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Commentary

Comprehensive Study on Progesterone and Allopregnanolone in Epilepsy

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DESCRIPTION

The neurological condition epilepsy affects around 50 million people globally. It is distinguished by recurrent seizures, which are brief bursts of electrical activity in the brain. While Antiepileptic Medicines (AEDs) can effectively treat the majority of persons with epilepsy, a considerable percentage of patients do not react to typical AEDs and are classified to have refractory epilepsy. In recent years, there has been an increase in interest in the potential use of neurosteroids like progesterone and allopregnanolone in the treatment of refractory epilepsy.

Progesterone and allopregnanolone are hormones that the body naturally produces. They are produced in the ovaries and adrenal glands and have a role in a range of physiological processes such as the menstrual cycle, pregnancy, and stress response. Furthermore, these hormones have been demonstrated to have neuroprotective characteristics, suggesting they may be useful in the treatment of neurological illnesses such as epilepsy.

The pharmacokinetics of progesterone and allopregnanolone in refractory epilepsy are critical considerations for assessing their therapeutic potential. The study of how medications are absorbed, transported, metabolized, and eliminated by the body is known as pharmacokinetics. Understanding the pharmacokinetics of progesterone and allopregnanolone can aid in optimizing dosage regimens and ensuring that these medicines are safe and effective for usage in refractory epilepsy patients.

Progesterone comes in a variety of forms, including oral pills, intramuscular injections, and vaginal gels. Progesterone pharmacokinetics differs depending on the mode of delivery. Progesterone is rapidly metabolized in the liver and has low bioavailability when taken orally. Progesterone intramuscular injections bypass the liver and provide better bioavailability; however, the period of effect is relatively limited, often lasting only a few days. Vaginal gels, on the other hand, provide persistent progesterone release and may be a more successful long-term therapy choice.

Several studies have been conducted to assess the pharmacokinetics of progesterone and allopregnanolone in individuals with intractable epilepsy. The researchers discovered that the pharmacokinetics of progesterone varied greatly amongst patients, with some having very high levels and others having very low levels. This variation may be attributable in part to variances in progesterone metabolism in the liver.

In another trial, 20 patients with refractory epilepsy were given intravenous allopregnanolone. Allopregnanolone was found to be well-tolerated and to have a rapid onset of effect, with seizure activity diminishing within minutes of treatment. However, the effects of allopregnanolone were brief, with seizure activity reverting to baseline in some individuals within 30 minutes. Recently, there has been increased interest in the usage of neurosteroids with enhanced pharmacokinetic properties. Brexanolone, for example, is a newly produced synthetic version of allopregnanolone.

When looking at the relationships between serum progesterone or allopregnanolone levels with treatment response during the steady state in the responder group *versus* the non-responder group, the results show that serum progesterone and allopregnanolone levels in the responder group are higher than those in the non-responder group by 6-10 and 2-6 times, respectively. In fact, *in vivo* study discovered that the serum allopregnanolone level was directly related to the degree of seizure frequency reduction. The latter is simply evidence that the decrease in seizure frequency is directly connected to higher levels of progesterone in the blood.

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