A RAPID AND SIMPLE METHOD FOR THE DETERMINATION OF MEXILETINE IN HUMAN PLASMA AND URINE BY GAS-LIQUID CHROMATOGRAPHY (GLC)

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There was a great interpatient variation in kinetics and plasma concentrations of mexiletine after intravenous and oral administration (Campbell et al, 1978). Plasma concentrations between 0.75 and 2.0µg per ml of the drug under normal urinary pH were usually effective to control ventricular dysrhythmias with minimum incidents of severe side effects (Campbell et al, 1975). Thus monitoring mexiletine levels in plasma should be of value in pharmacotherapy. Methods previously published for the measurement of mexiletine in plasma required chemical derivatisation prior to GLC analysis (Kelly, 1977). Such a technique is often time consuming for routine analysis.

We have developed a simple FID-GLC technique (using 3% OV17 on Gas Chrom Q 80-100 mesh in a 1.5metre, 4mm i.d. glass column at 150°C; nitrogen carrier at 30ml per min, hydrogen and air at 30 and 300ml per min respectively and a Perkin-Elmer Sigma 2 gas chromatograph fitted with a FID) which can measure therapeutic concentration of mexiletine in a 3ml plasma or urine sample without chemical derivatisation before GLC analysis. The method involves a preliminary extraction of the drug and internal marker (n,n diethyl-carbamyloxypyridine synthesised in own laboratory) into redistilled diethyl ether. The ether is evaporated to dryness and the residue is redissolved in redistilled methanol (10µl). An aliquot (2µl) is injected onto the GLC column.

The present method has several advantages over those previously reported: The stationary phase OV17 is more stable than the carbowax 20M used by Kelly (1977) at high temperature. It is a rapid and simple procedure and does not require butyryl derivative formation (Kelly, 1977) or acylation by heptafluorobutyric anhydride (Frydman, 1978) of mexiletine. It can be used adequately for routine monitoring of mexiletine in plasma after therapeutical dose (200mg or 400mg orally), and the minimum concentration measured accurately is 50ng per ml. This technique has been used to assess the bioavailability of Mexitil capsule and a modified preparation (encapsulating Mexitil capsule within a gelatin capsule). These capsules were prepared in a hospital pharmacy for a double blind trial involving the use of mexiletine and placebo. The bioavailability study was carried out using a cross over design in healthy volunteers under conditions of controlled acidic urinary pH as described previously for pethidine (Chan 1979). Results compared favourably with previously reported data on the kinetics of mexiletine after oral administration indicating that the present technique is reliable.

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