

Department of Clinical Laboratory Sciences

Graduate Masters Theses

Effect Of Accutane On Catecholamine Release.

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ABSTRACT

Isotretinoin (13-*cis*- retinoic acid, Accutane®) was approved for use by the Food and Drug Administration (FDA) of the United States in 1982 for the treatment of severe recalcitrant nodular acne. From the time of marketing there have been numerous published reports claiming this drug may be the cause of severe depression and suicide in patients being treated for acne with isotretinoin. Compared with all drugs in the FDA's Averse Event Reporting System database to June 2000, isotretinoin ranked within the top ten for number of reports of depression and suicidal attempts. Isotretinoin is the only non-psychotropic medication in the top ten ranked drugs for suicide attempts listed in the FDA's database. A definitive cause and effect relationship has not been established between isotretinoin and depression. Nevertheless, it has been reported that patients being treated with isotretinoin who in turn suffered from depression were alleviated of their symptoms when they discontinued therapy and their symptoms recurred when they continued with treatment. Contrary reports indicate that it is the presence of acne itself that causes the depressive moods and it is the improvement of the skin disorder through the use of isotretinoin that decreases depression. The exact causes of depression are not well understood. Health care providers are left with the undesirable task of treating the symptoms without ever curing the disease. Current successful treatments for symptoms of depression include selective serotonin reuptake inhibitors (SSRI's) and selective norepinephrine reuptake inhibitors (SNRI's). These drugs work by increasing the bioavailability of the monoamines serotonin and norepinephrine. We set out to determine if isotretinoin causes any changes in the amounts of monoamines released and taken up into nerve terminals of rat brain regions. The hippocampus and frontal cortex were taken from adult male Sprague Dawley rats. Tissues were either sliced (for release experiments) or homogenized (for uptake experiments). Tissues were incubated with either [³H] norepinephrine or [³H] serotonin and then exposed to different concentrations of isotretinoin. This study demonstrates that isotretinoin, at different concentrations, can cause an imbalance of monoamines released and taken up into regional rat brain tissues. These findings may indeed extend to alterations in behavior.