GI CARE FOR KIDS

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What families need to know about thiopurine therapy: Azathioprine & 6-Mercaptopurine

How these medications work:

Thiopurine medications are considered immunomodulator drugs and are important medications in controlling inflammatory bowel disease. The two drugs in this category are azathiopurine (AZA) and 6-Mercaptopurine (6-MP). Azathiopurine, also called Imuran®, is metabolized into 6-mercaptopurine, also called purinethol®. So, although these medications have different doses, their side effect profile is nearly identical. These medications work by interfering with the inflammatory activity of the body's immune system. Typically, this process takes 3-6months to fully work. During this time, steroid medications are often used.

Contraindications:

There are a few contraindications to receiving these medications, including allergy to these medications and prior chemotherapy with alkylating agents (eg cyclphosphamide, chlorambucil, melphalan). In addition, patients who are receiving allopurinol need very careful dosage adjustments to avoid toxicity (usually one-fourth to one-half the typical dose).

Monitoring Needed:

Patients taking these medications require frequent monitoring to avoid side effects. In many cases, routine blood tests (eg. CBC/diff, CMP, CRP) are checked about every two weeks for 1 month, then monthly for next 3 months, then every 3 months (the exact monitoring is determined by your physician). Also, most patients benefit from having their "TPMT" activity checked prior to therapy. "TPMT" is an abbreviation for thiopurine methyltransferase enzyme that helps break down these medications. One in 300 people do not have sufficient activity of this enzyme to safely receive these medications and ~10% of patients have reduced activity of TPMT which often requires a dose adjustment.

Strong Medications for Inflammatory Bowel Disease:

Overall the benefits of these medications outweigh the risks of these medications as these medications help induce a remission in inflammatory bowel disease (UC & Crohn's disease) between 40-70% of patients. As such, thiopurines (both AZA & 6-MP) allow many steroid-dependent patients to taper off corticosteroids. In general, the long term side effects and the effectiveness of thiopurines are much more favorable than those of corticosteroids.

Potential Side Effects:

Nevertheless, these medications have a number of possible side effects that patients and parents need to be aware of. These include the following:

1. Nausea, vomiting & diarrhea in some patients. Taking medications with meals often helps

2. Liver toxicity. Less than one person in a thousand has to stop the medication for this reason. Liver tests are monitored periodically.

3. Increased risk of non-Hodgkin's lymphoma cancer. This exact risk cannot be determined. Many large IBD studies have shown no increase risk of cancer beyond the risk already due to the IBD itself. More recent studies have indicated a likely low risk of 2-4 cases per 10,000 patients.

4. Pancreatitis. In many studies, it is difficult to identify this risk due to its low frequency; however, perhaps 1 in 100 patients develops pancreatitis with these agents. If these medications cause pancreatitis, they are invariably stopped because recurrent cases of pancreatitis usually occur.

5. Bone marrow suppression also called pancytopenia. This is where the bone marrow stops producing blood cells and platelets. This is also monitored. If bone marrow suppression occurs, this increases the chance for more serious infections.

6. Skin cancer. Non-melenoma skin cancer occurs more often in patients who have taken thiopurines; these cancers are not life-threatening. To minimize this risk, it is very important to limit sun exposure. Use of sunscreens, hats, and protective clothing is recommended.

7. Immunosuppression. Also, avoid "live-virus" vaccines unless given permission by your GI doctor. Examples of these vaccines include the ones for chickenpox (varicella), mumps/measles/rubella (MMR), NASAL flu mist, oral polio, yellow fever, rotavirus, and oral typhoid.

8. Many other infrequent side effects are possible and are listed in the package insert.

Conclusion:

Although reading about side effects increases the concern about the safety of these medications for many families, it is important to understand that these medications are very important in treating a serious disease. In almost all cases, not treating the disease adequately is far more dangerous than using these medications. Other alternatives to these medications also have the possibility of serious side effects and can be discussed with your gastroenterologist.

You can help avoid side effects by adhering to the correct dosage, using sunscreen, informing your GI physician if you are placed on other medications, and keeping your medical appointments/monitoring.

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