

MPTP Post-exposure Medical Protocol

Introduction

MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is a chemical used in research to provide insight to the mechanism responsible for the dopaminergic neurons in Parkinson's Disease. This chemical is used by Western University researchers to inject into mice at a dosage per mouse of approximately 30mg/kg. It is estimated that each mouse weighs approximately 20grams (0.02kg). As such, approximately 0.6mg of the MPTP is used per injection. Each mouse is injected once per day for five days.

Toxicology

MPTP is highly lipophilic and rapidly crosses the blood/brain barrier and has a complex metabolism. In the brain, it is metabolized to a MPDP⁺ (1-methyl-4phenyl-2,3-dihydropyridinium) by the enzyme monoamine oxidase B in non-dopaminergic cells. It is further oxidized to the active metabolite MPP⁺ (1-methyl-4-phenylpyridinium) to be taken by the dopamine transporter where it exerts its toxic effects. Both MPTP and its metabolites are excreted in urine and in feces.

According to the information provided by the University of California in San Francisco (UCSF), the probable human toxic threshold 0.001mg/kg for percutaneous exposure and 0.1mg/kg for GI and mucous exposure. A researcher is estimated to be weighed as low as 50kg. For percutaneous exposure, when 0.001mg/kg is multiplied by 50kg, the product equals 0.05mg. The full injection (0.6mg) is much higher than the potential toxic dose (0.05mg). As a result, post exposure medical prophylaxis is necessary.

Medical Prophylaxis

The current recommends medical treatment for exposure is a MAO-B Monoamine oxidase (inhibitor which prevents the conversion of MPTP to its toxic MPDP⁺ thereby reducing potential neurotoxicity). The evidence of the efficacy of this treatment is not fully confirmed. It has been suggested an initial large dose of the medication Selegiline should be 20mg (four, 5mg tablets be

taken orally at once). The need of additional daily treatment with the medication is controversial.

The University of California San Francisco recommended the treatment of 20mg Selegiline be administered immediately by mouth, followed by 5mg twice daily for the following four weeks.

The University of Washington recommends the use of Selegiline, but did not elaborate on the dose.

The University Health Network in Toronto also recommended the use of Selegiline hydrochloride 5mg, 4 tablets immediately, but did not elaborate on any further treatments.

Selegiline is a selective irreversible monoamine oxidase B inhibitor. In high doses (greater than 10mg/day), Selegiline behaves as a non-selective MAO inhibitor and it can precipitate a hypertensive reaction induced by tyramine rich foods and beverages (cheese, red wine, beer, pickled fish, caviar, smoked/cured meat, liver, yeast extract or meat extracts). It can also interfere with other medications, particularly birth control pills.

Policy at Western

All researchers working with MPTP must have safety training and medical evaluation prior to commencing work. These researchers must sign an informed consent to receive post-exposure treatment after the medical evaluation.

The researcher must report any exposure to MPTP immediately after first aid to the supervisor and to Workplace Health.

A dose of 4x5mg of Selegiline will be stored at the research site at the P.I.'s office. The researcher, with the counseling from Workplace Health, can take the medication shortly after exposure. If staff at Workplace Health is not immediately available, the Researcher can choose to take the medication on his/her own.

I _____(printed name) have been trained on the proper handling of MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). I also read and understood the treatment for exposure to MPTP. I have had the opportunity to ask questions about the treatment and the possible side effects.

I fully consent to take the treatment (Selegiline 5mg tabs x 4, and 5 mg twice a day for four weeks).

Signature

Date