

Review: Low-dose dopamine does not reduce mortality or need for renal replacement therapy

Friedrich JO, Adhikari N, Herridge MS, Beyene J. Meta-analysis: low-dose dopamine increases urine output but does not prevent renal dysfunction or death. *Ann Intern Med.* 2005;142:510-24.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Rheumatology ★★★★★☆☆

QUESTION

Does low-dose dopamine influence mortality, need for renal replacement therapy, or renal physiologic outcomes in patients with or at risk for renal dysfunction?

METHODS

Data sources: MEDLINE (1966 to January 2005), EMBASE/Excerpta Medica (1980 to week 5 of 2005), CANCELIT (1975 to October 2002), CINAHL (1982 to January 2005), Cochrane Central Register of Controlled Trials (Issue 4, 2004), Renal Health Library, and bibliographies of retrieved studies and reviews.

Study selection and assessment: Quasi-randomized and randomized controlled trials (RCTs) that compared low-dose dopamine ($\leq 5 \mu\text{g/kg}$ of body weight per min) with placebo or no infusion in any population and assessed clinical or physiologic outcomes. Quality assessment of individual studies included allocation concealment, blinding, and withdrawals.

Outcomes: All-cause mortality, need for renal replacement therapy, renal physiologic outcomes (urine output, serum creatinine level and creatinine clearance), and adverse effects (arrhythmia or myocardial, limb, or cutaneous ischemia).

MAIN RESULTS

61 RCTs and quasi-RCTs ($n = 3359$) met the selection criteria. Most trials included patients with normal or near-normal renal function; 6 RCTs ($n = 559$) used dopamine therapeutically in patients developing renal failure. Populations included patients having

cardiac surgery (18 RCTs), vascular surgery (4 RCTs), and other types of surgery (18 RCTs); receiving intravenous contrast dye (8 RCTs); receiving other nephrotoxic medications (3 RCTs); neonates (5 RCTs); and patients with miscellaneous indications (3 RCTs). The number of patients per trial ranged from 12 to 347. The median dopamine dose was $2.5 \mu\text{g/kg}$ per minute. 54 RCTs assessed mortality and need for renal replacement therapy; ≥ 1 death occurred in 15 RCTs, and ≥ 1 requirement for renal replacement therapy occurred in 12 RCTs. Pooled analysis using a random-effects model showed no effect of low-dose dopamine on all-cause mortality or need for renal replacement therapy (Table). An increase in urine output occurred the first day after dopamine

initiation (Table), which was not significant on day 2 or 3. A decrease in serum creatinine and increase in creatinine clearance were present only on day 1 (Table). Dopamine and placebo or no-treatment groups did not differ for adverse effects (Table).

CONCLUSIONS

In patients with or at risk for renal dysfunction, low-dose dopamine does not reduce mortality or need for renal replacement therapy. The improvement in physiologic parameters is short-lived and of questionable clinical importance.

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Low-dose dopamine vs placebo or no treatment for renal dysfunction to hospital or intensive care unit discharge*

Outcomes	Number (n) of trials	Weighted event rates		RRR (95% CI)	NNT
		Low-dose dopamine	Placebo or no treatment		
All-cause mortality	15 (1387)	15.2%	15.3%	4% (-19 to 22)	Not significant
Need for renal replacement therapy	12 (1216)	17.3%	15.2%	7% (-15 to 24)	Not significant
				RRI (CI)	NNH
Adverse effects†	18 (1660)	20.8%	16.3%	12% (-10 to 40)	Not significant
				Ratio of means (CI)‡	
Urine output at d 1	33 (1654)	1.24 (1.14 to 1.35)			
Creatinine level at d 1	32 (1807)	0.96 (0.93 to 0.99)			
Creatinine clearance at d 1	22 (1077)	1.06 (1.01 to 1.11)			

*Abbreviations defined in Glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from data in article using a random-effects model.
 †Calculated from data provided by author.
 ‡Ratio of means = mean value in dopamine group divided by mean value in placebo or no-treatment group.

COMMENTARY

Use of “renal dose dopamine” has been used to either prevent or treat renal insufficiency in critically ill patients for many years. The meta-analysis by Friedrich and colleagues of 61 randomized or quasirandomized trials enrolling 3359 patients is a model systematic review, with key steps done in duplicate, a comprehensive search, explicit selection criteria, detailed appraisal of trial quality, additional data obtained from authors, exploration of heterogeneity, use of a random-effects model to pool results, detailed analyses, and transparent reporting.

Among trials reporting mortality or need for renal replacement therapy, no effect was found. Among trials focused on physiologic outcomes, urine output was increased, serum creatinine was decreased, and creatinine clearance was transiently increased only after 24 hours of infusion. Between-study heterogeneity was significant and was partly explained by trial quality in that concealed or blinded trials tended to

generate neutral pooled estimates of effect compared with unconcealed or unblinded trials.

For clinicians who have abandoned the use of low-dose dopamine, this meta-analysis is consistent with their practice. After 15 years of trials on this topic, the most we can conclude is that low-dose dopamine temporarily increases urine output. However, the utility of this surrogate endpoint within the first 24 hours should be considered in light of current estimates of a trend toward increased tachyarrhythmias and no evidence of benefit with respect to renal replacement therapy or mortality. This meta-analysis also challenges us to generate plausible hypotheses and relative risk reductions for designing future trials that seek a clear role for low-dose dopamine.

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