Parkinson Update: New Tricks and Old Drugs

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New PD medications and treatments are being developed and novel uses for existing drugs are being discovered.

While there is no cure for Parkinson disease (PD) at this time, in the early stages of the disease, medications that mimic the action of dopamine and reduce the breakdown of dopamine are employed to control the motor symptoms patients experience. As researchers continue to learn more about the disease, new medications and treatments are being developed. Also, as described on the following pages, novel uses for existing drugs are being discovered.

New PD Treatment Strategy
♦ In a healthy brain, microglia cells serve as the first and primary immune response in the central nervous system.
♦ A flawed microglial inflammatory response could contribute to the neurodegeneration observed in PD.
♦ CU-CPT22 is a novel compound developed to suppress the misguided microglial inflammatory responses.
♦ The drug binds to microglia receptors to block inflammation.
♦ Researchers hope CU-CPT22 can be developed further as a PD treatment.

Receptor Responsible for PD Inflammation
♦ Alpha-synuclein (α-synuclein), although not completely understood, is a protein that likely helps maintain synaptic vesicles and regulate dopamine.
♦ In PD, α-synuclein accumulates, which may further trigger microglial inflammatory responses.
♦ Researchers found that α-synuclein triggers a proinflammatory microglial phenotype by interacting with toll-like receptor 1 and 2 (TLR1/2) at the microglial cell membrane.
♦ This reaction causes increases in the proinflammatory cytokines tumor necrosis factor-α (TNF-α) and interleukin-1β.
♦ Blocking the TLR1/2 receptor was found to reduce TNF-α secretion.
♦ A hypertension drug, candesartan cilexetil, inhibits TLR2 and reverses the cultured microglia proinflammatory phenotype exposed to α-synuclein.
♦ Candesartan cilexetil may be a future PD treatment.

PD Drug Also Used for Macular Degeneration?
♦ Levodopa (L-dopa) is a mainstay for the treatment of PD.
♦ L-dopa can cross the protective blood-brain barrier and replace the dopamine lost in PD.
♦ A study of over 15 million people taking L-dopa demonstrated that individuals are significantly less likely to develop age-related macular degeneration (AMD), a degenerative disease causing vision loss.
♦ When patients did develop AMD, age at onset was significantly greater.

Take Home Points
♦ A new drug called CU-CPT22 binds to microglia receptors to block inflammation, and could become a PD treatment.
♦ Candesartan cilexetil, a hypertension drug, inhibits TLR2, reverses the proinflammatory phenotype of cultured microglia exposed to α-synuclein, and may be a useful PD medication.
♦ A study of over 15 million people taking L-dopa demonstrated that they are significantly less likely to develop AMD.

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