

Huber W, Ilgmann K, Page M, Hennig M, et al. Effect of Theophylline on Contrast Material-Induced Nephrotoxicity in Patients with Chronic Renal Insufficiency: Controlled, Randomized, Double Blinded Study. Radiology 2002; 223(3); 772-779

S Farraher

Citation

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Abstract

WHAT IS THE QUESTION BEING ASKED?

Does the administration of intravenous Theophylline given thirty minutes prior to the introduction of intravascular contrast material reduce the risk of contrast induced nephrotoxicity in patients with underlying renal insufficiency?

WHY IS THIS IMPORTANT?

Contrast administration is integral in the diagnosis of pathology in multiple imaging modalities. Contrast administration is contraindicated in patients with underlying renal insufficiency because of the risk of progression of underlying renal disease.

WHAT IS THE BACKGROUND WORK?

Renal tubular production of adenosine is increased by irritation from the osmolal effects of intravascular contrast. Adenosine directly causes afferent vessel constriction in the kidney leading to decreased glomerular filtration rate (GFR), as well as increases the production of free radicals which can further damage renal parenchyma. Prior research on this topic includes the following:

1. Use of low osmolal contrast reduces the risk of contrast induced nephrotoxicity.
2. N-Acetylcysteine (antioxidant) administration has modest effects on lowering the incidence of induced nephrotoxicity in patients with mild renal insufficiency.

3. Theophylline (Adenosine antagonist) administration prior to intravascular contrast administration reduces incidence of contrast induced nephrotoxicity in studies with small population size, low contrast load, and subjects with mild renal insufficiency.

WHAT IS THE NULL HYPOTHESIS?

Theophylline will have no effect on decreasing the incidence of contrast induced nephrotoxicity in subjects with underlying renal insufficiency.

WHO IS THE TEST POPULATION?

The population studied included 100 patients referred for diagnostic imaging utilizing iodinated contrast material with a baseline creatinine >1.3. The patients were referred from multiple clinics including gastroenterology, cardiology, vascular surgery, and urology. Exclusion criteria included pregnancy, fluctuating creatinine (defined as a change >0.3 within 48 hours of the study), and contraindication to Theophylline administration. There were 82 females and 18 males evaluated. The mean patient age was 67.5. 72 intra-arterial contrast studies (54 cardiac catheterizations and 18 angiographic procedures), and 28 intravenous studies (24 computed tomography and 4 transjugular portosystemic shunt placement) were performed. The mean baseline creatinine level was ~2.0. The mean contrast load was ~200cc.

WHAT ARE THE METHODS USED?

The study design is a double blinded prospective study. The patients studied were randomized to receive 200mg IV Theophylline or Saline 30 minutes prior to imaging. Renal insufficiency was defined as baseline creatinine >1.3. Creatinine was measured at screening (within 48 hours of the exam), baseline (immediately before the exam), and at 24 and 48 hours after the administration of contrast. N-acetyl Beta-glucosaminidase (B-NAG), a substance secreted by the renal tubules when damaged, was measured at baseline, and at 4, 12, and 24 hours after the administration of contrast. A Chi squared exam was used to assess dichotomous factors (Theophylline vs. placebo).

RESULTS

Figure 1

Table 1: Incidence of Induced Nephrotoxicity

	Subject	Induced Nephrotoxicity	Incidence
Placebo	50	8	16%
Test	50	2	4%
Overall	100	10	10%

There was a statistically significant decrease in the incidence if contrast induced nephrotoxicity between the test and placebo groups ($p=0.046$).

THE LIMITATIONS TO THE STUDY INCLUDED

THE FOLLOWING:

- Predominantly intra-arterial contrast administration (72%).
- Study only evaluated the effects utilizing low osmolol contrast.
- Predominantly a female population (82%).
- Subjects received intravenous hydration 24 hours prior to the administration of contrast. What are the effects of Theophylline in the emergency setting when prior hydration can't be given?

FUTURE QUESTIONS TO BE ADDRESSED INCLUDE:

- Can the study results be repeated?
- Are the effects of Theophylline as effective with intravenous administration of contrast as with intra-arterial administration?
- Are the effects of Theophylline the same in the emergent setting when prior intravenous hydration is not possible?

References

Author Information

Steven Farraher, MD