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TITLE

ASPIRIN RESISTANCE: THE ROLE OF POOR BIOAVAILABILITY OF ENTERIC COATED ASPIRIN

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Aspirin plays an essential role in the prevention of cardiovascular events in high-risk patients. A poor response to aspirin (aspirin resistance) is associated with increased cardiovascular events. 75 mg aspirin has been shown to be the lowest effective dose and more recently has been replaced by 75 mg enteric-coated aspirin although there is a paucity of data to support its use. In formal bioequivalence studies in healthy volunteers (three two week cross over studies with 25 volunteers in each) different enteric-coated aspirin preparations were found not to be bioequivalent to each other and none of the enteric-coated preparations were bioequivalent to 75 mg plain aspirin. All volunteers on plain aspirin had complete inhibition while 13% on enteric aspirin had incomplete inhibition of serum thromboxane (TxA_2) production. These outliers were the heaviest volunteers in the study. To confirm this finding in a clinical environment 244 cardiovascular patients on low-dose aspirin were recruited. After confirming compliance 4% were shown to have inadequate inhibition (TxA_2 >10 ng/ml). This non-responding group was significantly heavier than those responding (92±19kg vs 106±22kg). When they were switched to 75 mg plain aspirin only 1% of patients had an incomplete response and these were heavier than the responders (120±31kg). Enteric aspirin is less effective than plain aspirin possibly due to poor absorbance at the higher pH of the intestines. This is more pronounced in heavier patients especially those over 90 kg. The use of enteric-coated aspirin in heavier patients may be responsible for the phenomenon of aspirin resistance.