



Evidence-Base Medicine

Dopamine use with improvement
in mortality of congestive heart
failure by R1鈕聖文



Asking a answerable question

- Does Dopamine affect mortality rate of congestive heart failure ?



PICO model

Patient	Congestive heart failure
Intervention	Dopamine
Comparison	Without Dopamine
Outcome	Mortality rate, symptoms relief



Key words

- Congestive heart failure
- Dopamine
- Mortality



Results

- EBMR: Cochrane Central Register of Controlled Trials → 0
- Cochrane Library → 3
- PubMed → 13
- MedLine → 3
- EBM Reviews - ACP Journal Club → 0

Cochrane



The Cochrane Library

Evidence for healthcare decision-making

[Home](#) | [About Cochrane](#) | [Access to Cochrane](#) | [For Authors](#) | [Help](#) | [Save Title to My Profile](#)



BROWSE

Cochrane Reviews: [By Topic](#) | [New Reviews](#) | [Updated Reviews](#) | [A-Z](#) | [By Review Group](#)

Other Resources: [Other Reviews](#) | [Clinical Trials](#) | [Methods Studies](#) | [Technology Assessments](#) | [Economic Evaluations](#)

[? More Info](#)

SEARCH

[Advanced Search](#) | [MeSH Search](#) | [Search History](#) | [Saved Searches](#)

There are 3 results out of 489167 records for: "Congestive heart failure and Dopamine in Keywords and Mortality in Keywords in The Cochrane Central Register of Controlled Trials" [Save Search](#)

[Edit Search](#)

View: 1-3

[Export All Results](#)

Record Information

Sort by: [Record Title](#) | [Match %](#) | [Year](#)

- | | |
|--------------------------|---|
| <input type="checkbox"/> | Neurohormonal activation in heart failure after acute myocardial infarction treated with beta-receptor antagonists.
Persson H, Andriksson K, Kahan T, Eriksson SV, Tidgren B, Hjendahl P, Hall C, Erhardt L
Year: 2002
Record |
| <input type="checkbox"/> | Renal function, neurohormonal activation, and survival in patients with chronic heart failure.
Hillege HL, Girbes AR, de Kam PJ, Boomsma F, de Zeeuw D, Charlesworth A, Hampton JR, van Veldhuisen DJ
Year: 2000
Record |
| <input type="checkbox"/> | Randomised study of effect of ibopamine on survival in patients with advanced severe heart failure. Second Prospective Randomised Study of Ibopamine on Mortality and Efficacy (PRIME II) Investigators.
Hampton JR, van Veldhuisen DJ, Kleber FX, Cowley AJ, Ardia A, Block P, Cortina A, Cserhalmi L, Follath F, Jensen G, Kayanakis J, Lie KI, Mancica G, Skene AM
Year: 1997
Record |

[Select All](#) (to export citations)

PubMed

9: [Massel D.](#)

[Related Articles](#), [Links](#)



Ibopamine and survival in severe congestive heart failure: PRIME II.
Lancet. 1997 Jul 12;350(9071):147. No abstract available.
PMID: 9228992 [PubMed - indexed for MEDLINE]

10: [Van Veldhuisen DJ.](#)

[Related Articles](#), [Links](#)



Treatment of mild heart failure: the place of diuretics and ibopamine.
Eur Heart J. 1997 May;18(5):712-4. No abstract available.
PMID: 9152639 [PubMed - indexed for MEDLINE]

11: [Hampton JR, van Veldhuisen DJ, Kleber FX, Cowley AJ, Ardia A, Block P, Cortina A, Cserhalmi L, Follath F, Jensen G, Kavanakis J, Lie KI, Mancica G, Skene AM.](#)

[Related Articles](#), [Links](#)



Randomised study of effect of ibopamine on survival in patients with advanced severe heart failure. Second Prospective Randomised Study of Ibopamine on Mortality and Efficacy (PRIME II) Investigators.
Lancet. 1997 Apr 5;349(9057):971-7.
PMID: 9100622 [PubMed - indexed for MEDLINE]

12: [Rolandi E, Sabino F, Cantoni V, Ghirardi P, Marchetti GV, Cicchetti V.](#)

[Related Articles](#), [Links](#)



Long-term therapy of chronic congestive heart failure with ibopamine: a multicenter trial.
J Cardiovasc Pharmacol. 1989;14 Suppl 8:S93-103.
PMID: 2483446 [PubMed - indexed for MEDLINE]

13: [Dei Cas L, Metra M, Nodari S, Visioli O.](#)

[Related Articles](#), [Links](#)



Efficacy of ibopamine treatment in patients with advanced heart failure: purpose of a new therapeutic scheme with multiple daily administrations.
J Cardiovasc Pharmacol. 1989;14 Suppl 8:S111-7.
PMID: 2483436 [PubMed - indexed for MEDLINE]

Display

Summary



Show 20



Sort by



Send to



Medline

Ovid: Search Form - Microsoft Internet Explorer

檔案(F) 編輯(E) 檢視(V) 我的最愛(A) 工具(T) 說明(H)

地址(D) http://gateway.ut.ovid.com/gw2/ovidweb.cgi

EPSON Web-To-Page 列印 預覽列印

Google G medline ovid Go 129 blocked Check Look for Map AutoFill Send to Settings

Ovid MEDLINE(R) 1996 to Present with Daily Update ovid web gateway

[Change Database](#) | [Ask a Librarian](#) | [Online Support](#) | [Help](#) | [LOGOFF](#)
[Personal Account \(for Searches\)](#) | [Saved Searches/Alerts](#)

#	Search History	Results	Display
1	Heart Failure, Congestive/th [Therapy]	4429	DISPLAY
2	Dopamine/tu [Therapeutic Use]	467	DISPLAY
3	1 and 2	3	DISPLAY

[Combine Searches](#) [Delete Searches](#) [Save Search/Alert](#)

Advanced Search **Basic Search** **Find Citation** [More Fields](#) [Search Tools](#)

Keyword **Author** **Title** **Journal**

Enter **Keyword** or phrase (use "\$" for truncation):
 Map Term to Subject Heading

SEARCH

Limits [More Limits](#)

Full Text Humans English Language
 Review Articles Abstracts Latest Update
 Core Clinical Journals (AIM)

開始 網際網路 下午 01:59

Google Scholar



management of acute heart failure syndromes"

進階學術搜尋
學術搜尋偏好
學術搜尋說明

搜尋所有網站 搜尋所有中文網頁 搜尋繁體中文網頁

學術搜尋 關於 "Reassessment of dobutamine, dopamine, and milrinone in the management of acute heart failure syndromes" 有 5 項搜尋結果，這是

所有結果

[M Bayram](#)

[L De Luca](#)

[M Massie](#)

[M Gheorghiade](#)

提示：請試試看，在搜尋時移去引號來得到更多搜尋結果。

[Reassessment of Dobutamine, Dopamine, and Milrinone in the Management of Acute Heart Failure ... - 3 個群組 »](#)

M Bayram, L De Luca, MB Massie, M Gheorghiade - *The American Journal of Cardiology*, 2005 - Elsevier

... doi:10.1016/j.amjcard.2005.07.021 How to Cite or Link Using DOI (Opens New Window)

Copyright © 2005 Elsevier Inc. All rights reserved. *Reassessment of Dobutamine, Dopamine, and Milrinone in the Management of Acute Heart Failure Syndromes*. Melike ...

[被引用 7 次](#) - [相關文章](#) - [網頁搜尋](#)

[Use of Nesiritide Before and After Publications Suggesting Drug-Related Risks in Patients With Acute ... - 3 個群組 »](#)

PJ Hauptman, MA Schnitzler, J Swindle, TE ... - *JAMA*, 2006 - Am Med Assoc

JAMA & ARCHIVES Select Journal or Resource, ...

[被引用 1 次](#) - [相關文章](#) - [網頁搜尋](#)

[Low cardiac output syndrome in children - 2 個群組 »](#)

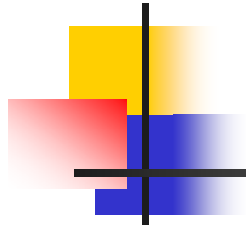
B Jones, M Hayden, JF Fraser, E Janes - *Current Anaesthesia & Critical Care*, 2005 - Elsevier

Quick Search: within All Full-text Sources Quick Search searches abstracts, titles, keywords, and authors. Click here for more information. *Current Anaesthesia & Critical Care* Volume 16, Issue 6, 2005, Pages 347-358. ...

...

[相關文章](#) - [網頁搜尋](#)

Evidence



- Reassessment of Dobutamine, Dopamine, and Milrinone in the Management of Acute Heart Failure Syndromes, *The American Journal of Cardiology*, 19 September 2005, Pages 47-58.



Evidence-Base - Aim

- They wanted to prove that acute, intermittent, or continuous use of inodilator infusions may increase morbidity and mortality in patients with acute heart failure syndromes.



Evidence-Base - Patient

- In this registry, which currently comprises >150,000 patients, <3% presented with a systolic blood pressure of <90 mm Hg and approximately 50% presented with relative preserved systolic function (PSF).



Evidence-Base - Patient

- Approximately 14% of the patients in ADHERE were treated with ≥ 1 acute infusions of inodilator agents (dobutamine 6%, dopamine 6%, and milrinone 3%) in the hospital.
- Furthermore, among home discharges of patients with a prior history of HF during this period, 1% were discharged on chronic dobutamine, and 1% on chronic milrinone infusion therapy.



Evidence-Base - Patient

- Abraham and coworkers compared in-hospital mortality in a subset of 65,180 patients, 15,230 of whom were receiving either intravenous vasodilator therapy (nitroglycerin or nesiritide) or inodilator therapy (dobutamine or milrinone).

Evidence-Base - Result



- Importantly, 15% of patients receiving inodilators had PSF.
- The inodilator-treated patients with preserved systolic function (PSF) had a higher mortality rate (19%) than all other inodilator-treated patients (14%).
- Patients with PSF who were treated with inodilators also had a higher mortality rate than patients with PSF who were not treated with inodilators (19% vs 2%, respectively).
- Among the inodilator-treated patients, those with PSF also had a longer hospital stay compared with all other inodilator-treated patients (mean, 12.9 vs 9.6 days).



Evidence-Base - Result

End Point [↕]	Dobutamine (n = 100) [↕]	Placebo (n = 99) [↕]	Levosimendan (n = 100) ^{↕↕}
1-mo mortality [↕]	14.0% [↕]	8.1% [↕]	6.0% * [↕]
6-mo mortality [↕]	42.0% [‡]	28.3% [↕]	18.0% [‡]

Adapted from Program and abstracts of the European Society of Cardiology, Heart Failure Update 2004⁴⁰ and *Eur J Heart Fail.*⁴¹ ↕

* p = 0.04 vs dobutamine. ↕

‡ p = 0.02 vs placebo. ↕

‡ p = 0.0001 vs dobutamine and 0.03 vs placebo. ↕

Evidence-Base - Result

Table 2. ↵

Short-term (acute) infusions: milrinone versus placebo trials ↵

Trial↵	<u>Milrinone</u> ↵	Comparison↵	Patient Population↵	Number↵	Follow-up↵	Outcome↵
Anderson et al 1987 ⁴⁶ , 1991 ⁴⁵ ↵	50 $\mu\text{g}/\text{kg}$ loading dose followed by infusion with 0.5 $\mu\text{g}/\text{kg}/\text{min} \times 1 \text{ hr}$ ↵	Placebo↵	NYHA class III-IV with CI $<2.5 \text{ L}/\text{min}/\text{m}^2$ or PCWP $>15 \text{ mm Hg}$ ↵	31↵	1 hr↵	<u>Milrinone</u> caused significant increases in CI (41%) and SV (32%) and decreases in PCWP (25%), SVR (24%), and MAP (5%) at 1 hr of infusion.↵
Seino et al, 1996 ⁴⁷ ↵	50 $\mu\text{g}/\text{kg}$ loading dose followed by continuous infusion with 0.5 $\mu\text{g}/\text{kg}/\text{min}$ for 6 hr↵	Placebo↵	Patients with acute heart failure with PCWP $>18 \text{ mm Hg}$ ↵	52↵	1 hr↵	37% decrease in PAOP, 39% decrease in RAP, 31% increase in CI, and 21% increase in SV at 15 min compared with decreased CI at 60 min and no other significant changes in placebo group. Subjective symptoms also improved compared with no improvement in placebo. 16% rate of ventricular arrhythmias in <u>milrinone</u> group.↵
Cuffe et al, 2002 ⁴⁴ ↵	48-72-hr infusion with 0.5 $\mu\text{g}/\text{kg}/\text{min}$ ↵	Saline placebo↵	NYHA class III-IV; mean LVEF = 0.23↵	951↵	2 mo↵	No significant difference in number of days hospitalized, in-hospital mortality, 60-day mortality, or composite incidence of death or re-admissions.↵
Felker et al, 2003 ⁴ ↵	48-72-hr infusion with 0.5	Saline placebo↵	NYHA class III-IV; mean	951↵	2 mo↵	<u>Milrinone</u> -treated patients with ischemic heart disease tended to have worse outcomes for the composite of death and <u>rehospitalizations</u> .↵

Evidence-Base - Result

Table 3. ↵

Results from the Outcomes of Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) ↵

Outcome ↵	Placebo (n = 472) ↵	<u>Milrinone</u> (n = 477) ↵	p Value ↵ ↵
Cardiovascular hospitalization within 60 days, mean days ↵	12.5 ± 14 ↵	12.3 ± 14 ↵	0.71 ↵ ↵
Death within 60 days ↵	8.9% ↵	10.3% ↵	0.41 ↵ ↵
Death or readmission within 60 days ↵	35.3% ↵	35.0% ↵	0.92 ↵ ↵
Treatment failures during the infusion period ↵	9.2% ↵	20.6% ↵	<0.001 ↵ ↵
New <u>atrial</u> fibrillation or flutter during index hospitalization ↵	1.5% ↵	4.6% ↵	0.004 ↵ ↵
Sustained hypotension during index hospitalization * ↵	3.2% ↵	10.7% ↵	<0.001 ↵ ↵

Adapted from JAMA,²¹ ↵

*Defined as a systolic blood pressure <80 mm Hg for >30 minutes, requiring intervention. ↵

Evidence-Base - Result

Trial [↗]	Milrinone [↗]	Dobutamine [↗]	Patient Population [↗]	N [↗]	Follow-up [↗]	Outcome [↗]
Biddle et al (1987) ⁴⁹ Open label [↗]	50 or 75 µg/kg bolus then 0.5–1 µg/kg/min infusion × 48 hr [↗]	Incremental doses of 2.5–15 µg/kg/min × 48 hr [↗]	NYHA class III–IV (stable for ≥2 wk before study) [↗]	79 [↗]	48 hr [↗]	No difference in hemodynamic effects between groups: SV increased, HR increased, SVR decreased, and PCWP decreased similarly in both groups. [↗]
Eichhorn et al (1987) ⁵⁰ [↗]	50 µg/kg bolus then 0.5 µg/kg/min [↗]	2.5–15 µg/kg/min (dose adjusted to achieve equal increases in CO) [↗]	NYHA class III–IV [↗]	14 [↗]	During hemodynamic and radionuclide recordings [↗]	24% increase in CI from baseline in both groups; increase in RV systolic performance. Significant RV afterload and PAESP reduction only in milrinone group. [↗]
Karlsberg et al (1996) ⁵¹ Open label [↗]	50 µg/kg bolus then 24-hr infusion of 0.25–0.75 µg/kg/min (titrated up similar to dobutamine) [↗]	24-hr infusion of 2.5–15 µg/kg/min (titrated up until >30% increase in CI or >25% decrease in MPCWP) [↗]	Within 12 hr to 5 days after acute MI [↗]	33 [↗]	24 hr [↗]	Criteria for decrease in MPCWP were met by 94% of the milrinone-treated patients and 57% of the dobutamine-treated patients (p = 0.03). Maximal reduction in MPCWP was greater for the milrinone (53.2% vs 31%, p = 0.01). Both improved global EF. [↗]
Feneck et al (2001) ⁵² Open label [↗]	50 µg/kg bolus then 0.5 µg/kg/min infusion × 4 hr [↗]	10–20 µg/kg/min infusion × 4 hr [↗]	Patients with low CO after cardiac	120 [↗]	4 hr [↗]	Dobutamine group had greater increases in CI, MAP, and LV stroke work index. Milrinone group had greater decreases in MPCWP. Dobutamine group had higher incidences of

Evidence-Base - Result

Trial [↵]	Dobutamine [↵]	Control [↵]	Patient Population (NYHA class) [↵]	Number [↵]	Follow-up [↵]	Outcome [↵]
Leier et al (1982) ⁶⁸ [↵]	IV infusion for 4 hr weekly × 24 wk [↵]	Matched control group [↵]	III–IV [↵]	26 [↵]	24 wk [↵]	No significant change in CI or resting LVEF. Improved functional classification ($p < 0.05$); increased exercise tolerance ($p < 0.05$). 2 of 15 died in <u>dobutamine</u> group vs 1 of 11 in control group. [↵]
Dies et al (1986) ⁶⁹ [↵]	IV infusion for 48 hr/wk × 24 wk [↵]	Placebo [↵]	III–IV, EF 0.20 ± 0.11 [↵]	60 [↵]	8 wk [↵]	Increased treadmill times; improved symptom scores. Increased mortality in treatment group (44% vs 17% in placebo group). [↵]
Erlemeier et al (1992) ⁷⁰ [↵]	8 × 24-hr infusions over a 4-wk period with at least 3 days in between [↵]	5% dextrose solution [↵]	IV [↵]	20 [↵]	3 days after last infusion [↵]	Increased exercise duration on treadmill test; decreased body weight. 1 death in treatment group (1/10) and 1 death (1/10) in control group. [↵]
Adamopoulos et al (1995) ⁷¹ [↵]	IV infusion 4 days/wk × 3 wk to raise HR to 70%–80%	Usual activity only [↵]	Mostly III, EF 0.23 ± 0.03 [↵]	20 [↵]	6 wk after intervention [↵]	Increased exercise tolerance at 3 and 6 wk; increased <u>chronotropic</u> responsiveness to exercise; improved symptoms; increased β -receptor density. No clinically significant arrhythmias and no deaths reported. [↵]

Evidence-Base - Result

Trial [↵]	Dobutamine [↵]	Control [↵]	Patient Population (NYHA class) [↵]	Number [↵]	Follow-up [↵]	Outcome [↵]
	maximum for 30 min/day [↵]					
Oliva et al (1999) ⁷² [↵]	Infusion for 48 hr/wk × 6 mo [↵]	Optimal standard treatment [↵]	III-IV, EF <0.30 [↵]	38 [↵]	8 wk for CI; 6 mo for other outcomes [↵]	Did not improve functional status; non-significant tendency toward decreased hospitalizations. <u>Nonsignificant</u> trend to improve exercise tolerance. No increase in ventricular arrhythmias. Did not significantly increase mortality. [↵]
Elis et al (1998) ⁷³ [↵]	24-hr infusion every 2 wk × 6 wk then every 3 wk × 6 mo [↵]	Placebo [↵]	III-IV, EF 0.30 (ischemia-induced HF) [↵]	19 [↵]	Until death or Dec. 1996 (survival analysis at 32 mo) [↵]	No difference in number of hospitalizations between groups at 6 mo. No significant difference between survival curves at 32 mo (p = 0.7) [↵]

CI = cardiac index; EF = ejection fraction; HF = heart failure; HR = heart rate; IV = intravenous; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.[↵]



Evidence-Base - Conclusion

- Randomized, controlled studies conducted to date do not support the use of intravenous inodilator agents (dopamine, dobutamine, and milrinone) in the acute, intermittent, or chronic setting.
- Despite the belief that these agents improve symptoms acutely and facilitate diuresis, this is not substantiated by data from randomized trials.



Evidence-Base - Conclusion

- In contrast, the use of these inodilators may induce hypotension and arrhythmias and may cause myocardial injury.
- In addition, short-term use of these agents has also been associated with increased postdischarge mortality, particularly in patients with ischemic heart disease.



Evidence-Base - Conclusion

- Data from recent registry studies indicate that these inodilator agents are being used in a significant number of patients with normal or high systolic blood pressure and PSF (preserved systolic function).
- Available clinical trial data do not support the use of dobutamine, dopamine, or milrinone in this population.



Evidence-Base - Conclusion

- The effects of inodilator therapy, when they are used specifically in patients with hypotension because of a low-output state, remain to be determined.
- Accordingly, we recommend that inodilator therapy with dopamine, dobutamine, or milrinone should only be used in patients who have low blood pressure because of low cardiac output in spite of a high LV diastolic pressure and who are not responding to other treatments.



Oxford centre for EBM levels of Evidence

- Systemic review of randomized central trial
 - Different population
 - Different clinical centers
 - Prospective cohort studies
- Level 1a



Are the results valid? (1)

- Was the assignment of patients to treatments randomized? → *Yes*
- Were all patients who entered the trial properly accounted for and attributed at its conclusion?
 - (1) Was follow-up complete? → *Almost*
 - (2) Were patients analyzed in the groups to which they were randomized? → *Yes*



Are the results valid? (2)

- Were patients, clinicians, and study personnel “blind” to treatment? → *Unknown*
- Were the groups similar at the start of the trial? → *Unknown*
- Aside from the experimental intervention, were the groups treated equally? → *Yes*



What are the results?

- How large was the treatment effect?
- How precise is the estimate of the treatment effect?



Will the results help me in my patient care?

- Can the results be applied to my patient?
- Were all clinically important outcomes considered?
- Are the benefits worth the harms and costs?



Thanks for your attention!!!
