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CHLORPROMAZINE LEVELS IN PLASMA AND MILK OF NURSING MOTHERS

Neuroleptic drugs are not uncommonly prescribed during the puerperium for control of psychiatric symptoms and some have been positively identified in the milk of nursing mothers. Studies with chlorpromazine (Blacker, Weinstein & Ellman, 1962; Citterio, 1964) were carried out when assay methods were relatively non-specific. Chlorpromazine has since been used as a reference drug for most neuroleptics and can now be reliably assayed in plasma and in breast milk.

Using a modification of Curry's (1968) gas chromatography method, details of which have been published elsewhere (Wiles, Kolakowska, McNeilly, Mandelbrote & Gelder, 1976) we have measured levels of chlorpromazine and some of its metabolites in the milk and plasma of four nursing mothers receiving the drug.

Chlorpromazine (CPZ) was detected in all milk samples tested and levels ranged from 7 ng/ml–98 ng/ml. 7-hydroxy-chlorpromazine was detected in two patients and monodesmethylated chlorpromazine in one chloromazine sulphoxide was present in all samples. Plasma levels of CPZ ranged from 16 ng/ml–52 ng/ml and in two patients were lower than milk CPZ levels, though there was no clear or consistent relationship between plasma and milk CPZ levels. Two of the mothers had fed their babies. One baby showed no adverse effects and the milk CPZ level was 7 ng/ml; the other baby was reported to be drowsy and lethargic — the milk CPZ level was 92 ng/ml.

These preliminary data suggest that levels of chlorpromazine can be higher in milk than in maternal plasma and might be associated with drowsiness and lethargy in the baby. There could therefore be cause for caution in allowing nursing mothers receiving CPZ, and presumably related neuroleptic drugs, to breast feed their babies, especially during the first few weeks after delivery.

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COMPUTER ASSISTED DISPLAY AND ANALYSIS OF SEQUENTIAL PEAK FLOW DATA

In patients with chronic bronchitis or asthma, frequent estimates of peak expiratory flow rate (PEF) provide an objective measure of variation in airway obstruction, and have been used both for the assessment of a patient's progress on a particular therapy (Falliers, Bates & Berman, 1971) and also for clinical trials of bronchodilator drugs (Lahdensuo & Alanko, 1976). More recently Turner-Warwick (1977) has described characteristic patterns of diurnal variations of PEF in asthma. In studies which may extend over several weeks, the many readings accumulated may prove time-consuming to examine and plot by hand and consequently are seldom analysed in depth. We have developed a system of computer storage, analysis and display of such data, to enable it to be handled rapidly and automatically.

Our hardware included a mini-computer (PDP 11/10) with 16K core store and a disk, with cassette archiving. Displays were produced by a digital to analogue converter (AR 11) linked to an X-Y plotter (Bryans 26000). Programs were written in assembler (RT 11 – Macro). The first application of the system was in the analysis of data from a clinical trial of an anti-allergic agent in asthma. Over a seven-week period patients recorded on daily diary cards the timing and values of duplicate PEF readings, the time and dose of inhaled drugs taken and a subjective assessment of their symptoms recorded on a visual analogue scale. Information from each patient was input through the keyboard into a file created by the computer on the disk. This file containing information on all the patients under study could then be further processed or manipulated by the program without the need for repetitive keyboard input. The program is interactive and options can be selected by responses from the keyboard.

During the trial over 250 PEF readings were obtained from each patient. Four possible ways in which the program can display such data are shown in Figure 1. In the first, all readings are plotted sequentially, irrespective of time of day or use of a bronchodilator aerosol. In the second, separate plots are produced for readings at similar times on successive days; these can be distinguished by colour coding on the plotter. In the third, readings likely to have been influenced by prior use of a bronchodilator aerosol (in this example readings up to 4 h – the 'invalid interval' – after inhalation of salbutamol) are shown separately as crosses, the time being selected by command from the keyboard; readings taken during the night when patients were woken by asthma are shown as squares. In the fourth, the separate plots of readings at similar times on successive days exclude those points likely to have been influenced by inhaler use, and are shown separately as crosses. The frequency of inhaler use is also plotted along the horizontal axis of each display. Individual graphs of any of these types can be produced by the system in about three minutes. In this trial duplicate readings of PEF were made; a further feature of the program is that the higher, lower or mean of each pair of readings can be selected for analysis by command from the keyboard. A separate routine is available to plot symptom scores.

While conventional plots permit direct visualisation of the data, trends may be obscured by variation within each day. Cumulative sum techniques (cusums) (Woodward & Goldsmith, 1964; Chaput de Saintonge & Vere, 1974; Wohl, 1977) may allow clearer appreciation of such trends; a reference value is subtracted from successive PEF readings and the remainders are then plotted on the same time scale in cumulative fashion (Figure 2). The reference value can either be arbitrarily chosen or be the mean of a group of data, for example the values before treatment began. The program allows cusum analysis of points at a given time of day, with or without inclusion of points likely to have been influenced by previous bronchodilator administration. The cusum plot may be used to relate to drug usage the points at which trends of PEF improve or deteriorate. An indication of the significance of an appropriately scaled plot may be