Review: Fenoldopam reduces acute kidney injury and death in critical illness

Landoni G, Biondi-Zoccai GG, Tumlin JA, et al. **Beneficial impact of fenoldopam in critically ill patients with or at risk for acute renal failure: a meta-analysis of randomized clinical trials.** Am J Kidney Dis. 2007;49:56-68.

Clinical impact ratings: Critical Care ★★★★★★☆ Nephrology ★★★★★★☆

QUESTION

In critically ill patients, does fenoldopam reduce acute renal failure (ARF) requiring renal replacement therapy?

METHODS

Data sources: BioMedCentral, Cochrane Central Register of Controlled Trials, PubMed (to 30 October 2005), conference proceedings, bibliographies of retrieved articles, and experts in the field.

Study selection and assessment: Randomized controlled trials (RCTs) in any language that evaluated fenoldopam in critically ill patients (surgical or intensive care unit [ICU]). Studies related to renal protection in the setting of angiographic contrast media exposure were excluded. 16 RCTs (n = 1290) met the selection criteria. Fenoldopam dosages ranged from 0.025 to 0.1 µg/kg per minute; 1 trial used 0.3 µg/kg per minute. Control group treatment was placebo (10 RCTs) or best available treatment (usually low-dose dopamine [5 RCTs]) or was not reported (1 RCT). Assessments of the quality of individual studies were based on the Cochrane Handbook and included assessing risks for selection, performance, attrition, and adjudication biases and allocation concealment.

Outcomes: ARF requiring ≥ 1 episode of renal replacement therapy and all-cause hospital mortality. Secondary outcomes were ARF, ICU length of stay (LOS), hospital LOS, peak serum creatinine level, and hypotension.

MAIN RESULTS

Meta-analysis using fixed-effects models showed that fenoldopam reduced risks for ARF, requirement for renal replacement therapy, and all-cause mortality (Table). Fenoldopam was also associated with shorter ICU LOS, borderline shorter hospital LOS, and lower peak serum creatinine levels (Table). Groups did not differ for hypotensive episodes (Table).

CONCLUSION

In critically ill patients, fenoldopam reduces acute renal failure requiring renal replacement therapy and all-cause mortality.

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Fenoldopam vs placebo or best available treatment (control) in critically ill patients*

Outcomes	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		Fenoldopam	Control		
ARF requiring RRT	11 (1094)	5.9%	10%	43% (15 to 64)	23 (16 to 67)
All-cause mortality	11 (1118)	13%	19%	31% (7.4 to 50)	17 (11 to 72)
ARF	11 (1094)	15%	28%	49% (33 to 60)	8 (6 to 11)
				RRI (CI)	NNH
Hypotension	10 (1042)	23%	19%	24% (–5.8 to 58)	Not significant
		Weighted mean difference (CI)			
ICU LOS (d)	8 (840)	–0.61 (–0.99 to –0.23)			
Hospital LOS (d)	8 (695)	–1.07 (–2.16 to 0.01)			
Peak serum creatinine (mg/dL) [µmol/L]	14 (1187)	–0.20 (–0.24 to –0.16) [–18 (–21 to –14)]			

*ARF = acute renal failure; RRT = renal replacement therapy; ICU = intensive care unit; LOS = length of stay. Other abbreviations defined in Glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from data in article using a fixed-effects model.

COMMENTARY

Augmenting renal blood flow is an attractive strategy for prevention and early treatment of ARF in high-risk patients. Low-dose dopamine, which acts on several adrenergic and dopaminergic receptors in a dose-dependent manner, has been extensively studied for this purpose. Pooled data show that dopamine improves renal physiology, but these effects are small and temporary and do not improve clinical outcomes (1). In contrast to dopamine, the newer agent, fenoldopam, vasodilates renal arterioles by binding to DA-1 receptors more selectively.

The comprehensive systematic review by Landoni and colleagues evaluated fenoldopam to prevent ARF in critically ill patients in the ICU and having surgery. Pooled analyses suggested patient-important benefits (decreased renal replacement therapy and mortality) and a clinically tolerable increased risk for hypotension. Although the authors included RCTs in which the control group received active therapy, estimates of treatment effect were similar when analyses were restricted to placebo-controlled RCTs. However, most trials were small (only 5 enrolled > 100 patients), limiting the number of outcome events, and most had low-to-moderate methodological quality. The estimates of treatment effect may, therefore, be overly optimistic. Industry funding, another potential source of bias, was not discussed. Furthermore, the review excluded contrast-induced nephropathy, and a recent RCT of 315 patients showed that fenoldopam did not prevent this complication in high-risk patients (2). Although physiologic arguments may support the efficacy of fenoldopam in ischemic but not contrast-induced renal injury, this lack of consistency may simply reflect methodological limitations of the RCTs included in the review.

Fenoldopam is a promising therapy for ARF. Given the limitations of current evidence, we agree with the authors that a large multicentered RCT powered to detect improvements in patient-important outcomes is justified and required.

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