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CLINICAL RESEARCH

Diuretics versus volume expansion in acute submassive pulmonary embolism

Traitement diurétique versus remplissage dans l'embolie pulmonaire aiguë avec dysfonction ventriculaire droite

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KEYWORDS
Pulmonary embolism;
Diuretic;
Fluid loading

Summary
Background. — The benefit of volume expansion (VE) in submassive pulmonary embolism (PE) with right ventricular (RV) dysfunction is unclear.
Aim. — To compare the effects of diuretic treatment versus VE in patients hospitalized for PE with RV dysfunction.
Methods. — We prospectively included 46 consecutive patients with submassive PE treated on admission with a 40 mg bolus of furosemide (D group, $n = 24$) or 500 mL of saline infusion (VE group, $n = 22$). The primary endpoint was the timing of normalization of B-type natriuretic peptide and troponin Ic concentrations. The secondary endpoints were variations in RV function variables, recorded at baseline, at the 4th hour after treatment initiation (H4) and every day until discharge, and a clinical composite endpoint of thrombolysis or death at 7 and 30 days.

Abbreviations: BNP, B-type natriuretic peptide; H4, the 4th hour after initiation of treatment; H24, the 24th hour after initiation of treatment; HR, heart rate; IVC, inferior vena cava; LV, left ventricular; PASP, pulmonary arterial systolic pressure; PE, pulmonary embolism; RV, right ventricular; SBP, systolic blood pressure; S'-DTI, peak systolic velocity of tricuspid annulus by Doppler tissue imaging; TAPSE, tricuspid annular plane systolic excursion; TTE, transthoracic echocardiography; VE, volume expansion.

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Results. — No differences were observed between patients at baseline. The primary endpoint occurred earlier in the D group than in the VE group (67.5 ± 34.8 vs 111.6 ± 63.3 hours; $P = 0.006$). Furosemide treatment on admission was well tolerated, and was not associated with serious adverse events. At H4, substantial improvements were observed in the D group versus the VE group in terms of heart rate reduction (−8.15 ± 21.0 vs −0.71 ± 6.30 beats/min; $P < 0.01$) and peak tricuspid annular systolic velocity (Doppler tissue imaging) (11.4 ± 2.10 vs 9.90 ± 2.80 cm/s; $P = 0.02$). There was no significant difference between groups in terms of severe outcomes at 7 and 30 days.
Conclusions. — In the acute management of submassive PE patients, a single furosemide bolus on admission seems to produce significant and earlier improvements in RV function markers compared with VE, without adverse events.

MOTS CLÉS
Embolie pulmonaire ;
Traitement diurétique ;
Remplissage

Résumé
Introduction. — Le bénéfice du remplissage dans l'embolie pulmonaire (EP) aiguë avec dysfonction ventriculaire droite (VD) est incertain. Nous avons comparé les effets d'un traitement diurétique versus un remplissage chez des patients hospitalisés pour EP avec dysfonction VD.
Méthodes. — Nous avons prospectivement inclus 46 patients consécutifs hospitalisés pour une EP aiguë avec dysfonction VD traités à l'admission soit par un bolus de 40 mg de furosémide (groupe D, $n = 24$), soit un remplissage de 500 cm^3 de chlorure de sodium (groupe R, $n = 22$). Le critère de jugement principal était le temps de normalisation du *Brain natriuretic peptide* (BNP) et de la troponine Ic. Les critères de jugement secondaires étaient l'analyse de paramètres cliniques, biologiques et échographiques enregistrés à l'admission, après 4 heures de traitement, puis quotidiennement jusqu'à la sortie d'hospitalisation et la survenue d'un critère clinique composite (décès ou thrombolyse) aux 7e et 30e jours.
Résultats. — Il n'y avait pas de différence significative entre les 2 groupes à l'admission. La normalisation du BNP et de la troponine Ic est survenue plus rapidement dans le groupe D que dans le groupe R (67,53 ± 4,8 vs 111,6 ± 63,3 heures, $p = 0{,}006$). L'administration de furosémide à l'admission était bien tolérée et ne s'est pas compliquée d'effets indésirables graves. À la 4e heure, une réduction significative de la fréquence cardiaque et une amélioration significative du pic de vitesse systolique tricuspide (onde S, évaluée en doppler tissulaire pulsé) étaient observées dans le groupe D avec respectivement −8,15 ± 21,0 vs −0,71 ± 6,30 bpm dans le groupe R, $p < 0{,}01$ et 11,4 ± 2,10 vs 9,90 ± 2,80 cm/s dans le groupe R, $p = 0{,}02$. Il n'y avait pas de différence significative en termes de décès ou thrombolyse aux 7e et 30e jours entre les 2 groupes.
Conclusion. — Dans la prise en charge de l'EP aiguë avec dysfonction VD, un bolus de furosémide à l'admission entraîne une amélioration rapide et significative de paramètres pronostics cliniques, biologiques et échographiques sans survenue d'effets indésirables graves.

Background

Submassive acute pulmonary embolism (PE) is a frequent and severe condition characterized by right ventricular (RV) dysfunction and a high rate of in-hospital mortality [1]. RV failure constitutes an emergency for the prevention of cardiogenic shock and death [2].

According to the current guidelines, fibrinolysis therapy is the cornerstone for patients with massive PE complicated with cardiogenic shock [3–6]. However, in intermediate-risk PE (RV injury with preserved blood pressure), the recent PEITHO trial [7], involving 1005 patients, showed no benefit from fibrinolysis therapy in terms of in-hospital or long-term mortality, but a high rate of bleedings. For intermediate-risk PE, except for anticoagulation therapy, initial haemodynamic management remains empirical, and consists of reasonable volume expansion (VE) [8] and close monitoring. In the above-mentioned randomized trial, no more information concerning concomitant therapies was given, except the potential use of dopamine infusion. Although careful VE is the standard of care in this particular situation, the volume and speed of administration are not well defined, and are at the discretion of the physician.

In submassive PE, pulmonary vascular resistances increase dramatically, leading to RV overload. One of the main consequences is RV dilatation, then both wall stress

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