Intravenous Milrinone for Symptomatic Cerebral Vasospasm: A Single Center Case-control Study

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Learning Objectives

By the conclusion of this session, participants should be able to: 1. Describe the pathophysiology of cerebral vasospasm. 2. The morbidity and mortality associated with cerebral vasospasm. 3. The standard treatment of cerebral vasospasm. 4. Resume and critics the clinical trials about cerebral vasospasm.

Introduction

Cerebral vasospasm (CV) remains a serious cause of morbidity and mortality following subarachnoid hemorrhage. Milrinone, a type III phosphodiesterase inhibitor with positive inotropic and vasodilatory properties, has been increasingly used in the treatment of CV. However, data on its safety and clinical efficacy remains limited.

Methods

We performed a retrospective study on 93 consecutives patients with symptomatic cerebral vasospasm treated between 2000 and 2010 (Figure 1): 60 received standard hyperdynamic therapy (SHT) and intravenous milrinone, whereas 33 received SHT without milrinone. The proportion of new onset CV-related infarcts on CT-scan, the clinical outcomes (mRS) at 3 months and 2 years and mortality were compared between the 2 groups. Logistic regression was used to study the relationship between Fisher, Hunt & Hess grade, radiological CV severity, CV-related infarct, the use of milrinone and clinical outcome.

Figure 1

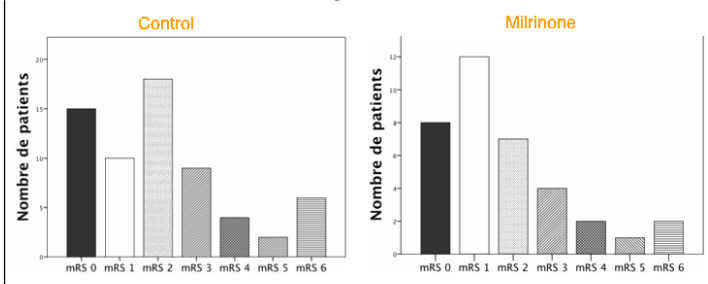
	Group control (*N*=38)	Group milrinone (*N*=67)	*P*-value
Age (years)	50.5 ± 11.7	54.5 ± 11.3	0.089
Gender			0.477
Male	9 (23.7%)	12 (17.9%)	
Female	29 (76.3%)	55 (82.1%)	
Hunt & Hess			0.281
1-3	34 (89.4%)	54 (80.6%)	
4-5	4 (10.6%)	13 (19.4%)	
Modified Fisher score			0.099
1-2	10 (26.4%)	9 (13.4%)	
3-4	28 (73.6%)	58 (86.6%)	
Hypertension	13 (34.2%)	28 (41.8%)	0.444
Smoking	20 (52.6%)	35 (52.2%)	0.969
External ventricular derivation	18 (47.4%)	37 (55.2%)	0.439
Norepinephrine	19 (50%)	48 (71.6%)	
Severity of vasospasm			0.765
Mild	5 (13.2%)	11 (16.4%)	
Moderate	18 (47.4%)	27 (40.3%)	
Severe	15 (39.5%)	29 (43.3%)	

Population caracteristics

Results

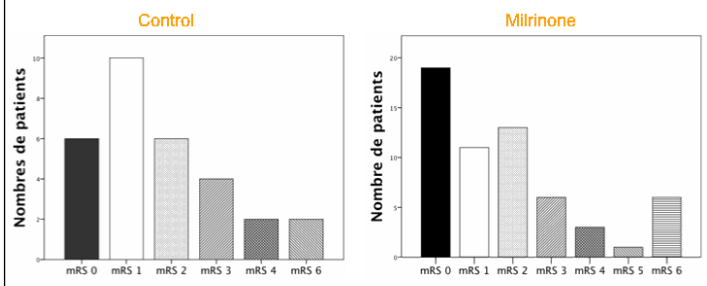
Sixty patients received milrinone for an average of 6.1 ± 3.3 days (range : 1-16). There were no complications related to milrinone. A new-onset CV-related infarct occurred in 51.6 % of patients who received IV milrinone compared to 57.6 % of patients who did not received milrinone. A favorable clinical outcome (mRS= 2) was observed in 63.3% (n=38) of patients receiving milrinone compared to 57.6% (n=19) not treated with milrinone. No statistically significant differences were observed between patients treated with and without milrinone in terms of CV-related infarcts, mortality and functional outcome.

Figure 2



Clnical outcome at 3 months

Figure 3



Clinical outcome at 2 years

Figure 4

Secondary variables	Control	Milrinone	P-value
Angioplasty	11 (28.9%)	19 (28.4%)	0.949
Hospitalisation (days)	29.0 +/- 23.0	23.9 +/- 12.2	
Death	2 (5.3%)	5 (7.5%)	1.000
Radiological infarctions	23 (60.5%)	37 (57.2%)	0.598

Outcomes for secondary variables

Conclusions

Milrinone seems to be safe for the treatment of symptomatic CV, but no clear advantage as compared to SHT have been demonstrated in this retrospective study. A prospective randomized study is needed to evaluate its efficacy.