急性心不全に対する利尿薬の用量調節

DOSE：体液貯留に対しループ利尿薬は持続投与でもボーラス投与でも結果は同等であるが高用量フロセミド投与の方が有効である可能性がある

DOSE: Loop diuretics have similar results whether given by continuous infusion or bolus, but high-dose furosemide may be better for fluid overload

急性心不全で入院した患者に対し、高用量または低用量の利尿薬を持続的または間歇的に投与しても総合的な症状改善または腎機能変化には有意な差がないとの研究結果が第59回American College of Cardiologyで発表された。利尿薬の最適な使用法の評価（Diuretic Optimization Strategies Evaluation：DOSE）スタディにおいて、急性非代償性心不全および体液貯留を有する患者308人を高用量または低用量フロセミド静脈内注射（それぞれ常用経口投与量の2.5倍または常用経口投与量と同用量）を投与する群に無作為に割り付けた。二重無作為化アプローチにより患者らはまた、静脈内投与を12時間ごとあるいは持続的に投与する群に無作為に割り付けられた。その結果、高用量フロセミドを72時間投与することにより全体の徴候の改善がより認められる傾向にあった。高用量のフロセミド投与による腎機能の有意な悪化（ベースラインから72時間後までの血清クレアチニンレベルの変化の中央値で計測）はみられなかった（高用量群で0.06mg/dLに対し低用量群で0.01mg/dL）。全体の体液量減少および体重変化のような体液量オーバーロード改善に対するフロセミドの有効性などいくつかの二次計測項目に関しても高用量フロセミド群で良好な傾向にあった。

Full Text

In patients hospitalized with acute heart failure, there is no significant difference in overall symptom relief or change in kidney function whether a diuretic is delivered at high or low doses or by continuous or intermittent infusion, according to research presented at the American College of Cardiology's 59th annual scientific session.

The Diuretic Optimization Strategies Evaluation (DOSE) Study did suggest, however, that high-dose furosemide may be more effective than low-dose furosemide at improving several individual measures of fluid overload and symptom severity. Furthermore, significant deterioration in kidney function, although more common with high furosemide doses, tended to be transient. DOSE is the largest randomized controlled trial of diuretic strategies ever conducted in patients hospitalized for sudden worsening of heart failure. It is the first clinical trial completed by the National Heart, Lung, and Blood Institute's Heart Failure Clinical Research Network, which was established to promote innovative clinical research in heart failure.

"Despite decades of clinical experience, high-quality data supporting the safety and effectiveness of furosemide in acute heart failure are sparse," said G. Michael Felker, M.D., MHS, a co-principal investigator and an associate professor of medicine in the Divisions of Cardiology and Clinical Pharmacology at Duke University Medical Center, Durham, NC. "DOSE was an attempt to take the principles of evidence-based medicine-prospective, randomized, controlled trials-that we use to evaluate new drugs and apply them to old drugs like furosemide that we prescribe every day. These results give us a more precise understanding of the trade-off between relief of congestion and the risks of renal dysfunction."

Diuretics such as furosemide are used to treat more than 90 percent of patients who are hospitalized for acute decompensated heart failure (ADHF), to reduce fluid overload and make it easier to breathe. However, because high-quality data are not available to guide the use of furosemide, there is a great deal of variation among clinicians and hospitals in both the total dose and the way the intravenous drug is administered. Observational data have suggested that higher doses of furosemide may be associated with worsening kidney function, abnormal concentrations of sodium and potassium in the blood, low blood pressure, and death. In addition, some small studies have suggested that giving furosemide as a continuous infusion may be the safest and most effective approach, but most clinicians still use intermittent "bolus" dosing.

For the study, researchers recruited 308 patients with ADHF and fluid overload from nine regional medical centers and their referring hospitals in the U. S. and Canada. Patients were randomly assigned to treatment with either high- or low-dose intravenous furosemide (delivered at 2.5 times their usual daily oral dose or at the same level as their usual daily oral dose, respectively). In a double-randomization approach, patients were also assigned to intravenous dosing either every 12 hours or to a continuous infusion.

Researchers observed a trend suggesting greater global symptom resolution with high-dose furosemide over 72 hours. This was not associated with significant deterioration in renal function as measured by the median change in serum creatinine level from baseline to 72 hours (0.06 mg/dL for high-dose furosemide vs. 0.01 mg/dL for low-dose). Several secondary measures of the effectiveness of furosemide in relieving fluid overload, such a net volume loss and change in body weight, also tended to favor high-dose furosemide.
"These findings suggest that high-dose furosemide may be preferable to low-dose," Felker said. "The price seems to be a transient and relatively small deterioration in kidney function."

The infusion strategy used for delivering furosemide (intermittent vs. continuous) made no difference in the global measure of symptom resolution or in the change in serum creatinine level (0.04 mg/dL for both groups).

"Given that there has been no adequately sized clinical trial of diuretic dose or route of administration to date-and because of the encouraging trends in the high-dose group-these results may have an immediate impact on the care of hospitalized heart failure patients," said Christopher O'Connor, M.D., the study's senior co-principal investigator, a professor of medicine and director of the Duke Heart Center.

"We will change our standard of care today, and the results may be reflected in future guidelines."

DOSE was sponsored by the National Heart Lung, and Blood Institute. Drs. Felker and O'Connor have no potential conflicts of interest to report.

ACC2010特集