

The patient population that may respond or may be the target for therapeutic treatments beyond levothyroxine, usually are patients that do not feel OK on levothyroxine alone. Do not have any obvious underlying comorbidity that can explain they are not feeling well, and they usually they're requesting this therapy.

Very seldom providers prompt themselves to start a different type of formulation. So generally speaking, the patients initiated that request to do something about it. And again, symptoms can be very disabling from the patient's perspective, and they need to be addressed by the provider.

Another, I will call it the circumstantial evidence that may lower the threshold from the provider standpoint to initiate alternative treatments, is the observation of low T3 levels in patients that are treated with levothyroxine alone. Again, in the absence of symptoms I would be hard pressed to make any therapeutic change. But if the patient is not doing well and I see a T3 level low or below normal range, that would probably prompt me to consider alternative treatments.

The problem of going on alternative treatments particularly when we add the T3 which is liothyronine, is that the current formulation of liothyronine require if we look at the pharmacokinetics twice a day administration. We have experimental evidence that the liothyronine has a very short equilibration phase in its pharmacokinetics.

Equilibration phase means that immediately after absorption the liothyronine is rapidly distributed in the zero pole, resulting in a rise of T3 level often above normal range. And then a relatively quick disappearance of from zero. That causes peaks and troughs of T3 levels. If we are giving a relatively dose on a single daily administration.

So, if our goal is maintaining a relatively steady level of T3, we should look for a twice a day administration. In terms of dosing, currently available dose of liothyronine are 5, 25, and 50 micrograms. The usual dosing of liothyronine is everywhere between 2.5 and 5 micrograms on twice daily administration.

This is really not carved in stone, the only society that gives some degree of recommendation is the European Thyroid Association, which aims to the equivalent of 3.75 micrograms twice a day. Which is very difficult to achieve in the setting of what we have here in the United States.

Once we decide to go on combination therapy, we also may want to consider whether using dessicated thyroid extracts. Dessicated thyroid extracts have been around since 1851, and they were the primary way of treating patients with hyperthyroidism.

One thing that we need to recognize is that those are thyroid extracts, meaning that the content of T3 is higher as compared to the circulating levels of T3 in the ratio T3 to T4 in circulation in humans. So even dessicated thyroid extracts which are definitely not real, are not as physiological as we'd like them to be. And the ratio of T3 to T4 is skewed toward the relative presence of T3 as compared to what would be normal in circulation in humans.

When it comes to assessing the success of the therapy, then we need to look at two different parameters. One is serum thyroid hormone in TSH levels, and then comparing these parameters with the patient's symptoms.