

Conclusion

Anti-viral treatment of HCV has possible intrinsic time-dependent relationship with DM development.

Diabetes Mellitus and Glucose Metabolism

TYPE 1 DIABETES MELLITUS

An Unusual and Enigmatic Etiology for Diabetic Ketoacidosis: Safety Needles

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Diabetic ketoacidosis is associated with a mortality rate of upto 6.1% and accounts for an estimated 115000 hospital discharges per year in the United States. In order to reduce mortality related to DKA, precipitating causes must be identified and addressed. The most common precipitant for DKA is infection with other precipitating factors including acute illness, medications and inadequate insulin therapy (1).

A 76 year-old woman with type 2 diabetes was transferred from her assisted living facility for hyperglycemia. This was her fifth admission in the last month and a half attributed to either hyperglycemia or DKA. Her medications included insulin glargine and insulin aspart. She mentioned compliance with her insulin as well as her diabetic diet. In the ER, her vitals were stable with physical examination showing an obese woman in no acute distress. Her labs showed a blood glucose of 780, an anion gap of 17 and positive serum ketones. Further investigation did not reveal a source of infection or ischemia. The patient was treated in the ICU with intravenous insulin and fluids with resolution of her ketoacidosis. The patient was discharged with a 67% increase in her prandial insulin. On further review, her facility had recently required safety needles to be used for insulin pens. Patient was asked to demonstrate her technique with observation that patient was not pushing down enough to allow for the needle to enter her skin with subsequent trapping of her insulin within the needle. Prior to discharge, she was educated on proper administration of her insulin and since her discharge, she has had no subsequent readmissions for hyperglycemia.

Hospitals and long-term facilities are the primary utilizers of needles with a retractable safety shield. Reduction of accidental puncture, elimination of reuse of needles and helping patients overcome anxiety about needles are some of the key advantages of these needles. Upon application of pressure onto the skin, the automatic shield or plastic cannula retracts and thus hides the needle before, during and after the injection. The major disadvantage is insulin being deployed while the needle is outside the body if incorrectly applied. Therefore, appropriate administration must be taught to the patient, including perpendicular insertion of the needle into the subcutaneous tissue and ensuring a more firm surface by injecting into a lifted skin fold. Legislation in the US has been passed requiring safety-engineered devices when feasible. In situations where the safety-engineered devices can impair effectiveness or cause

harm, alternative approaches can be utilized, including insulin syringes or self-administration of insulin along with safe work procedures (1).

1. Yu Catherine H.Y.. "Safety" technology: a hidden cause of diabetic ketoacidosis. *Canadian Medical Journal Journal*. 2012 Mar 20;184(5):557–558.

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

The Effect of Soybean Isoflavones in Developing Cerebellum

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Abstract ENDO 2020

The effect of soybean isoflavones in developing cerebellum Thyroid hormone (TH) receptor (TR) and estrogen receptor (ER) play crucial roles in cerebellar development. TR and ER are involved in Purkinje cells dendrite growth, spines and synapse formation. They also regulate the functional maturation, intracellular metabolism, and migration of neuron and glial. Soybean isoflavones especially genistein, daidzein, and daidzein metabolite, S-equol were known to exert their action through TR, ER, and GPR30, that is a G-protein-coupled ER. However, the mechanisms of soybean isoflavone action on cerebellar development and function have not yet been extensively studied. We evaluated the effects of soybean isoflavone, such as genistein, daidzein, and S-equol, using mouse primary cerebellar culture, astrocyte-enriched culture, and C6 clonal cells. Soybean isoflavone augmented TH- or estradiol (E2)-mediated dendrite arborization of Purkinje cells. Such augmentation was suppressed by G15, a selective G-protein coupled ER (GPR30) antagonist, and ICI 182.780, an antagonist for ERs in both cultures. It also increased mRNA expression level of TH-responsive genes including *Mbp*, *Bdnf*, *Rc3*, *Ntf3*, *Camk2b*, and *Hr*. Moreover, genistein and daidzein also increased mRNA expression level of *Syn1*, *Syp* and *Psd95* that are involved in synaptic plasticity.

On the other hand, in astrocytes, soybean isoflavone activated cell migration and F-actin rearrangements. Such effects were suppressed by G15, but not by ICI 182.780. Knockdown of GPR30 by RNAi also suppressed the cells migration. Protein expression levels of p-Akt (Ser473), p-Rac1/cdc42 (Ser71), RhoA, Rac1/2/3, and cdc42 also increased by soybean isoflavone. Co-exposure with Rhosin HCl, a selective RhoA inhibitor, reduced the cells migration and formation of stress fibers. These findings indicate that soybean isoflavone may affect cerebellar development by acting to both neurons and astrocytes through several signaling pathways, including TR, ER, and GPR30.

Keywords:

EDC, ER, TR, GPR30, Neuron, Astrocyte