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Study reveals potential for NT-proBNP as a marker to predict cardiovascular risks from anti-inflammatory drugs

Roche has announced the results of a pilot study evaluating the use of N-terminal pro-B-type natriuretic peptide (NT-proBNP) in predicting the risk of cardiovascular adverse events (CV-AE) in patients treated with non-steroidal anti-inflammatory drugs of the COX inhibitor class.

Non-steroidal anti-inflammatory drugs (NSAIDs) – for example, acetylsalicylic acid and ibuprofen – are the best known inhibitors of COX (cyclo-oxygenase), an enzyme involved in the inflammation pathway. This inhibition provides relief from the symptoms of the inflammation process; for example, fever and pain. These drugs are routinely used to treat patients with osteoarthritis, rheumatoid arthritis and other pathologies associated with inflammation. However, studies with newer NSAIDs such as the selective COX-2 inhibitors (also called coxibs) have resulted in concern that there might be an increase in the risk of heart attack, thrombosis or stroke associated with long-term, high-dosage use of coxibs. Traditional NSAIDs (tNSAIDs) demonstrate comparable risks in observational studies.

Cardiovascular risk could be predicted

A pilot study¹ examined whether the risk of CV-AE could be predicted by measuring the NT-proBNP concentration in patients taking anti-inflammatory drugs. Baseline samples were measured by Elecsys proBNP (Roche Diagnostics) in 433 patients with osteoarthritis of the knees, with or without osteoarthritis of the hands, during an observational period of 200 days. Cardiovascular adverse events – including myocardial infarction, stroke, new or worsening of pre-existing arterial hypertension, congestive heart failure, and several less severe CV events – were monitored and retrospectively related to the use of coxibs, tNSAIDs and glucocorticoids.

NT-proBNP value of 100 ng/L as cut-off

The results of the pilot study showed that NT-proBNP values greater than 100 ng/L could be linked to an increase in the cardiovascular risk. Of the 433 patients, 82 mild-to-serious CV-AE were observed (18.9%) during the 200 days. Most of these events were observed in patients with NT-proBNP concentrations ≥ 100 ng/L. The risk for CV-AE in patients with NT-proBNP values ≥ 100 ng/L was 1.95-fold higher ($p < 0.05$) for patients treated with any of the inhibitors (tNSAIDs, glucocorticoids or coxibs), 7.41-fold higher ($p < 0.01$) for patients treated with coxibs (alone or in addition to tNSAIDs or glucocorticoids), and 3.74-fold higher ($p < 0.05$) for patients treated with two or more anti-inflammatory drugs. These patients were compared to those in the corresponding group with NT-proBNP values < 100 ng/L. For instance, in the coxib group only 9% of patients with NT-proBNP values < 100 ng/L showed CV-AEs compared to 41% of patients with NT-proBNP values ≥ 100 ng/L. NT-proBNP concentrations < 100 ng/L were associated with a negative predictive value (NPV) of 85.5% across all treatment groups. With the highest NPV of 90.9% the potential of NT-proBNP to predict CV-AE was strongest for the coxibs group.



Conclusions

The results of this pilot study confirm the potential value of NT-proBNP for risk stratification. "Based on the result of this study, it appears that patients with values below 100 ng/L of NT-proBNP have a low risk of CV-AE from treatment with anti-inflammatory drugs", supposed Evangelos Giannitsis, Department of Internal Medicine, University Hospital of Heidelberg, Germany – a key investigator of the pilot study.¹ When confirmed with additional, larger data sets with more reliable endpoints, monitoring NT-proBNP could provide a promising screening strategy for predicting cardiovascular risk in patients with osteoarthritis, and possibly other pathologies associated with the use of anti-inflammatory drugs. Further studies, however, are necessary. "This study suggests a new, important application that could offer routine screening and monitoring for the risk of cardiovascular adverse events to physicians and patients", Dr. Giannitsis said.

The complete results of the study are available in the publication¹ or can be obtained by contacting Roche.

1) Brune K, Katus HA, Moecks J, Spanuth E, Jaffe AS, Giannitsis E. The Concentration of N-Terminal Pro-B-type Natriuretic Peptide Predicts the Risk of Cardiovascular Adverse Events from Antiinflammatory Drugs: A Pilot Trial. Clin Chem. May 1, 2008 (electronic publication ahead of print), to be published in July 2008.

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