Drug-Induced Valvulopathy

Bryan S Judge, MD
LLSA Medical Toxicology Review
ACMT Spring Conference – San Juan, Puerto Rico
March 28, 2009

- Cabergoline and pergolide significantly associated with cardiac-valve disease
- Aortic, mitral, and tricuspid valves affected
- Amantadine associated with an increased risk of valvular heart disease

- Clinically significant regurgitation was discovered only in patients taking cabergoline or pergolide.
- Rates of drug-induced valvulopathy were high.
- Drug-induced insufficiency was evident in aortic, mitral, and tricuspid valves.
Norfenfluramine  Cabergoline

Pergolide  Methylergonovine

Extracellular space

Intracellular space

Nucleus

Left atrium

Mitral valve

Chordae tendinae

Left ventricle

Proliferation

5-HT$_{2B}$  Gaq  G$\beta y$

ERK1/2  P  P

Parkin  P  P

GTP  PLC-$\beta$

DAG  PKC

Rb-P

G$\alpha q$

TGF-$\beta$
Take Home Points

- 5-HT\(_{2B}\) receptors are abundant in human cardiac valves
- Several drugs are potent 5-HT\(_{2B}\) agonists
- Several studies have implicated activation of 5-HT\(_{2B}\) receptors as a key step in initiating drug-induced valvulopathy
- Two recent studies have associated cabergoline and pergolide with valvular disease
- Avoid prescribing drugs that are potent 5-HT\(_{2B}\) agonists