LISA-CHE

Measurement of the activity of Acetyl- and Butyryl-Cholinesterase

Literature Overview

Overview of some literature dealing with cholinesterase activities in connection with various diseases.

Butyrylcholinesterase activity, cardiovascular risk factors, and mortality in middle-aged and elderly men and women in Jerusalem.

Calderon-Margalit R[1], Adler B, Abramson JH, Gofin J, Kark JD.

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Abstract

BACKGROUND: The association of butyrylcholinesterase (BuChE) with Alzheimer disease and the association of this disease with cardiovascular risk factors raise interest in the association of BuChE activity with cardiovascular risk factors and mortality.

METHODS: A baseline cross-sectional study was conducted between 1985 and 1987, encompassing residents > or =50 years of age living in a Jewish neighborhood in western Jerusalem. Interviews were followed by examinations and nonfasting blood sampling (available for 1807 participants). Follow-up data to April 1996 on mortality and causes of death were obtained through record linkage with the Israeli Population Registry.

RESULTS: BuChE activity was inversely related to age and was positively associated with serum concentrations of albumin ($r = 0.35$; $P <0.001$), cholesterol ($r = 0.31$; $P <0.001$), and triglycerides ($r = 0.30$; $P <0.001$). Enzyme activity was associated with measures of overweight, obesity, and body fat distribution (e.g., body mass index, $r = 0.20$; $P <0.001$). In multivariate analysis, the associations of enzyme activity with serum cholesterol, triglycerides, and albumin persisted strongly. After adjustment by Cox proportional hazards regression for other predictors of mortality in this population, individuals in the lowest quintile of BuChE activity had significantly higher mortality than those in the highest quintile [hazard ratios (95% confidence intervals): all-cause mortality, 1.62 (1.15-2.30); cardiovascular deaths, 1.79 (1.05-3.05)]. The association was attenuated by introduction of serum albumin into the models.

CONCLUSIONS: This is the first study to report on the association between BuChE and mortality. The relatively strong association of BuChE with serum lipid and albumin concentrations requires elucidation. Our results suggest that low BuChE activity may be a nonspecific risk factor for mortality in the elderly.

Butyrylcholinesterase as a Diagnostic and Therapeutic Target for Alzheimer's Disease.

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Abstract

The serine hydrolase butyrylcholinesterase (BChE), like the related enzyme acetylcholinesterase (AChE), co-regulates metabolism of the neurotransmitter acetylcholine. In the human brain BChE is mainly expressed in white matter and glia and in distinct populations of neurons in regions that are important in cognition and behavior, functions compromised in Alzheimer's disease (AD). AD is a neurodegenerative disorder causing dementia with no cure nor means for definitive diagnosis during life. In AD, BChE is found in association with pathology, such as β-amyloid (Aβ) plaques, particularly in the cerebral cortex where BChE is not normally found in quantity. Up to 30% of cognitively normal older adults have abundant Aβ deposition in the brain. We have designed an imaging agent that can detect, through autoradiography, BChE-associated Aβ plaques in the cerebral cortex of AD brains, but does not visualize Aβ plaques in brains of cognitively normal individuals. Furthermore, in an AD mouse model with BChE gene knocked out, there are up to 70% fewer fibrillar Aβ brain plaques, suggesting diminished BChE activity could prove beneficial as a curative approach to AD. To that end, we have examined numerous N-10-carbonyl phenothiazines that are specific inhibitors of human BChE, revealing important details of the enzyme's active site gorge. These phenothiazines can be designed without potential side effects caused by neurotransmitter receptor interactions. In conclusion, BChE is potentially an important target for diagnosis and treatment of AD.

Cholinesterases as biomarkers for parasympathetic dysfunction and inflammation-related disease.

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Abstract

Accumulating evidence suggests parasympathetic dysfunction and elevated inflammation as underlying processes in multiple peripheral and neurological diseases. Acetylcholine, the main parasympathetic neurotransmitter and inflammation regulator, is hydrolyzed by the two closely homologous enzymes, acetylcholinesterase and butyrylcholinesterase (AChE and BChE, respectively), which are also expressed in the serum. Here, we consider the potential value of both enzymes as possible biomarkers in diseases associated with parasympathetic malfunctioning. We cover the modulations of cholinesterase activities in inflammation-related events as well as by cholinesterase-targeted microRNAs. We further discuss epigenetic control over cholinesterase gene expression and the impact of single-nucleotide polymorphisms on the corresponding physiological and pathological processes. In particular, we focus on measurements of circulation cholinesterases as a readily quantifiable readout for changes in the sympathetic/parasympathetic balance and the implications of changes in this readout in health and disease. Taken together, this cumulative know-how calls for expanding the use of cholinesterase activity measurements for both basic research and as a clinical assessment tool.

Low preoperative plasma cholinesterase activity as a risk marker of postoperative delirium in elderly patients.

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Abstract

BACKGROUND: delirium is a frequent neuropsychiatric syndrome affecting medical and surgical elderly patients. Cholinergic dysfunction has been implicated in delirium pathophysiology and plasmatic acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) activities are suppressed in patients with delirium. In this cohort study, we investigated whether these changes emerge during delirium or whether they are present before its onset.

METHODS: plasma activities of AChE and BuChE were measured pre- and postoperatively in consecutive patients ≥60 years old undergoing elective total hip replacement surgery. In addition to a comprehensive clinical and demographic baseline evaluation, venous blood samples were collected from each subject in the morning of hospital admission's day and in the morning of the first postoperative day. Delirium was screened daily with confusion assessment method (confirmed with diagnostic and statistical manual of mental disorders (DSM-IV)-TR).

RESULTS: preoperatively, plasma esterase activity was significantly lower in patients who developed delirium compared with the remaining subjects. Following surgery BuChE activity was lower in the delirium group but this difference disappeared after controlling for preoperative values. Plasma cholinesterase activity correlated positively with calcium and haemoglobin and negatively with total bilirubin and international normalised ratio.

CONCLUSION: plasma cholinesterase activity can be a useful candidate biomarker to identify subjects at greater risk of developing postoperative delirium.

Low Serum-Butyrylcholinesterase Activity as a Prognostic Marker of Mortality Associates with Poor Cardiac Function in Acute Myocardial Infarction.

Sun L, Qi X, Tan Q, Yang H, Qi X.

Abstract

BACKGROUND: Recently, butyrylcholinesterase (BChE) activity seems to have an independent prognostic role in acute coronary syndrome (ACS). However, the underlying mechanisms remain unclear. A previous study showed that serum BChE activity had a diagnostic value for chronic heart failure. This raises a question: whether BChE activity is associated with cardiac function in ACS, and if so, is this association related to the predictive value of BChE? The aim of this study was to determine the association between BChE activity with cardiac function assessed by Killip class and left ventricular ejection fraction (LVEF) in acute myocardial infarction (AMI) and to evaluate the independent prognostic role of BChE with consideration of these two indicators.

METHODS: A total of 350 consecutive patients with AMI were retrospectively included. Serum BChE activity was measured upon admission. All patients were divided into two groups according to median value of BChE activity. All-cause death was defined as endpoint. The prognostic value of mortality was assessed by using Cox regression analysis.

RESULTS: BChE activity was higher in patients with low Killip class (I or II) than that in those with high Killip class (III and IV) (7.0 +/- 1.3 or 7.0 +/- 1.5 vs. 6.2 +/- 1.6, p < 0.01). BChE activity was positively correlated with LVEF (r = 0.24, p < 0.001). During a mean follow-up period of 29 +/- 7 months, 25 patients died. BChE activity was significantly higher in surviving patients compared with non-surviving ones (7.0 +/- 1.4 vs. 5.7 +/- 1.3, p < 0.001). The survival rates were 89% and 97%, respectively, in the low and high groups of BChE activity. In a multivariate Cox proportional hazards regression analysis, after adjusting for potential confounders, BChE activity was an independent predictor of mortality after myocardial infarction [Hazard Ratio (HR) 0.65, 95% CI 0.46 - 0.91; p = 0.0131. However, when introducing Killip class and LVEF into the model, BChE activity was not in the equation.

CONCLUSIONS: Low BChE activity as a predictor of mortality in AMI might be related to its association with poor cardiac function.

Reduced serum butyrylcholinesterase activity indicates severe systemic inflammation in critically ill patients.

Zivkovic AR[1], Schmidt K[1], Sigl A[1], Decker SO[1], Brenner T[1], Hofer S[1].

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Abstract

Systemic inflammation is an immune response to a nonspecific insult of either infectious or noninfectious origin and remains a challenge in the intensive care units with high mortality rate. Cholinergic neurotransmission plays an important role in the regulation of the immune response during inflammation. We hypothesized that the activity of butyrylcholinesterase (BChE) might serve as a marker to identify and prognose systemic inflammation. By using a point-of-care-testing (POCT) approach we measured BChE activity in patients with severe systemic inflammation and healthy volunteers. We observed a decreased BChE activity in patients with systemic inflammation, as compared to that of healthy individuals. Furthermore, BChE activity showed an inverse correlation with the severity of the disease. Although hepatic function has previously been found essential for BChE production, we show here that the reduced BChE activity associated with systemic inflammation occurs independently of and is thus not caused by any deficit in liver function in these patients. A POCT approach, used to assess butyrylcholinesterase activity, might further improve the therapy of the critically ill patients by minimizing time delays between the clinical assessment and treatment of the inflammatory process. Hence, assessing butyrylcholinesterase activity might help in early detection of inflammation.

Reduced serum cholinesterase activity indicates splenic modulation of the sterile inflammation.

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Abstract

BACKGROUND: Sterile inflammation is an immediate and well-coordinated immune response to surgical injury. The cholinergic system plays a pivotal role in the inflammatory response. Induced inflammation stimulates the vagus nerve, which in turn activates anti-inflammatory nonneuronal processes. Serum cholinesterase (butyrylcholinesterase [BChE]) is an enzyme that hydrolyzes acetylcholine. Measuring the activity of the BChE in blood might indicate the level of the nonneuronal cholinergic activity. The spleen is a major organ of the immune system playing an important role during inflammation. A functional connection of the neuroimmune reflex has thus far been described only in experimental settings.

MATERIALS AND METHODS: In 48 patients receiving major pancreatic surgery, BChE activity was measured by applying point-of-care-testing, in addition to standard laboratory tests.

RESULTS: The BChE activity decreased in patients receiving surgery. This reduction emerged much earlier than changes in C-reactive protein concentration, an inflammatory biomarker broadly used in the clinical environment. A milder reduction in the BChE activity was observed in patients subjected to surgery with splenectomy than in those with a preserved spleen.

CONCLUSIONS: The use of the point-of-care-testing system for quick bedside diagnostics and the rapid effects of inflammation on BChE levels provide a method and a marker to facilitate the early detection of systemic inflammation. Furthermore, this study provides evidence that the experimentally documented neuroimmune interaction is part of the physiological response to surgery-induced sterile inflammation. Splenic function plays an essential role in modulating the cholinergic anti-inflammatory response.

Serum Butyrylcholinesterase Activity: A Biomarker for Parkinson's Disease and Related Dementia.

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Abstract

OBJECTIVE: This study aim to determine changes of serum butyrylcholinesterase (BChE) activity in PD patients and related dementia.

PATIENTS AND METHODS: Consecutive PD patients and healthy controls were included and clinical data were collected. Fast serum BChE activity was determined and compared between healthy controls and PD patients. Independent risk factors were performed for BChE activity, PD, and related dementia. The relationship between BChE activity and disease severity was also evaluated. Receiver operating characteristic (ROC) curves were obtained to explore serum BChE activity in distinguishing PD patients and related dementia.

RESULTS: Serum BChE activity mainly independently correlated with gender, albumin, triglyceride, body mass index, and PD. Serum BChE activity decreased in PD patients compared with healthy controls. Based on the ROC curve, the optimal cut-off point was 6864.08 IU/L for distinguishing PD patients, and the sensitivity and specificity values were 61.8% and 72.1%. It inversely correlated with Unified Parkinson's Disease Rating Scale score. BChE activity decreased in PD-related dementia compared with those without dementia. The sensitivity and specificity values were 70.6% and 76.3%, respectively, with an optimal cut-off point of 6550.00 IU/L.

CONCLUSIONS: Serum BChE activity can be regarded as a biomarker for PD and related dementia.

Serum butyrylcholinesterase predicts survival after extracorporeal membrane oxygenation after cardiovascular surgery.

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Abstract

INTRODUCTION: Risk stratification in patients undergoing extracorporeal membrane oxygenation (ECMO) support after cardiovascular surgery remains challenging, because data on specific outcome predictors are limited. Serum butyrylcholinesterase demonstrated a strong inverse association with all-cause and cardiovascular mortality in non-critically ill patients. We therefore evaluated the predictive value of preoperative serum butyrylcholinesterase levels in patients undergoing venoarterial ECMO support after cardiovascular surgery.

METHODS: We prospectively included 191 patients undergoing venoarterial ECMO therapy after cardiovascular surgery at a university-affiliated tertiary care center in our registry.

RESULTS: All-cause and cardiovascular mortality were defined as primary study end points. During a median follow-up time of 51 months (IQR, 34 to 71) corresponding to 4,197 overall months of follow-up, 65% of patients died. Cox proportional hazard regression analysis revealed a significant and independent inverse association between higher butyrylcholinesterase levels and all-cause mortality with an adjusted hazard ratio (HR) of 0.44 (95% CI, 0.25 to 0.78; P = 0.005), as well as cardiovascular mortality, with an adjusted HR of 0.38 (95% CI, 0.21 to 0.70; P = 0.002), comparing the third with the first tertile. Survival rates were higher in patients within the third tertile of butyrylcholinesterase compared with patients within the first tertile at 30 days (68% versus 44%) as well as at 6 years (47% versus 21%).

CONCLUSIONS: The current study revealed serum butyrylcholinesterase as a strong and independent inverse predictor of all-cause and cardiovascular mortality in patients undergoing venoarterial ECMO therapy after cardiovascular surgery. These findings advance the limited knowledge on risk stratification in patients undergoing ECMO support and represent a valuable addition for a comprehensive decision making before ECMO implantation.

Serum Total Cholinesterase Activity on Admission Is Associated with Disease Severity and Outcome in Patients with Traumatic Brain Injury.

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Abstract

BACKGROUND: Traumatic brain injury (TBI) is one of the leading causes of neurological disability. In this retrospective study, serum total cholinesterase (ChE) activities were analyzed in 188 patients for diagnostic as well as predictive values for mortality.

METHODS AND FINDINGS: Within 72 hours after injury, serum ChE activities including both acetylcholinesterase and butyrylcholinesterase were measured. Disease severity was evaluated with Acute Physiology and Chronic Health Evaluation (APACHE) II score, Glasgow Coma Score, length of coma, post-traumatic amnesia and injury feature. Neurocognitive and functional scores were assessed using clinical records. Of 188 patients, 146 (77.7%) survived and 42 (22.3%) died within 90 days. Lower ChE activities were noted in the non-survivors vs. survivors (5.94±2.19 vs. 7.04±2.16 kU/L, p=0.023), in septic vs. non-infected patients (5.93±1.89 vs. 7.31±2.45 kU/L, p=0.0005) and in patients with extremely severe injury vs. mild injury (6.3±1.98 vs. 7.57±2.48 kU/L, p=0.049). The trajectories of serum ChE levels were also different between non-survivors and survivors, septic and non-infected patients, mild and severely injured patients, respectively. Admission ChE activities were closely correlated with blood cell counts, neurocognitive and functional scores both on admission and at discharge. Receiver operating characteristic analysis showed that the area under the curve for ChE was inferior to that for either APACHE II or white blood cell (WBC) count. However, at the optimal cutoff value of 5 kU/L, the sensitivity of ChE for correct prediction of 90-day mortality was 65.5% and the specificity was 86.4%. Kaplan-Meier analysis showed that lower ChE activity (<5 kU/L) was more closely correlated with poor survival than higher ChE activity (>5 kU/L) (p=0.04). After adjusting for other variables, ChE was identified as a borderline independent predictor for mortality as analyzed by Binary logistic regression (P=0.078).

CONCLUSIONS: Lowered ChE activity measured on admission appears to be associated with disease severity and outcome for TBI patients.

The Association of Blood Cholinergic Esterases and Other Risk Factors on the Development of Postoperative Delirium

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Abstract

Study Objective: Delirium is an important complication after surgical intervention. One of the potential risk factors for cognitive disorders is deterioration in cholinergic neurotransmission including anticholinergic medications. We hypothesize that changes in blood cholinesterases (CHE) are associated with postoperative delirium.

Design: Prospective cohort study.

Setting: Postoperative delirium was assessed at least once daily in all included patients (n=103) preoperatively and on the first and third postoperative day during their stay on the intensive care unit (ICU) or in hospital.

Patients: undergoing a surgery on the head were included.

Interventions and Measurements: Postoperative delirium was assessed using the Intensive Care Delirium Screening Checklist (ICDSC). Blood samples were taken parallel to delirium testing and analyzed for serum anticholinergic activity (SAA) using radioactive competitive assay; acetyl- and butyrylcholinesterase activities (ACHE, BuCHE) were measured spectrophotometrically. Furthermore, patients' characteristics and medication were recorded. Logistic regression analysis was used to evaluate potential predictors of postoperative delirium.

Main Results: Postoperative delirium was identified in 32% of patients and was associated with significant longer duration of surgery, prolonged artificial ventilation, and longer stays on the ICU and in hospital. In contrast to ACHE and SAA, a significantly reduced BuCHE (mean of n=3 time points ± SD, U/l) was associated with delirious patients (2918.9 ± 645) compared to non-delirious (3484.0 ± 928.4). Reduction in BuCHE was associated with a higher number of administered drugs with greater anticholinergic potency (≥ 1, classified according to the Anticholinergic Drug Scale).

Conclusion: Patients with reduced pre- or postoperative BuCHE activity are at higher risk for the development of postoperative delirium, this may be because of polypharmacy with anticholinergic drugs.

The cholinergic system and inflammation: common pathways in delirium pathophysiology.

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Abstract

OBJECTIVES: To investigate whether delirium is associated with an unbalanced inflammatory response or a dysfunctional interaction between the cholinergic and immune systems.

DESIGN: Cohort observational study.

SETTING: General hospital orthopedic ward.

PARTICIPANTS: One hundred one individuals aged 60 and older with no previous cognitive impairment undergoing elective arthroplasty.

MEASUREMENTS: Incidence of postoperative delirium, plasma cholinesterase activity (acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE)) and inflammatory mediators (C-reactive protein (CRP), interleukin (IL)-1 beta, tumor necrosis factor alpha, IL-6, IL-8, IL-10) before and after surgery.

RESULTS: Thirty-seven participants developed postoperative delirium and had greater production of CRP and proinflammatory to anti-inflammatory ratio after surgery. In participants with delirium, but not in controls, preoperative levels of plasma cholinesterase activity correlated with ΔCRP (AChE: $\rho = 0.428$, $P = .008$ and BuChE: $\rho = 0.423$, $P = .009$), ΔIL-6 (AChE: $\rho = 0.339$, $P = .04$), and ΔP/A ratio (AChE: $\rho = 0.346$, $P = .04$).

CONCLUSION: Delirium was associated not only with an unbalanced inflammatory response, but also with a dysfunctional interaction between the cholinergic and immune systems. Comprehensive understanding of the relationship between the cholinergic and immune systems is crucial to developing new insights into delirium pathophysiology and novel therapeutic interventions.

The Effect of Cholinesterase Activity on the Diagnosis and Prognosis of Sepsis

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Abstract: Background: There are many biomarkers defined for systemic inflammation and sepsis. Cholinesterase and its biological role is not entirely known but in recent studies, it was seen that cholinesterase levels had a diagnostic value in predicting both sepsis and mortality. Objective: The purpose of this study is to establish the role of cholinesterase activity as a biomarker in the early diagnosis and treatment planning of sepsis which is an uncontrolled inflammatory response of the host to an infection. Materials and Method: This is a controlled, observational, and prospective clinical study and has been carried out on patients admitted to the intensive care unit with sepsis. The demographic features, the medical history and vital findings of the patients were recorded. According to the intensive care monitoring and treatment procedures, the complete blood count test, urine test and routine biochemical assessments particularly the CRP, procalcitonin and blood gasses tests were performed and the serum cholinesterase activity was assessed. The data was digitalized and then analyzed using the SPSS 15.0 software package. Results: The cholinesterase levels detected in the patient group were lower than the cholinesterase levels of the control group and there was a significant difference between the groups ($p< 0.001$). A statistically significant association was detected between the severity of sepsis and the cholinesterase levels of the patients. There was also a statistical relationship between the cholinesterase levels and being connected to mechanical ventilation and the use of vasopressors ($p<0.05$). There was a significant association between mortality and cholinesterase levels ($p= 0.009$). As the cholinesterase activity decreased the mortality rate increased. As a result of the ROC analyses performed to establish the diagnostic value of the patients' cholinesterase levels in predicting sepsis and morality it was seen that cholinesterase levels had a diagnostic value in predicting both sepsis and mortality. Conclusions: We believe that the cholinesterase activity investigated in our study is an extremely useful biomarker in the diagnosis and prognosis prediction of the sepsis syndrome that progresses with systemic inflammation.

Value of Serum Cholinesterase Activity in the Diagnosis of Septic Shock Due to Bacterial Infections.

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Abstract

BACKGROUND: We aimed to investigate whether serum cholinesterase (SChE) activity can be helpful for the diagnosis of septic shock and to evaluate its usefulness in comparison with procalcitonin (PCT) and C-reactive protein (CRP).

METHODS: A prospective single-blinded study conducted in an intensive care unit of university hospital. Patients were classified as having cardiogenic shock, septic shock, or hemorrhagic shock. We also included a control group without neither hemodynamic instability nor sepsis. For all included patients, SChE, PCT, and CRP were simultaneously sampled.

RESULTS: The comparison of sepsis markers between all groups showed that the mean values of PCT and CRP were significantly higher in patients with septic shock. However, SChE activity was significantly lower in this group. The SChE activity was found to be more accurate than PCT and CRP for the diagnosis of septic shock. In fact, an SChE activity ≤ 4000 UI/L predicted the diagnosis of septic shock with a sensitivity of 78%, a specificity of 89%, a predictive negative value of 97%, and a predictive positive value of 65%. However, the prognostic value of SChE activity was poor in multivariate analysis.

CONCLUSION: The SChE activity level was significantly decreased in patients with septic shock. However, its prognostic value is poor. Our results suggest that SChE activity is useful for the diagnosis of septic shock. Further studies are warranted to confirm our findings.