The Importance of Accurate Cystine Level Testing

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The importance of measuring white cell (leucocyte) cystine

The importance of white cell cystine measurements in the diagnosis and clinical management of patients with cystinosis cannot be over emphasised. The measurement is particularly valuable in determining how well Cystagon treatment is working, but there are problems, specifically in relation to the time of blood sampling time, that can lead to misleading results. The purpose of this "essay" is to discuss some critical points that, hopefully, will lead to be a better understanding of the white cell cystine test.

Diagnosis

Increased white cell cystine concentrations are only observed in individuals with cystinosis. Despite improved genetic diagnosis, the measurement of white cell cystine remains the easiest and quickest test to confirm or rule out a clinical diagnosis of cystinosis. A blood sample for a diagnostic test can be taken at any time, and under virtually any circumstance, provided the white cells are correctly prepared within 24h of sampling. Our experience, and that of the majority of other laboratories offering a diagnostic service for cystinosis, is that an elevated white cell cystine concentration (>1 µmol ½ cystine/g protein) is diagnostic of the disease.

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Although critical for diagnosis, the real importance of white cell cystine measurement in cystinosis, is as a measure of how well the Cystagon treatment is working. Before treatment with cysteamine/Cystagon became available, the long term outlook for patients with cystinosis was extremely poor. However, since the introduction of cysteamine/Cystagon therapy, though some problems persist, life can be fun and fulfilling. Growth can be significantly improved and end stage renal failure can be delayed for many years. Consequently, it is vital that your doctor can accurately check how well your prescribed dose of Cystagon is working.

How to check how well Cystagon is working

Checking how well a drug is working is very important in deciding the dose required and how often it needs to be given. If you have high blood pressure and you are prescribed a drug to lower blood pressure, then it is easy to check how well the drug is working, simply by measuring blood pressure. In cystinosis, the pioneering studies on cysteamine/Cystagon demonstrated that reductions in average white cell cystine concentrations were associated with better growth and slower progression of kidney

disease. Consequently, the check on how well Cystagon is working in any patient, is the measurement of their white cell cystine level.

How constant is your white cell cystine level?
If appropriate decisions about dose/frequeny of Cystagon are to be made it is important that your clinician has confidence in the white cell cystine results. In this respect, it is very important to realise that your white cell cystine level is not constant. There will be some variation both during the day and from day to day, depending on your mealtimes, diet, growth, and any infection. However, these changes, except perhaps for infection, tend to be small compared with the lowering effect of Cystagon.

How does Cystagon affect your white cell cystine level?
Following a dose of Cystagon, it is absorbed in the gut and appears in the blood. Some of the Cystagon will get into cells and start to reduce cystine levels. The biggest fall in white cell cystine level is usually 1-2h after taking the dose of Cystagon. After this time, the level will slowly increase back towards the pre-dose level. This means that a blood sample should never be taken for white cell cystine level <4h after a dose of Cystagon, as the level could be very misleading.

If the white cell cystine level is changing how can measuring it be of value to the doctor?
BE CONSISTENT. This applies to clinic staff and patients. Try to make sure that your blood samples for white cell cystine measurement are always taken at around the same time after a dose of Cystagon. In addition, it is vital that the time of your last dose, the actual dose, and the time the blood sample was taken are accurately recorded.

What is the best time to have my blood taken for white cell cystine levels?
The best time is just before your next scheduled dose of Cystagon. This will tell your doctor the highest level that your white cell cystine will be on your current dose/frequency prescription; most of the time the level will be lower.

Examples:
Frequency of Cystagon dosing, 4 times a day.
If you take your morning dose at 07:00 try to have your blood sample taken at 13:00. If you know that normally you will not have your blood taken until 15:00 then take your dose at 09:00.
Frequency of Cystagon dosing, 3 times a day.
If you take your morning dose at 07:00 try to have your blood sample taken at 15:00.

What should I do if my clinic appointment is usually early or mid-morning?
This is not a problem. The best thing to do is to delay your first dose of the day until after your blood sample has been taken. This may mean that instead of 6h between dose and blood sampling the time may be extended to 10h or more. Provided this interval is the same, within an hour or two, every time you have a white cell cystine blood test, it will allow your doctor to manage your Cystagon dose/frequency with confidence.

The important question.
All the advice suggests that, on Cystagon treatment, the target white cell cystine concentration should be <1 µmol ½ cystine/g protein. I am taking a high dose of Cystagon, 3 times a day, but my blood samples for white cell cystine levels are usually taken 12h after my last dose and the results are usually around 1.2 to 1.3 µmol ½ cystine/g protein. Is my Cystagon dose/frequency effective?

Yes. The result tells your doctor that when you are taking your Cystagon dose every 8h your white cell cystine level is <1 µmol ½ cystine/g protein for most, if not all of the time.

The important points to remember:

1. TAKE THE PRESCRIPTION. If there any problems with the dose of Cystagon or maintaining the frequency, then discuss them with your doctor or nurse specialist so that the best dose and frequency for you can be organised.

2. BLOOD SAMPLING FOR WHITE CELL CYSTINE LEVELS - BE CONSISTENT. Try to organise that the blood is always taken at around the same time after a dose of Cystagon, preferably just before your next scheduled dose.

3. It is vital that the time of your last dose, the actual dose, and the time the blood sample was taken are accurately recorded.

With a bit of understanding, effort, and discussion between patient and doctor or nurse specialist, every patient with cystinosis will get the maximum benefits of Cystagon treatment.