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Comparison of the diagnostic role of BNP and N-terminal proBNP in adults and pediatric patients

Brain natriuretic peptide (BNP) is a recently discovered cardiac neurohormone that is secreted in ventricular myocardium in response to increased ventricular wall tension caused by volume expansion and pressure overload (13). BNP belongs to the group of natriuretic peptides, which intensify natrium and water elimination through glomerulal filtration increase, inhibition of natrium reabsorption, and reduction of rennin and aldosteron release. Moreover, these peptides dilate capillaries, counteracting to vessel contracting factors, such as angiotensin II and vasopressin (5). As natriuretic peptides are synthesized as preprohormones, in serum we can find biologically active 32-amino acid peptides of BNP and its amino-terminal fragments (NT-proBNP). Many studies confirmed that BNP and NT-pro BNP are specific markers of ventricular dysfunction (2, 11, 18).

In adults with congestive heart failure (CHF), measurement of plasma BNP and NT-proBNP levels is increasingly used to aid diagnosis, assess prognosis, and adjust therapy (2, 11). The present studies show that evaluation of NT-proBNP in heart ventricles dysfunction is practically equivalent to BNP. The latest findings show even some NT-pro BNP diagnostic superiority, in comparison to BNP, due to its long stability in gained samples (18).

The most important and the most efficient diagnostic use of cardiac natriuretic peptides is the possibility of exclusion of left ventricle systolic dysfunction in patients with symptoms suggesting heart failure. In cases when NT-pro BNP limits are normal (<125 pg/ml), the heart failure can be excluded in 98–99%. Negative predictive value of NT-proBNP rises when connected with EKG. In symptomatic heart failure there is a well-defined correlation between NT-proBNP concentrations and progression of CHF expressed by New York Heart Association (NYHA) classification. Moreover, the BNP concentration is strongly correlated with left ventricle ejection fraction and enables to detect its decrease with good diagnostic sensitivity and specificity (18). Nevertheless, natriuretic peptides should not be used as independent diagnostic parameters, rather in wide clinical context, in compliance with interview and physical examination (18).

According to the data from literature the role of NT-pro BNP as a prognostic marker is already well grounded (3, 6, 8, 9, 12, 18). Kirk et al. (8), Hartmann et al. (6), Gardner et al. (3) and Kistorp et al. (9) in their papers underline that this is the best predictive index for both, sudden death and cardiac events in CHF patients. Many data also indicate the potential role of NT-proBNP in monitoring the treatment in patients with heart failure (21, 22). In the opinion of Richards et al. (21) and Wu et al. (22), the NT-pro BNP concentration reduction over 30% in the course of treatment is connected with better prognosis. The clinical value of this biochemical tests is confirmed by the fact of including them to guidelines of diagnosis and treatment of the European Society of Cardiology (4) and regarding their usefulness by American cardiac societies (ACC, AHA) (1) and National Institute

of Clinical Excellence in Great Britain (15). Nevertheless, according to the same guidelines, cardiac peptides evaluation can not substitute imaging techniques in heart failure diagnosis.

There is an increasing interest in BNP and its N-terminal pro-peptide not only in adults but also in pediatric patients. Although less common than in adults, heart diseases, especially congenital heart malformations, are significant cause of morbidity and death in infants and children. Recent studies suggest that the BNP ant NT-proBNP may be a useful diagnostic tools in children with heart disease.

Several authors tried to evaluate plasma concentration ranges in control healty infants and children. Results published by Nir et al. (16), Mir et al. (14), Rauh and Koch (20) showed that after marked increase in the first day of life, the NT-proBNP levels decreased and became stable after newborns period. The same authors (20) observed no differences in NT-pro BNP plasma levels between male and female children.

Many authors agree that BNP and NT-proBNP plasma levels might be a new additional diagnostic tool that could result in more precise diagnosis of congenital heart defects in children (10, 13, 16). Performed studies revealed a very strong negative correlation between left ventricular systolic function and BNP plasma concentrations. According to Mir et al. (13), Nir et al. (16), and Koch et al. (10), increasing plasma BNP concentration with decreasing left ventricular shortening fraction and significant relationship between NT-proBNP and left ventricular ejection fraction were found. Koch et al. (10) revealed that in children with left-to-right shunt, an increased plasma BNP correlated with shunt volume, systolic right ventricular pressure, mean pressure in the pulmonary artery and pulmonary resistance. These data are very consistent to the current conception of BNP released by the ventricular myocytes in response to volume and pressure overload. In pediatric patients with aortic or pulmonary stenosis most of the BNP plasma levels were within normal limits. Moreover, patients with tetralogy of Fallot featuring systemic pressure in the right ventricle and increased ventricular mass again had normal BNP levels (10). Patients with univentricular heart had higher plasma BNP levels than normal subjects.

In fact, there are a lot of data suggesting a much more complicated role for BNP than only to be a myocardial answer to pressure overload. Puddy et al. (19) indicated that plasma BNP could be a predictor of haemodynamically significant PDA in preterm infants. Yoshimura et al. (23) evaluated plasma BNP in 30 patients after total cavopulmonary connection and in 30 children after definitive repair for Fallot's tetrallogy. They found out that BNP levels during early postoperative period were significantly lower in patients from the first group than in patients from the second group. There are some data that B-type natriuretic peptides can be used for monitoring cardiotoxicity in children undergoing chemotherapy in course of malignancies (7). In the opinion of Nir et al. (17), natriuretic peptides have a great diagnostic value in children with predominant dyspnea symptom, helping in effective differentiation between cardiac and noncardiac causes.

In future, BNP may change the current strategies for clinical management of congenital heart disease. However, data on adult patients can not be directly transferred to children and the clinical impact of measuring plasma BNP levels has to be evaluated separately for each entity, before we can use this marker in clinical routine (10).

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SUMMARY

Brain natriuretic peptide (BNP) and its amino-terminal fragment (Nt-proBNP) are recently discovered factors of a heart origin. They are secreted in ventricular myocardium in response to increased ventricular wall tension caused by volume expansion and pressure overload. These peptides are widely recognized as heart failure markers. They can be also used for monitoring treatment. Nowadays, attempts to estimate their possible role in pediatric cardiology are made. In the future, BNP may change the current strategies for clinical management of congenital heart disease. However, data on adult patients can not be directly transferred to children

Porównanie diagnostycznych zastosowań BNP i Nt-proBNP u dorosłych i dzieci

Mózgowy czynnik natriuretyczny (BNP) i jego amino-terminalny fragment (Nt-proBNP) są niedawno odkrytymi peptydami pochodzenia sercowego. Wydzielane są przez mięśniówkę komór serca w odpowiedzi na wzrost napięcia ściany komór, spowodowany przeciążeniem objętościowym i ciśnieniowym. Czynniki te zyskały szerokie uznanie jako wskaźniki niewydolności serca u dorosłych. Mogą być również wykorzystywane do monitorowania leczenia. Obecnie podejmowane są próby zastosowania ich w diagnostyce kardiologicznej w pediatrii. W przyszłości BNP może zmienić postępowanie diagnostyczne u dzieci z wrodzonymi wadami serca. Jednakże dane uzyskane na dorosłych pacjentach nie mogą być bezpośrednio przeniesione na dzieci.