

Drug Therapy in the Elderly

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This is based on the B.Pharm thesis of Ms. M. Scicluna B.Pharm. entitled 'Dosage forms in the Elderly'. (All drawings and tables are reproduced from her thesis.)

Introduction

In the last decades, life expectancy has substantially increased. The proportion of elderly in a population, vary according to the social, development and economic status of a country. In rich countries, it can now be as high as 16% and may become 25-30% by the end of the century, while in underdeveloped countries it may be as low as 4%. Comparing the percentage of population aged 60 and over in Malta to those of the major areas of the world as shown in Fig. 1, it is seen that 11.9% of the Maltese are over the age of 60.

In developed countries, the percentage increase in elderly subjects is a result of a falling birth rate and an increase in life expectancy in general related with the improvement in the country's hygiene and health services. The sit-

uation in Malta is similar to that of developed countries.

From data obtained through the demographic review, a study of the absolute number of elderly subjects in the Maltese population shows that it has increased considerably over the past 6 year, Fig. 2. In 1983, 13.04% of the population was over 60 years of age, and by the year 2000 this figure is expected to be 13.3%. Such figures emphasise that the needs of the geriatric patients will constitute an increasing important aspect of medical care of the future.

We are an aging society with both a greater relative proportion and a greater actual number of our population considered elderly. Old people form a disproportionately high part of the work of doctors in general practice. The health care needs are certain to increase and with that, as people live longer, they are more likely to suffer from one or two chronic health conditions such as heart disease, hypertension, diabetes and rheumatic diseases. Few of these diseases can be treated with just one drug which usually must be taken over a long period frequently for the rest of the patient's life. From research carried out in the United States it was found that the elderly take about 31% of all drugs dispensed.

Drug Therapy in the elderly

Drug therapy in the elderly is still uncertain, complicated and difficult. Numerous articles have been written about the overall impact of drugs and their use in the elderly. Guidelines for prescribing drugs are yet to be developed and perhaps that is the reason why adverse drug reactions occur more frequently in older than in younger patients. Prescribing for the elderly must be based on sound clinical principals to ensure that they are not denied adequate therapy where this is indicated, nor needlessly exposed to potentially toxic drugs. In addition, geriatric patients are likely to take their medication incorrectly, which may result in decreased efficacy or increased toxicity.



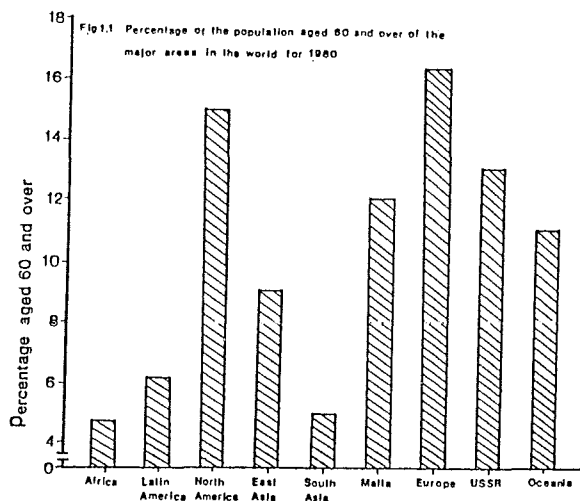


Fig. 1. Percentage of the population aged 60 and over of the major areas in the world for 1980.

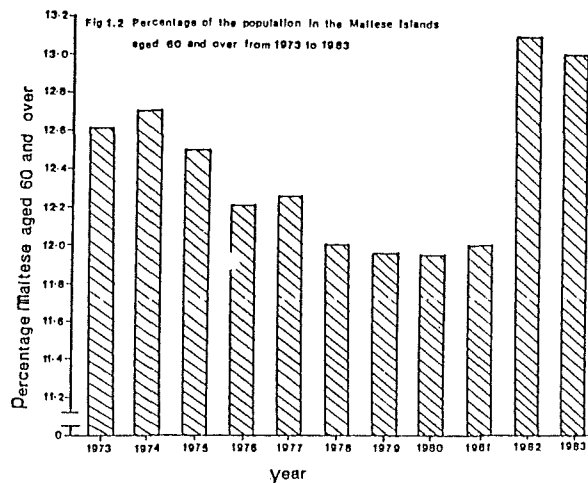


Fig. 2 Percentage of the population in the Maltese islands aged 60 and over from 1973 to 1983.

A new approach to minimize the undesirable effects of drugs is the intense application of pharmacokinetics and pharmacodynamic principles to geriatric drug therapy.

cially when the drug administered has a low therapeutic index as Digoxin. In these cases the dose is very critical and it is important to frequently monitor drug levels.

Table 1. Principals for Prescribing Drugs for the Elderly

1. Is drug therapy required?
2. Is the choice of drug correct?
3. Is the patient asked to take more drugs than he can tolerate or manage?
4. Which type of preparation is to be used?
5. Should the standard dosage schedule be modified?
6. Which side effects are likely to occur?
7. Is the drug correctly packed and labelled?
8. Can the medication be stopped?
9. Can self medication be achieved?

Pharmacokinetic and pharmacodynamic influence

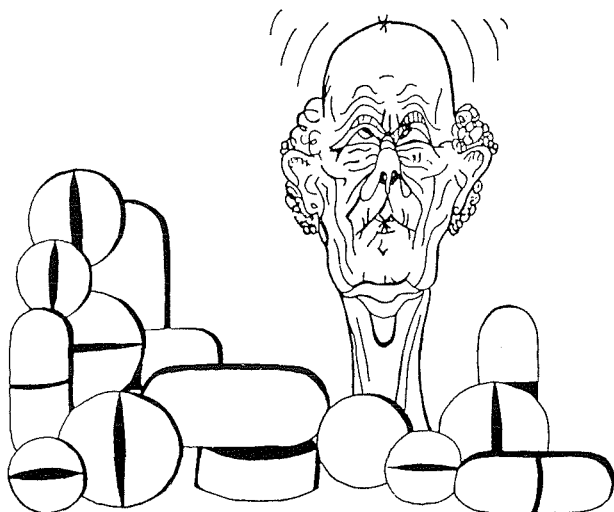
Though there is no evidence that drugs have a quantitatively different effect on the elderly patients than on younger patients, observations in practice suggest that with quite a number of drugs, pharmacokinetic characteristics deviate significantly in the elderly. Change in absorption, distribution, hepatic metabolism, excretion and other related physiological changes take place in the elderly. Because of these changes, the required dose differ in elderly patients, espe-

Absorption

A large number of drugs are administered by the oral route. Most drugs are absorbed by passive diffusion process which is partially dependent on the pH of the surrounding fluid. With advancing age, there is a general rise in gastric pH, reduction in gastric fluid volume, and in the intestinal blood flow. These changes cause a decrease in rate of disintegration and dissolution of tablets and capsules. Weakly acidic drugs such as acetaminophen and acetylsalicylic acid are less readily absorbed. Administration of these weakly acidic drugs in liquid form is better.

By contrast absorption of weakly basic drugs, such as Diazepam and Erythromycin is from the small intestine. Due to a decrease in the gastric emptying rate, and a decrease in intestinal motility, there is a delay or decrease in absorption of weak bases.

Active transport is impaired in old age due to altered cyclic AMP levels in senescent cells. Absorption of some sugars, vitamins and iron and potassium is diminished, as these are absorbed by active transport. This explains why elderly people develop iron deficiency anaemia, hypokalemia, or osteomalacia, and why combinations of potassium and diuretics are not usually very effective in counteracting hypokalaemia in patients on diuretics. Elderly patients on diuretics therapy usually require 94 mmol of potas-



sium supplement daily. Whatever the preparation used, serum levels of potassium should be monitored in all patients.

Drugs which increase bowel motility as laxatives, may prevent adequate absorption, particularly of slow-release preparations.

Distribution

Once the drug enters the blood stream it is distributed in the fluids and tissues of the body to reach sites of action. In the elderly there is a decrease in lean body mass relative to fatty tissues even in the absence of overall weight changes. The extracellular fluid remains unchanged whereas the intracellular fluid is reduced. Drugs which are mainly distributed in lean body mass or body water as Acetaminophen will demonstrate a higher blood level if the dose remains unchanged.

Fat soluble drugs as Phenobarbitone, Diazepam and Lidocaine, which normally are stored in fat tissue will have a greater volume of distribution in the elderly due to an increase in body fat with age. This will produce lower plasma levels and decreased intensity of action. A prolonged half-life of the drug reflecting a prolonged duration of action also results. If highly fat-soluble drugs are given in the usual dose and for a prolonged period of time, they tend to accumulate in the elderly and produce toxic effects. In these cases a wider dosing interval is necessary.

Although the volume of distribution changes with age for some drugs, it remains unaffected for others, such as Lorazepam, Nitrazepam and Propranolol.

Protein Binding

Plasma albumin levels decrease with age due to reduced albumin synthesis, increased albumin catabolism or both. Many drugs as, Warfarin, Phenytoin and Carbenoxolone are reversible bound to plasma proteins. Reduced plasma proteins allows more drug to diffuse in the circulation and a stronger pharmacological effect is observed. In the case of Phenytoin, reduced protein binding exposes a greater amount of drug to its sites of elimination, leading to a faster clearance from the body and a less intense pharmacological effect.

Hepatic Metabolism

Most drugs are metabolised via hepato monooxygenase enzymes. Subcellular and molecular mechanisms underly age-related decline in hepatic drug metabolism. Hypothesis lately has accumulated that strongly supports this evidence. A decrease in cytochrome P450 is responsible for oxidative drug metabolism, reduces total drug clearance and/or increases steady state plasma levels with repeated dosing in older patients. The half life of drugs such as Warfarin, Acetoaminophen, and Diazepam is increased. Other drugs such as Allopurinol, where its metabolite, oxyourinol, contributes significantly to its therapeutic effect, reduction in effectiveness may occur.

Additionally, hepatic blood flow may show substantial decrease with age; liver size decreases and related decreases in blood-flow clearances may occur.

Other changes in hepatic function, whether organic or induced by alcohol or drug ingestion, may present other clinical variances in the older individual.

Reduction in first pass metabolism is advantageous as lower doses of the drug are required, reducing the likelihood for toxic effects. Propranolol, chormethiazol, labetotol and glyceryl trinitrate show a substantial increase in peroral bioavailability in the elderly due to a low first pass clearance.

Sublingual Administration Absorption

Elderly complain of a dry mouth due to a decrease in salivation. When a drug is to be administered sublingually it will not dissolve readily and absorption through the mucous membrane is decreased. In these cases it is advisable to

Table 2. The Value of Various Dosage Forms in the Elderly

1. Mixtures	Colour, taste, stability, dysphagia, self administration.
2. Powders	Taste, stability, self administration, local irritation.
3. Tablets and Capsules	Colour, shape, size, self administration, obscure taste, dysphagia, packaging, confusion.
4. Parenteral	Onset of action, stability, pain.
5. Suppositories	Absorption, inconvenience, first pass effect
6. Aerosols	Local rapid effect, difficulty in use, fewer side effects.
7. Eye Preparations	Difficult self administration.
8. Ointments/Creams	Very easy to administer, compliance.

drink a glass of water before administering the drug.

Renal Excretion

The major age-related change responsible for altered pharmacokinetics is their reduced excretory ability. Both glomerular filtration and renal tubular secretion decline with advancing years. Kidney function is reduced by 30-40% in the elderly. Fortunately, decreases in renal clearance of drugs excreted mainly unchanged by the kidney (many antibiotics) often correlate well with creatinine clearance. Thus, correct determination of kidney function can diminish the effect of reduced kidney function and reduce the hazard of cumulation of drugs due to altered kidney function. This decrease capacity to eliminate drugs may lead to accumulation of certain drugs like chlorpropamide, aminoglycosides antibiotics and digoxin.

These age-related changes, make the elderly patient more prone to medication problems, particularly side effects from drug accumulation which is probably one of the main reasons for increased sensitivity to these drugs. It is clear that for certain drugs, dose reductions and in some cases dosage form change should be considered.

Since it is not yet possible to draw firm guidelines on all the effects of ageing, drug pharmacokinetics and pharmacodynamics, many more carefully designed studies are required involving normal healthy volunteers.

This is necessary for many drugs already undergoing wide use amongst the elderly and for the new drugs likely to be extensively prescribed.

Manufacturers should provide information for this kind and give recommendations for starting and maintenance dosage to elderly patients.

Such recommendations will provide guidelines to individualise therapy.

Compliance of elderly patients to different dosage forms

The elderly are prone to ingest medications only when they think they need them, making compliance a problem. Some elderly patients are unable to deal with drugs presented in unusual ways, however appropriate these may be. Others may find it difficult to use certain dosage forms and would prefer other forms of drug presentation.

The problem of non compliance increases with the number of drugs a patient is taking concurrently. According to Steward and Cliff (1972) the percentage of medication errors among the elderly ranges between 25% and 59%. Errors include dose omission, inaccurate dosage improper timing and sequences, inaccurate knowledge about the intended therapy or omission of medication.

Poor compliance can have serious repercussions. It can be life-threatening in cases of insulin or digoxin omission. Unintentional overdose may result in toxicity. To see whether such compliance problem exists with elderly Maltese patients, a 15-day survey was conducted to estimate the percentage non-compliance of such patients to different dosage forms. In the study 230 patients were interviewed at different Government Dispensaries using standard Questionnaires. Table 3 summaries the results.

This survey showed that polypharmacy is evident among uninstitutionalized elderly Maltese patients. The patients interviewed were prescribed an average of 3.8 different drugs during any one period, 57% were prescribed more than 4 different types of drugs.

Table 3. Compliance of Elderly Maltese Patients to Different Dosage Forms

Dosage Form	Number of Elderly Patients taking the dosage form	Number of Elderly Patients Non-Compliant to the dosage form	Percentage of Elderly Patients Non-Compliant to the dosage form
Tablets/Capsules	226	97	42.9%
Injections	32	3	9.4%
Aerosols	13	1	7.7%
Oral mixtures	11	3	27.3%
Suppositories	18	10	55.6%
Eye drops	7	3	42.9%
Ear drops	—	—	—
Ointments/Creams	—	—	—

Gibson and O'Hare (1968) suggested that the elderly can usually only manage to take three prescriptions at a time, and that this number of different drugs given to an elderly person should not be exceeded. 10.3% of the interviewed patients not compliant to tablets blamed the complex medication programme prescribed to them. Patient compliance may benefit from minimizing the complexity of the therapeutic regimen and restricting drugs to the absolute minimum essential number.



To alleviate compliance problems in the elderly who tend to forget

(1) a 'daily calendar' detailing each day's drug treatment in chronological order or

(2) a 'table identification card' bearing samples of the medication and details of the administered schedule. These can be used apart from standard instructions and suitable labelled and packaged medication for alleviating specific compliance problems in individual patients.

Major Reasons for Non-Compliance

1. Standards of labelling.
2. Packaging.
3. Social isolation.
4. Mental frailty.
5. Complex therapeutic regimens.
6. Nature of medication.
7. Side effects.
8. Deliberate deviation.
9. Lack of Doctor/Pharmacist report.
10. Inadequate patient education.

Little attention is paid to the patient's dislike of some dosage forms. The number, colour, size, shape, odour, taste and ease of administration of formulations should be considered before prescribing a medication schedule to an elderly patient. Suitable labelling and packaging of dosage forms should be adapted.

Intentional premature discontinuation of a course of treatment may occur for a variety of reasons. In a chronic asymptomatic illness such as mild hypertension, motivation may be lacking. Some elderly patients believe that once they begin to feel better, treatment can be taken as required or stopped altogether. Occasionally, therapy is stopped because the patient is concerned about habituation or the development of new symptoms which may be ascribed rightly or wrongly to the drug.

The incidence of uncomfortable side-effects such as gastric irritation with Indomethacin capsules, blurred vision caused by Pilocarpine eye drops, frequent urination with diuretics can lead to discontinuation of therapy. Patients should be informed about the possible side effects of a drug on commencing treatment.

Table 5. Maximizing Compliance

Direct	Careful prescription history Consider non drug therapy Use only essential drugs Make sure regimen is appropriate Review regimen every 6 months Reduce daily number of doses.
Observation	Look for mental status changes Look for anticholinergic effects Look for incontinence induced by high-potency diuretics Watch for drugs that can cause falls and fractures by impairing alertness, mobility, or normal cardiovascular tone and blood pressure.

Role of the Pharmacist

Pharmacists have an important role in educating the elderly to comply with the medication and not to engage in excessive self medication.

Elderly patients respond favourably to increased care, concern and interest. Traditionally they viewed the pharmacist as a vital link in the health care team. The pharmacist must insure that all medicaments dispensed are in adequate containers, strong enough to withstand frequent handling, but capped in a way that render medicine accessible to elderly patients. The instructions on the label should be clear, simple and specific.

Before dispensing the medication, the pharmacist must counsel the patient in simple language about each drug. Information should include: purpose of medication, method of administration, time of drug intake, selected side-effects, storage advice, warning etc. As oral instructions may be quickly forgotten, reinforcement with printed information is necessary. Apart from the labelling of dosage forms, the use of memory cards are important to increase compliance.

The pharmacist can also improve patient care by monitoring for dose related side effects and evidence of adverse effects. Prompt recognition of these adverse reactions may minimize patient discomfort. The pharmacist in addition can impact on medical care by providing accurate drug and pharmacokinetic information to physicians at the time decisions are made as to the selection of the most appropriate medication for a particular patient.

At the government dispensaries, no permanent pharmacist is present and the patient receive their medications sealed in a bag without

a word of advice. It can be worth considering, the possibility of patients receiving their free drugs from a retail pharmacy of their choice, where they can depend on the pharmacist present for drug related advice. Successful management of the elderly demands good communication between pharmacist and the patient.

Conclusion

The field of geriatric pharmacy is newly evolved, and most pharmacists have little or no formal education on geriatric study. Departments of pharmacy need to increase their research in this area and to develop educational programmes in geriatric, clinical pharmacology and therapeutics for both under-graduate and post-graduate curriculum.

We are an aging society with both a greater actual number and a greater relative proportion of our population considered elderly.

More knowledge is required about the aged and aging; and more dissemination of the sizeable and growing body of knowledge about health and disease in old age.

Scientists working in drug product development should consider creating more adequate dosage forms for the elderly patients.

There is absolutely no reason why in today's medicated society, the elderly patient should be condemned to that Shakespearean state of mere oblivion, "sans teeth, sans taste, sans everything."

References

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