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[www.principlepharmacy.com](http://www.principlepharmacy.com)**CORTICOSTEROID TREATMENT AND INTENSIVE INSULIN THERAPY FOR SEPTIC SHOCK IN ADULTS: A RANDOMIZED CONTROLLED TRIAL**

In a recent edition of JAMA, a multicenter randomized 2x2 factorial study was done in patients' with septic shock, an infectious disease complication which carries a mortality rate of 60%. The study was designed to determine if normalization of blood glucose with intensive insulin treatment improved mortality in patients with septic shock who had a poor response to fluids and vasopressors. In addition, the investigators set out to determine if the addition of fludrocortisone to hydrocortisone have any added benefit. The study had 2 study groups: continuous IV insulin (n=255) and conventional insulin (n=254). Both of these groups were subdivided into hydrocortisone 50 mg bolus Q6H x7days or hydrocortisone at the previous dose and fludrocortisone PO 50 mcg every day x7days. The study found that in hospital deaths were higher in the continuous IV insulin group and there was no difference found on the combined corticosteroids versus hydrocortisone only. Investigators concluded that aggressive treatment of hyperglycemia in patients with severe septic shock had no positive effect on mortality and at this time is not recommended.

Conclusion: Patients with septic shock should be treated with hydrocortisone and their blood glucose levels should not be intensively maintained between 80-110 mg/dL.

**STUDY SHOWS THAT RASAGILINE IMPROVES PARKINSONS' DISEASE**

Standard therapies for Parkinson's disease (PD) will improve the motor abnormalities of the disease but, until now, no available therapy can slow the progression of the disease. A study in the New England Journal of Medicine was designed to show the potential disease modifying effect of rasagiline, an inhibitor of monoamine oxidase type B, on PD.

The study was an 18 month long multi-center trial of 1,176 patients with untreated PD who were randomly assigned to receive rasagiline at a dose of either 1mg or 2mg per day for 72 weeks (early start group) or placebo for 36 weeks and rasagiline for 36 weeks (late start group).

Positive results were measured with the Unified Parkinsons' Rating Scale (UPRS). The scale is a 176 point scale, in which higher numbers indicate more severe disease. The study measured superiority of early start treatment with rasagiline to placebo by 3 measurements:

1. By the rate of change in the UPRS score between weeks 12 and 36
2. Superiority to the delayed start treatment in the rate of change in the score between baseline and week 72,
3. Noninferiority to delayed – start treatment in the rate of change between weeks 48-72

Early start treatment with 1mg/day met all the endpoints in the primary analysis. However, all three endpoints were not met by the 2mg day dose since changes in the UPRS between baseline and week 72 were not significant.

The results of the study showed that early treatment with rasagline at a dose of 1mg daily provided benefits in Parkinsons' disease that were consistent with a possible disease modifying effect, but early treatment with 2mg did not.<sup>(1)</sup>

## Drugs That Induce Fever

### Most Common

- Amphotericin B
- Asparaginase
- Atropine
- Barbiturates
- Cephalosporins
- Interferon
- Penicillin
- Primadone
- Procainamide

### Less Common

- Allopurinol
- Azathioprine
- Cimetidine
- Hydralazine
- Iodides
- Imipenem/cilastin
- INH
- Rifampin
- Streptokinase

## SOURCES

1. N Eng J Med 361-1268-78, 2009
2. ASHP daily report 2/9
3. FDA medwatch safety summary 2010

## Drug Warnings Interactions

### PAROXETINE MAY INCREASE THE RISK OF DEATH FROM BREAST CANCER IN PATIENTS TAKING TAMOXIFEN

An article published in British Medical Journal showed that the anti-depressant paroxetine (Paxil) can interfere with tamoxifen, a drug that is used in thousands of breast cancer patients, for a 5 year period. The study, which included over 2,400 women taking tamoxifen, concluded that women taking the antidepressant were more likely to die from breast cancer and slightly more likely to die from any other cause, compared to women not taking the drug. In fact, women taking the two agents for more than three years were almost twice as likely to die from breast cancer as those taking paroxetine only briefly. The study reported that for every 20 patients who took the two drugs together for just under two years one extra woman would die of breast cancer. The authors conclude that women who require an antidepressant currently taking tamoxifen should not be given paroxetine and patients on paroxetine and tamoxifen should be switched to another antidepressant.<sup>(2)</sup>

### CLOPIDOGREL INEFFECTIVE IN POOR METABOLIZERS

The FDA has mandated that a black box warning be added to the label of clopidogrel (Plavix) an antiplatelet drug. The warning will give healthcare professionals the following information :

- Reduced effectiveness in patients who are poor metabolizers of Plavix
- Test are available to determine differences in CYP2C19 function
- Consider the use of other anti-platelet medications or alternative dosing strategies for Plavix in patients who are poor metabolizers.<sup>(3)</sup>

## FROM THE DIRECTOR'S DESK

