The effect of diethylaminobenzaldehyde, an inhibitor of aldehyde dehydrogenase, on primitive haematopoiesis during zebrafish embryonic development

73

ACH Ma, RHS Liang, AYH Leung
Department of Medicine, The University of Hong Kong, Hong Kong

Introduction: Aldehyde dehydrogenase (Aldh) are a group of enzymes involved in the biosynthesis of retinoic acid as well as the metabolism of amino acid, fatty aldehydes, ethanol and cyclophosphamide. Despite the widely reported expression in primitive haematopoietic stem and progenitor cells (HSPC), its function during haematopoiesis was unclear. Inhibition of Aldh with diethylaminobenzaldehyde (DEAB) in vitro delays differentiation and expand human HSPC due to inhibition of retinoic acid biosynthesis. In this study, we examine the effect of DEAB in vivo on zebrafish embryos with particular reference to its effect in primitive haematopoiesis.

Methods: Wild-type and transgenic [Tg(gata1:gfp), Tg(fli1:gfp)] embryos were treated with DEAB (1 μmol/L) between 1-cell to long-pec stage. Treated embryos were evaluated in terms of morphology, flow cytometry, in-situ hybridisation (ISH) and Q-RT-PCR.

Results: At 36 hpf, the intermediate cell mass where primitive haematopoiesis happens was significantly expanded without detectable vascular abnormality. Genes associated with HSC (*scl*, *lmo2*), erythropoiesis (*gata1*, and *embryonic hemoglobins*) and myelopoiesis (*spi1*) were also significantly up-regulated as shown by ISH and Q-RT-PCR. Upon DEAB treatment, there was a significant increase in GFP^+ cells (representing erythroid cells) in Tg(gata1:gfp) embryos, which could be ameliorated by concomitant treatment of all-trans retinoic acid (ATRA) [control: 4.39±0.11%; DEAB: 6.15±0.29%; DEAB+ATRA: 4.46±0.12%; P=0.012].

Conclusion: DEAB treatment induces expansion in primitive haematopoiesis in zebrafish embryos probably through the inhibition of Aldh and retinoic acid synthesis.

Intracerebral haemorrhage complicating anticoagulant therapy among Hong Kong Chinese

74

KC Teo[1], NR Mahboobani[1], R Lee[2], RTF Cheung[3], SL Ho[3], CT Tse[1], KH Chan[3]
[1]Department of Medicine, LKS Faculty of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[2]Department of Diagnostic Radiology, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[3]Research Centre of Heart, Brain, Hormone and Healthy Aging, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

Background: Anticoagulation is effective to prevent cardioembolism in patients with atrial fibrillation (AF) and prosthetic heart valves, but carries risk of potentially life-threatening intracerebral haemorrhage (ICH). The ideal international normalised ratio (INR) for Chinese patients on warfarin treatment is uncertain. We aimed to study the clinical and radiological characteristics of Chinese patients who developed acute ICH while on warfarin.

Methods: Patients with diagnostic code of ICH from January 2000 to December 2008 were reviewed, those who had ICH while taking warfarin were studied.

Results: Among 1114 patients with ICH, 54 patients had 58 episodes of ICH while taking warfarin. Four patients were excluded due to inadequate data, 50 patients (31 for AF, 14 for prosthetic heart valves, 5 for DVT) with 54 ICH episodes were studied. Their mean age was 72.2 (range, 34-94) years, 25 (50%) were male. Their mean INR on presentation with ICH was 2.6 (range, 1.2-6.8). Sites of ICH revealed on CT scan were supratentorial (32), infratentorial (17), multifocal (2), intraventricular haemorrhage (2), and unknown (1). The mean Glasgow Coma Scale score (GCS) at presentation was 12.26 (range, 3-15). Importantly, 27 (50%) of the 54 ICH episodes resulted in mortality; among the 27 ICH episodes that did not result in mortality, 23 (42.6%) episodes had good neurological recovery and 4 (7.4%) episodes had poor recovery. *t* Test revealed that patients with poor outcome (defined as mortality, or neurological disability leading to ADL dependency/ADL requiring moderate assistance) had shorter duration of warfarin therapy (P=0.014), lower GCS at presentation (P=0.000), greater pulse pressure at presentation (P=0.022), higher pulse rate at presentation (P=0.028), higher mean systolic BP on day 1 (P=0.018) but lower mean systolic BP (P=0.001), mean diastolic BP (P=0.018) and mean arterial pressure (P=0.001) on day 2, greater BP fluctuations on day 1 (P=0.001), and higher white blood count at presentation (P=0.015) than patients with good outcome (ADL independent/requiring mild assistance). Logistic regression analysis revealed that presence of intraventricular extension (P=0.000, OR=28.8), GCS <12 on presentation (P=0.005, OR=20.6) and smoking (P=0.047, OR=5.3) predicted poor clinical outcome.

Conclusion: Warfarin-related ICH accounted for approximately 5% of ICH in this hospital-based study and occurred with a mean INR of 2.6. It is a serious condition with mortality rate of 50%. INR on presentation did not affect clinical outcome.