Erythropoiesis-stimulating agents and thrombotic events in dialysis patients

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Introduction

- Erythropoiesis-Stimulating Agents (ESAs) have been associated with a higher cardiovascular event and mortality rate
- Risk of arterial thrombosis is mainly based on composite endpoints of anemia correction trials
- ESA associated risk of venous thrombosis has not been studied in dialysis patients

Aim

- To determine the association between ESA use and dose with arterial and venous thrombosis in a population of incident dialysis patients

Methods

- Necosad is a prospective cohort study in which incident adult dialysis patients were included
- Data on ESA use and dose, co-morbidities and laboratory parameters were routinely collected every 6 months
- Patients were categorized according to ESA treatment (yes or no) and tertiles of ESA dose (units per week)
- Fatal and non-fatal arterial and venous thromboses were collected by chart review of 805 patients from 6 participating centers
- 755 patients were still alive and participating in the study at 3 months after the start of dialysis (baseline)
- Crude and adjusted time-dependent Cox regression was performed to calculate hazard ratios (HR) with 95% confidence interval (CI) for ischemic stroke, myocardial infarction and venous thrombosis

Conclusion & Discussion

- No excess of thrombotic events in ESA treated dialysis patients
- Our results for myocardial infarction are in line with meta-analysis
- A protective effect of ESA on ischemic stroke is not previously shown
- Our observational cohort reflecting common practices in a general dialysis population might explain the difference in results for ischemic stroke from anemia correction trials
- Further investigation is needed to enlighten the true mechanism of the ESA associated mortality

Results

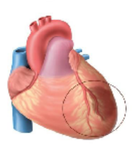
- Patients with ESA had a 2 times lower stroke rate than patients without ESA
- ESA treated patients had a HR of 1.12 (0.58-2.14) for myocardial infarction
- No evident dose response effect was present
- Only 13 patients with venous thrombosis

Ischemic stroke

58 patients

33.6 (25.8-43.2)^

Myocardial infarction



110 patients

IR 59.9 (49.4-71.9)^

Venous thrombosis

13 patients

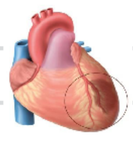
IR 7.31 (4.1-12.2)^

^IR = incidence rate per 1000 person years

Table 1. Hazard ratios for ischemic stroke in different ESA categories

	ESA (dose units/week)	Unadjusted (95% CI)		Adjusted (95% CI)*	
Ischemic stroke	yes vs no	0.50	(0.26-0.95)	0.45	(0.23-0.90)
	no ESA	1.93	(0.92-4.05)	2.13	(0.99-4.58)
	≤ 4000	ref		ref	
	4001-8000	0.93	(0.45-1.92)	0.85	(0.41-1.79)
	>8000	0.97	(0.47-1.97)	1.02	(0.48-2.18)

Table 2. Hazard ratios for myocardial infarction in different ESA categories

	ESA (dose units/week)	Unadjusted (95% CI)		Adjusted (95% CI)*	
Myocardial infarction	yes vs no	1.19	(0.64-2.22)	1.12	(0.58-2.14)
	no ESA	0.89	(0.45-1.76)	0.89	(0.45-1.78)
	≤ 4000	ref		ref	
	4001-8000	0.98	(0.59-1.62)	0.88	(0.53-1.46)
	>8000	1.21	(0.75-1.95)	1.13	(0.68-0.88)

*Adjusted for age, sex, primary kidney disease, comorbidities (venous thrombosis, myocardial infarction, ischemic stroke, malignancy, diabetes mellitus), dialysis modality, nutritional status, residual renal function, ferritin and albumin

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FP7-project

51ERA-EDTA 482--SP

M) Dialysis. M3) Cardiovascular complications in in CKD 5D.

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DOI: 10.3252/pso.eu.51era.2014

Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014

PosterSessionOnline.com