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How Do Once-weekly Basal Insulins Work?

Announcer:
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Dr. Tsimikas:
This is CME on PACE CME and ReachMD, and I'm Dr. Athena Philis-Tsimikas from San Diego, California, and I'll be speaking to you today about the mode of action of once-weekly basal insulins.

As you may know, there are a number of once daily basal insulins that we can offer people with type 2 diabetes. If you remember, one of our initial insulins is human insulin NPH that could be used in two ways, either in the evening, to be given overnight to try and suppress hepatic glucose output and provide with a better morning glucose, or it can be given twice a day in order to try and achieve a very flat glucose throughout the day and evening.

Subsequent to NPH, we have our newer analogue basal insulins, which were introduced beginning with detemir and glargine. Both of those have a longer half-life lasting between 17 to 24 hours. Those can be given once a day, although in some situations, might have a reduction in their action, tending towards the 24-hour time period. But overall work very well to control and manage that blood sugar, especially overnight.

There were, beyond that, even longer-acting once-daily insulins which were introduced, and those include degludec and glargine U300.Both of those had somewhat differing mechanisms of action, but both resulted in yet a longer half-life, lasting a true 24 hours, and could be used once a day, morning or evening, in order to achieve a target blood glucose.

All of these basal insulins require a once-a-day injection. Really, requiring someone to think about and remembering to take that injection every day.

There are currently two options for a once weekly insulin. These are currently either completed in phase 3 clinical trials, and in some countries are approved for use.

So, the mechanism of action, let's start out with icodec, and this is a modified human insulin that has had a fatty diacid moiety attached to the insulin molecule. What does this do? This allows a gradual continuous release of active icodec from an albumin-bound inactive circulating depot. So, this molecule attaches to albumin in the plasma and then allows a slow release of this. This then prolongs its activity and buffers against any dosing variation so that you don't have high-release, low-release. It also leads to a very steady release of insulin for use. And its half-life is approximately 1 week, allowing once-weekly injections.

The other insulin is efsitora alpha. This is a fusion protein of two different molecules. It consists of a single chain variant of insulin combined with a human immunoglobulin G FC domain.

This immunoglobulin FC domain extends the plasma half-life by promoting the FC receptor that exists on the cell surface to recycle and

allow it to be visible over an extended period of time. This also attenuates the insulin receptor binding site and reduces clearance in the kidneys. All of these mechanisms of action actually allow an extension of the half-life and lead to a 17-day half-life for efsitora alpha. It can be dosed once a week with a flat basal delivery of insulin over that time period.

So, these are some of the newer insulins. They have been tested and show demonstrable efficacy both in lowering glucose values and doing this with a low rate of hypoglycemia. This is something that we can offer our patients that might allow them to reduce the number of injections that they need to take, as well as still being able to manage those blood sugars and achieve the treatment targets.

I hope this has been valuable. It's been a pleasure speaking to you today.

Announcer:
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