

GENETIC POLYMORPHISM OF CYP2C9 AND WARFARIN DOSE REQUIREMENTS IN KOREAN PATIENTS

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The cytochrome P450 CYP2C9 is known to be responsible for the metabolism of S-warfarin. Six distinct polymorphisms in the genetic sequence encoding CYP2C9 protein have been identified to date. Several population-based studies indicated that 2C9*2 (Arg144Cys) and 2C9*3 (Ile359Leu) polymorphisms are associated with hypersensitivity to warfarin and bleeding complications. The variant *2 and *3 alleles are present in approximately 35% of Caucasian individuals; however, these alleles are significantly less prevalent in other ethnic populations. In our studies, genotypes of CYP2C9 in Korean population were characterized to investigate their relation with individual variation in warfarin dosages. Ninety-six Korean patients receiving warfarin were recruited. Genotyping of 2C9 genes was carried out by matrix assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry. Five of 96 subjects were heterozygous for CYP2C9*3 (allele frequency, 0.030; 95% confidence interval of 0.17 to 6.3%) and one subject with CYP2C9*2 allele was observed (allele frequency, 0.01; 95% confidence interval of 0.2 to 2.8%). No other known alleles including CYP2C9*4 and *5 alleles were observed. When reference single nucleotide polymorphisms (SNPs) published in dbSNP database at NCBI were also investigated, one polymorphism called CYP2C9*X was identified at the same allele frequency as 2C9*3 and found to be associated with CYP2C9*3. The significance of these CYP2C9 polymorphic alleles in warfarin sensitivity will be discussed.

살서제(Bromadilone,superwarfarin) 중독으로 인한 장기간의 응고장애

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서론: 살서제(殺鼠劑)로, 과거에는 쿠마린 유도체가 사용되었으나 내성으로 인해 더 이상 시판되지 않으며, 현재는 superwarfarin 그룹이 사용되고 있다. 이중 하나인 brodifacoum은 생체 반감기가 120일로 급성 중독에 의해 응고장애가 수주에서 수개월까지 지속될 수 있는 것으로 알려져 있다. 이에 살서제(bromadilone)중독 후 장기간의 응고장애를 보인 1례를 경험하였기에 보고하는 바이다.

중례: 26세 남자가 출혈경향과 두통을 주소로 내원 하였다. 과거력상 환자는 우울증으로 치료 중이었으며 내원 3개월전 사살기도로 살서제(bromadilone 300mg) 음독 후 나 병원에서 2주간 입원치료 하였고, 퇴원후에도 지속적인 잇몸출혈과 쉽게 멍이 드는 증상을 보였다. 내원당시 생체징후는 안정적이며, 양측 상지 진박외 부위에 혈종이 관찰되었다. 백혈구 11,300/mm³, 혈색소 11.8g/dl, 혈소판 261,000/mm³였으며, PT >180 sec, aPTT>180 sec, bleeding time 3분, clotting time 7분 이었다. 그 외 protein C activity <10%, protein S activity 24%, factor IV11%, factorVIII (negative), factorIX (negative) 몰 보였다. 입원 2일째부터 vitamine K₁ 10mg iv daily, HHP(총 13 pints) 투여하였으며 내원 26일째, PT(INR) 3.36, aPTT 52.4sec로 호전 양상을 보이고 있다.

