

# The Story of Prazosin in Alzheimer's

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Agitation and aggressive behaviors are the most common reason an exhausted family finally places their loved ones with Alzheimer's disease into long-term care. Irritability, uncooperativeness with necessary care, anger outbursts, and pressured pacing and sleep disruption can exhaust even the most devoted family. The antipsychotic drugs (such as quetiapine and olanzapine) most commonly used to treat agitation/aggression in Alzheimer's disease often are not effective. In addition, these antipsychotics produce side effects such as excessive sedation, symptoms similar to those experienced by persons with Parkinson's disease, and increase the risk of stroke and death. Clearly, research is needed to develop new treatments for these life altering behavioral problems of the later stages of Alzheimer's disease that plague patients.

Elaine Peskind, MD, and ADRC investigators have taken a novel approach to discovering effective treatments for agitation/aggression in Alzheimer's disease. Working with ADRC neuroscientist Patti Szot, PhD, they discovered a cause of agitation in Alzheimer's disease: over activity of the brain "adrenaline" arousal system that uses the messenger chemical norepinephrine.

Decades ago, drugs had been developed to lower high blood pressure without producing sedation by blocking excess effects of norepinephrine on blood vessels. Dr. Peskind reasoned that if one of these "adrenaline blocker" drugs could enter the brain it might reduce agitation/aggression in Alzheimer's disease. Prazosin (formerly marketed as "Minipress") is just such an inexpensive generic drug – and it worked! In a small pilot study in 22 persons with Alzheimer's disease agitation/aggression, prazosin was markedly more effective than placebo for reducing these distressing symptoms and did not produce sedation or other problem side effects.

The National Institute on Aging was so impressed with Dr. Peskind's pilot study results that they awarded her a one million dollar grant to perform a larger definitive study of prazosin in one hundred Alzheimer's disease patients living with a caregiver in the community who have problematic behaviors such as uncooperativeness with care, irritability/anger, physically aggressive behavior or restlessness which occur at least two times per week.