare but it's been found in malabsorption syndromes like Crohn's disease and my guess would be also ulcerative colitis and maybe diverticulitis and severe leaky gut. I haven't really looked at that carefully or see not but my guess is that. The study that they have done are with long-term parental nutrition which is IV, stick all the nutrient in there and if they do that, or nasogastric tube, if they do that for a long time and the formula they are given is depleted in molybdenum that can trigger a molybdenum deficiency in the kind of symptoms that would occur with that.

The way that it is typically supplemented is in the form of ammonium molybdate, around 160 mcg a day. Here's a picture of the sulfur metabolism pathway and you can see the sulfate, sulfite to sulfate down here at the bottom here. This is the molybdenum-containing dependent enzyme, sulfate oxidase. This is how your acid gets produced and you see the xanthinoxidase right there. Let's look at a couple of these mutations. The MOSC1 gene controls the first step in the synthesis of these molybdenum-dependent protein. It causes the conversion of guanosine triphosphate into cyclic PMP (cPMP). Daily administration of this resolves all metabolic abnormalities associated with defective sulfite oxidase and xanthine oxidase pathways. What does that mean?

Well, if you've got this deficiency in this MOCS1 gene and they supplement with the cPMP then it turns that around.

The problem is when this is not working properly there is neurologic deterioration as a result. The cyclic, and I say just PMP because it's hard to say pyranopterin monophosphate (cPMP). Those with the MCOS lack the cyclic PMP. Let's look at the clinical uses. That's where we really want to be.

How can we use molybdenum? Well if somebody has sulfite sensitivity, and you know the people who say well I can't eat food at a salad bar, if I eat dried fruit I get really sick or I have to be careful about wine. This can be a molybdenum deficiency so if somebody has sulfite reactive asthma attacks as a result of these sensitivities molybdenum can be really helpful. It's been used as an anti-cancer agent by helping to detox cancer causing chemicals. It's been used to prevent cavities. It seems to increase the anti-carey effect of fluoride. In Wilson's disease, which is that copper toxicity disease I mentioned earlier which creates neurologic complications, the tetrathiomolybdate form of molybdenum forms a complex with copper and blocks the absorption of the copper so that way we reduce the copper toxicity.

It actually does also protect the thyroid because the amino acid cystine requires molybdenum as a cofactor to be metabolized to glutathione. If you think about somebody's taking NaC and acetylcysteine and were taking it because we want them to produce more glutathione the molybdenum can be really helpful.

Let's look at molybdenum toxicity. Toxicity is really rare. They've studied up to 1500 mcg a day which is quite a bit more than the recommended amount and the kinds of things that we see in molybdenum toxicity is gout-like symptoms where there's joint pain, really severe big, swollen joints like the big toe especially has been affected by that so gout-like symptoms have been reported in an Armenian population where they consume very much, a lot of molybdenum, up to 10 to 15 mg. The upper limit, the safe upper limit is set to be 2 so these gout-like symptoms are reported when they are consuming quite a large number.

When we look at the toxicity is rare with intakes up to 1500 mcg, that 1.5 grams so we haven't really looked too much at the higher doses. What's the recommended required? It's all different depending on whether you're a kid or you're an adult, you're pregnant or you're nursing, etc. Anywhere from 17 mcg for a little one all the way up to 45 mcg but still we're talking microgram doses, we're talking very, very small amounts. Think about some of the other things we given microgram doses like chromium we might have given 800 mcg a day or vitamin B6 we may give 1000 mcg a day. It's very, very small doses and there's a small range of toxicity.

These are some good molybdenum sources. You can see that all the veggie kind of foods are good, namely legumes. Lentils, dried peas, lima beans, kidney beans, soy beans, black beans, pinto beans, garbanzo beans. We've also got it in tomatoes, romaine lettuce, cucumber, celery, and fennel.

It sounds like if you sit down to a big salad with romaine lettuce, cucumber, celery and tomatoes, you put a few leaves of fennel on it and then you throw one of these kind of beans over it you've got a very good meal containing a lot of molybdenum.

Well according to WH Foods, these are the foods that are highest so we're given a cup, which is a reasonable serving size, a cup of lentils or dried peas or lima beans or kidney beans or all those beans we just mentioned, has anywhere, they're very close in their molybdenum content. The lowest has 123 at garbanzo beans and the highest was the lentils at 148 so not a lot of variation between then. Actually, quite a good way to get those nutrients into the body. What else do we have on here? The romaine, you can see it's a substantial difference between romaine, cucumber, celery which are barely above 10 with the actual numbers up above.

Molybdenum supplementation. The way that it's supplemented is either with a sodium molybdate or ammonium molybdate. That's basically it. There's 2 different forms of it. Drug interactions? The only drug interactions I could find was with acetaminophen. High doses of molybdenum inhibit the metabolism of acetaminophen. How do we test for molybdenum? Well, you can use a urine heavy metal test kit and if you want it to be really super accurate for 3 days prior to testing don't eat leafy greens, don't take supplements, and don't take antacids and use the heavy metals test kit. There's your references. There's a lot of good studies you can look at if you want to go deeper with molybdenum. You've got our textbook which is Advanced Nutrition and Human Metabolism. Another one that's good that I have on my shelf, I'm not sure if I have the 10th edition, though, Modern Nutrition in Health and Disease and then there is Metabolic and Molecular Basis of Inherited Disease and the PDR, the Linus Poly Institute has a lot of good stuff on a lot of different nutrients and we'll leave it there for you.