59. Pharmacokinetics of C1-inhibitor in patients with acute myocardial infarction

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Introduction: C1-inhibitor (C1-INH) is used for the treatment of patients with hereditary angioedema. Recently, beneficial effects of high-dose C1-INH treatment on myocardial ischemia have been reported in animal models and in man. We investigated the pharmacokinetic behavior of C1-INH in patients with acute myocardial infarction (AMI) to calculate the amount of C1-INH required for optimal efficacy.
Methods: Twenty-two patients received an intravenous loading dose followed by 48 hours of continuous infusion of C1-INH. Changes in the endogenous production of C1-INH were checked in sixteen control patients with AMI. A two-compartment model was used to estimate the Fractional Catabolic Rate (FCR), the Transcapillary Escape Rate (TER) and the Extravascular Return Rate (ERR) constants of C1-INH. Software that was specially designed for solving a system of dynamic differential and algebraic equations was used to fit the experimental data against the three-parameter model.
Results: With fixed values for TER and ERR (0.014 and 0.018 h^{-1} respectively), 20 of the 22 cases gave well-determined values for FCR, and simultaneous fitting resulted in an FCR of 0.011± 0.001 h^{-1} (median ± 95% confidence interval) versus 0.025 h^{-1} as reported in healthy controls. Simultaneous estimation of all three parameters resulted in ill-defined values of TER and ERR, but left the median value of FCR unchanged.
Conclusion: Dose calculation of C1-INH in patients treated with massive doses of C1-INH requires turnover parameters different from those found in healthy subjects, possibly due to suppression of continuous C1-INH consumption by target proteases.

60. Evaluation of a new routine hs-CRP method on the Synchron LX®20

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Background: High sensitivity CRP (hs-CRP) is considered as an important risk factor for coronary heart disease and introduction, as a routine laboratory parameter is obvious. To report reliable CRP results regardless of the clinical context, it is of course most practical if one CRP method is used for the complete measuring range. We report here the evaluation of a hs-CRP method for the Beckman Synchron LX®20 (measuring range 0.2-380 mg/l).
Methods: Routine C-reactive protein (CRP) and hs-CRP were both measured on the Beckman Synchron LX®20. A special measuring device Synchron LX®20 PRO, was implemented to allow analysis of the hs-CRP method. The hs-CRP method was compared (521 samples) with the BNA from Dade Behring and the IMMAGE from Beckman Coulter. The influence of sample turbidity, a known major problem of the present Synchron LX®20 CRP method, was also examined.
Results. Total imprecision (CV) remained less than 8% over the whole measuring range. In the low range (0-10 mg/l) very good agreement was found between the different hs-CRP methods based on Deming regression analysis and Bland-Altman plots, whereas in the high range (above 100 mg/l) large discrepancies between the methods were seen. The Synchron LX®20 PRO hs-CRP method was not influenced by sample turbidity.
Conclusions. Based on its performance in the low range, the Synchron LX®20 PRO hs-CRP method appears suitable for cardiovascular risk stratification. However, to allow the use of one CRP method for the complete measuring range, standardisation should be improved, especially in the high range.

61. Determination of the antioxidant capacity of polyphenols in red wine

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Introduction: Epidemiological studies have shown that moderate intake of red wine reduces the risk of coronary heart disease. It has been proposed that the antitherogenic effects is due to the antioxidant effect of polyphenols and ethanol. We have determined the reaction rates of superoxide with four different polyphenols and ethanol.
Methods: The superoxide reaction rates were determined at 37°C and pH 7.4 using competitive spin trapping and Electron Paramagnetic Resonance (EPR) spectroscopy.
Results and discussion: Ethanol did not scavenge superoxide. For the polyphenols we do find significant superoxide scavenging. For Catechine, Epicatechine, Gallic Acid and Quercetine we find rate constants of respectively 2.3 10^4, 2.2 10^4, 2.3 10^3 and 1.7 10^4 $(M.s.)^{-1}$. In order to estimate the capacity of the polyphenols to exert an antioxidant effect in vivo, it is necessary to see them in perspective of their respective plasma concentrations and a known antioxidant, e.g. vitamin C. The plasma concentration of the polyphenols is reported to be in the low nM range. In comparison: Vitamin C has a rate constant of 2.7 10^5 $(M.s)^{-1}$ and a plasma concentration of approximately 10 - 100 µmol/l. Therefore, the in vivo antioxidant effect of red wine polyphenols and ethanol is negligible in comparison to vitamin C.
Conclusions: At concentrations found in vivo, the antioxidant effect of red wine polyphenols and ethanol is negligible. The antiatherogenic effects must be caused by a mechanism other than direct scavenging of superoxide.