

Reserpine

Can lessons be learned from the past? The drug reserpine was first isolated in 1952 and soon was being used for treatment of hypertension. Within 5 years of it being isolated literature began to appear in the late 1950s suggesting reserpine caused increase risk severe depression and increased risk of suicides in patients.

The mechanism of action of reserpine is to block reuptake of monoamine neurotransmitters (serotonin, dopamine, norepinephrine and epinephrine) into the presynaptic neuron leading to depletion of these neurotransmitters. Writings from the 1950s and 1960s put forth the observations that when reuptake of monoamine neurotransmitters is blocked there is increase destruction (metabolism) of these neurotransmitters by the MAO leading to depletion of the monoamine neurotransmitters.

Numerous writings credit the experience with reserpine at the time as being the basis for “The Monoamine Theory” of medicine which was put forth in the 1960s, over 40 years ago. The monoamine theory basically states, “Low levels of monoamine neurotransmitters in the synapse cause disease”. The Monoamine Theory has been the basis for treatment of disease for the last 40 years and is still the basis for the current reuptake inhibitors used in medicine. “The Bundle Damage Theory” was put forth by me in peer reviewed writings in this year. The Bundle Damage theory notes that regulation of function in the brain is not controlled by a single neuron but by multiple neurons that act as bundles, when enough of the components making up the electrical conduction pathway are damaged flow of electricity is compromised, function is no longer regulated properly causing symptoms of disease develop.

The main source of damage to neuron bundles leading to chronic disease symptoms is neurotoxic insult with Parkinson’s disease being the prototype. There are other sources of damage to the electric conductivity pathway such as trauma, and biologic which can lead to compromised electrical flow.

The most notable difference between the Monoamine Theory and the Bundle Damage Theory is that the monoamine theory predicts that returning synaptic neurotransmitter levels to normal will cause relief of symptoms whereas the Bundle Damage Theory states that neurotransmitter levels must be increased higher than normal in proper balance to compensate for the damaged structures conducting electricity.

Now back to reserpine, it is still available for treatment of hypertension as a second line drug. Effective management of the problem with neurotransmitter depletion leading from reserpine, and now the current reuptake inhibitors, leading to severe depression and suicide have not been addressed until this research project.

For 50 years medicine has lived with reuptake inhibitors that deplete neurotransmitters, make the cause of the problem worse (neurotransmitter levels that are not high enough), and can induce suicide in patients. Virtually every reuptake inhibitor on the market now carries a black box warning of suicide risk.

As noted in previous peer reviewed writings current reuptake inhibitors are not very effective in the treatment of depression. Meta-analysis of over 20 double blind placebo controlled University studies

found in peer reviewed literature, that were not funded with drug company money, revealed that two things:

1. The placebo effect in treatment of depression is very large with 30% to 45% of patients taking placebo showing relief of symptoms.
2. The effectiveness of reuptake inhibitors in treatment of depression in adults is very low. In general 7% to 13% of patients in studies achieved relief of depression symptoms better than placebo. In some studies the odds of developing a drug side effect are more probable than achieving relief of symptoms greater than placebo.

The peer reviewed literature has been noting for over 50 years that reuptake inhibitor drugs deplete neurotransmitters at which point the reuptake inhibitor drugs pills no longer work, symptoms of disease returning or getting worse, and most important patients taking them are at risk for suicide.

Obviously we need to treat our patients, so what can be done? Reuptake inhibitors need to be administered in such a way as to not deplete neurotransmitters. From a clinical stand point neurotransmitter depletion is easy to spot. It is the patient who has been taking a reuptake inhibitor then presents in clinic complaining that the drug is no longer working. Drugs that work with neurotransmitters do not work if there are not enough neurotransmitters in the system to work with. At the point where the drug quits working the neurotransmitter levels have just been depleted below the point needed to keep the drug working.

The only way to increase monoamine neurotransmitter levels in the brain is by administering amino acid precursors (in proper balance). With 12 years of experience administering amino acid precursors to patients on a large scale I can confidently assert that this is safe approach. All patients taking reuptake inhibitors need to take NeuroReplete 4 pills in the AM and 4 PM with CysReplete 2 pills 3 times a day (first dose at noon).

This research project started by looking for a way to keep reuptake inhibitor drugs working in 1997, simply giving this same dosing of amino acids to all patient taking reuptake inhibitors (especially those that have experienced the drugs to quit working) is the only way to prevent reuptake inhibitors for depleting neurotransmitters, prevent the patient's symptoms from getting worse, preventing severe depression brought on by the drug, and most important prevent the risk of suicide during treatment. These reuptake inhibitor problems have been with us in medicine for over 50 years it is time we start to address them properly.

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