TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Spironolactone

Spironolactone is marketed by G. D. Searle & Co. Ltd. under the trade name Aldactone-A.

It is one of a series of synthetic steroidal spirolactones which have a molecular structure resembling that of the adrenocortical salt-retaining hormone aldosterone. Doubtless because of this stereochemical similarity spirolactones compete for the sites in the renal tubule upon which aldosterone acts, and are therefore aldosterone antagonists.

Pharmacology

Aldosterone exerts an effect only on the distal part of the renal tubule, where it promotes the reabsorption of sodium from the luminal fluid and in exchange enhances the secretion of potassium ions. This action is prevented to a greater or lesser degree by spironolactone, but it has no action on water or electrolyte excretion in the absence of aldosterone such as occurs in adrenalectomized animals[1] or in patients with Addison's disease.[2]

Most of the excessive renal reabsorption of sodium in patients with oedema occurs in the proximal convoluted tubules and the ascending loops of Henle. The sodium retention promoted by aldosterone in the distal renal tubule plays only a secondary and often relatively insignificant part in the pathogenesis of the oedema formation. However, when there is excessive secretion of aldosterone the reabsorption of sodium in the distal tubule may assume significant proportions and the enhanced secretion of potassium may contribute to depletion of the total body potassium. This is likely to happen when the oedema is caused by a persistent condition which is unresponsive to radical treatment, so that symptomatic treatment by prolonged administration of potent conventional diuretics which act on the proximal convoluted tubule or the ascending limb of Henle is necessary. Thus hyperaldosteronism and significantly important retention of sodium in the distal tubule are especially common in patients with oedema and ascites secondary to hepatic cirrhosis,[3] and also in some, but not all, patients with nephrosis or long-standing oedema secondary to cardiac failure.[4 5]

Given by mouth spironolactone exerts its anti-aldosterone effect relatively slowly, not achieving a maximum response for two to three days. This activity persists for about the same length of time after administration is stopped. So spironolactone is most effective when given regularly each day over a period of time, in contrast with conventional diuretics, which have a short-lived action measured in hours and are usually administered intermittently in order to reduce the risk of potassium depletion.

Clinical Use

Given by itself spironolactone is a relatively weak diuretic, compared with the more conventional agents that act on the proximal renal tubule, though in some mild cases spironolactone alone eliminates oedema. More often it is not by itself potent enough, and it finds its main use in combination with the thiazides, mersalyl, ethacrynic acid, or frusemide in the treatment of patients with relatively refractory oedema,[6 7] particularly when caused by cirrhosis of the liver. In these cases spironolactone is given three or four times daily, and the more potent agent administered intermittently or even daily in particularly unresponsive cases. Not only does spironolactone enhance the natriuresis and water diuresis, it also diminishes the urinary elimination of potassium. However, the degree of potassium sparing is seldom sufficiently great to obviate completely the need for supplements of potassium chloride,[8] and furthermore the diuretic effectiveness of spironolactone is often enhanced by co-administration of potassium.[9] Thus in practice spironolactone has proved of most value in refractory cases when conventional diuretics have failed to eradicate the oedema. Such patients are likely to be found in hospital, where monitoring of the serum potassium level and the daily urinary excretion of sodium and potassium can be carried out. If this regimen of treatment is necessary after the patient has returned home the serum potassium level must be measured weekly until it is clear that a steady state has been achieved.

Like the thiazide diuretics spironolactone has been used as an antihypertensive agent,[10] but for this purpose it is expensive, and its action in lowering the blood pressure is disputed.[11 12]

Toxic and Side Effects

Spironolactone is seldom the cause of any toxic reactions. Rarely headache, rashes, ataxia, and mental confusion have been attributed to its use. It may, however, cause gynaecomastia, and in patients with severe renal insufficiency it may induce hyperkalaemia. It is much less likely to cause a rise in blood urea, as occurs in a proportion of patients given triamterene, an agent which has similar indications and a similar site of action, although not an aldosterone antagonist, being effective in adrenalectomized animals.

Cost and Dosage

Spironolactone is supplied as Aldactone-A in tablets containing 25 mg. of the active material. The dosage is 25–50 mg. three or four times daily.

The basic N.H.S. cost of Aldactone-A is 20s. 2d. for 30 tablets.

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