

03 - Drug interactions

Drug interactions

628 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 6 and diuretics). Older people demonstrate an exaggerated response to central nervous system (CNS)-active drugs such as benzodiazepines and opioids. This is partly because of an age-related decline in CNS function and partly due to increased pharmacodynamic sensitivity to these drugs (due to increased blood-brain barrier permeability).^{2,3} Therapeutic response to medication can also be delayed; for example, older adults may take longer to respond to antidepressants than younger adults.⁴ Older people may be more prone to developing serious adverse effects such as agranulocytosis⁵ and neutropenia⁶ with clozapine, stroke with antipsychotic drugs⁷ and bleeding with selective serotonin reuptake inhibitors (SSRIs).⁸ How ageing affects drug therapy (altered pharmacokinetics)^{9,10}

Absorption Gut motility decreases with age, as does secretion of gastric acid. This leads to drugs being absorbed more slowly, resulting in a slower onset of action. In general, the same amount of drug is absorbed as in a younger adult, but the rate of absorption is slower. **Distribution** Older adults have more body fat, less body water and less albumin than younger adults. This leads to an increased volume of distribution and a longer duration of action for some fat-soluble drugs (e.g. diazepam), higher concentrations of some drugs at the site of action (e.g. digoxin) and a reduction in the amount of drug bound to albumin (increased amounts of active 'free drug'; e.g. warfarin, phenytoin). **Metabolism** The majority of drugs are hepatically metabolised. Liver size is reduced in the elderly, but in the absence of hepatic disease or significantly reduced hepatic blood flow, there is no significant reduction in metabolic capacity. The magnitude of pharmacokinetic interactions is unlikely to be altered but the pharmacodynamic consequences of these interactions may be amplified. **Excretion** Renal function declines with age: 35% of function is lost by the age of 65 years and 50% by the age of 80. More function is lost if there are concurrent medical problems such as heart disease, diabetes or hypertension. Measurement of serum creatinine or urea can be misleading in the elderly because muscle mass is reduced, so less creatinine is produced. It is particularly important that estimated glomerular filtration rate (eGFR)¹¹ is used as a measure of renal function in this age group. It is best to assume that all elderly patients have at most two-thirds of normal renal function. Most drugs are eventually (after metabolism) excreted by the kidney. A few do not undergo biotransformation first. Lithium and sulphuride are important examples. Drugs primarily excreted via the kidney will accumulate in the elderly, leading to toxicity and adverse effects. Dosage reduction is likely to be required (see Chapter 8). **Drug interactions** Some drugs have a narrow therapeutic index (a small increase in dose can cause toxicity and a small reduction in dose can cause a loss of therapeutic action). The most commonly prescribed ones are digoxin, warfarin, theophylline, phenytoin and lithium.

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