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Pharmacokinetics in Older Person's

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ABSTRACT
Older person's have physiologic changes in organ function related to ageing or to specific diseased conditions. Aged person is characterized by impairment in the function of many regulatory processes that provide functional integration between cells and organs. Therefore, there may be failure to maintain homeostasis under conditions of physiological stress. The change in homeostatic ability disturbs different regulatory system. These changes can affect drug pharmacokinetic in older individuals. Pharmacokinetics is also called ADME (Absorption, Distribution , Metabolism and excretion) study. Pharmacokinetic changes includes increase in volume of distribution and reduction in renal and hepatic clearance. This article review focus on the main age-related physiological changes affecting different organ system and their implications for pharmacokinetics of drugs.
Keywords : Ageing, pharmacokinetics and homeostasis

I. INTRODUCTION

Ageing is the progressive accumulation of more or less random changes. Ageing is not a single entity but collective term representing the sum of cumulative local effects at the molecular cellular and tissue level. The most consistent is the time-related loss of function units. These units are small in structure but capable of performing the specific physiological activities (e.g. nephrons, alveoli or neurons.) Aged persons have impairment of some of the regulatory processes that give functional integration between cells and organs. Consequently, there is a failure to maintain homeostasis under conditions of physiological stress. Ageing produces anatomical and physiological changes which might lead to decompensation of the relevant system when they progress beyond threshold. Some main age-related physiological changes are discussed. This is followed by description of the age-related changes in pharmacokinetics.

Pharmacokinetics Implications

- **Drug Absorption**

Earlier studies reported some age-related effects including reduced gastric acid secretion[1,2] and gastric empting and reduced [3]absorption capacity of small intestine,[4] probably due to the effects of disease conditions, More recent reports have not confirmed these kind of changes in healthy person. [5,6,7,8]
The absorption of vitamin B12, Iron and calcium through active transport is reduced.[9,10]
Absorption of Levodopa is increased.
Transdermal absorption may be delayed in case of water soluble drugs.

- **First-pass metabolism and bioavailability**

Ageing is associated with a reduction in first-pass metabolism. This is probably due to the reduction in liver mass and blood flow[11]. As results, the bioavailability of drugs undergoing first-pass metabolismsuch as propranolol and labetalol can be significantly increased [12,13].
Several ACE inhibitors are pro-drugs and need to be activated in the liver. Therefore, their first-pass activation might be slowed or reduced with advancing age[14,15].

- **Drug Distribution**

As a significance of the age-related changes in the body composition[16], water-soluble drugs tend to have smaller volume of distribution (Vd) resulting in higher serum levels in older person's.
Lipid soluble or non-polar drug's have higher Vd with age.
The main effect of the increased Vd is a prolongation of half-life. Increased Vd andt1⁄2have been observed for some drugs as diazepam, lignocaine and thiopentone[17,18].
The reduction in Vd for water-soluble drugs tends to be balanced by a reduction in renal clearance (CL).

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Vd is affected by protein binding, acid drugs such as diazepam, warfarin and salicylic acid binds to albumin.
Basic drugs like lignocaine, propranolol binds to alpha1 acid glycoprotein.
Although no substantial age-related chances in the concentration of both there proteins have been observed.

- **Drug Metabolism and Excretion**

The primary organis liver and it's mass significantly reduced with advancing age.
The drug clearance is also depends on liver on the capacity to extract the drug from the blood passing through the organ and the amount of hepatic blood flow.
The latter is dependent on the metabolism capacity of the liver
Several studies have shown significantly reduction in the clearance of many drugs metabolism by phase-1 reaction in the liver[19,20]. The main factor is probably represented by the age-related changes in liver size and hepatic blood flow.
Some pharmacokinetics studies have reported that factors such as cigarette smocking do not induce drug metabolism in older people to same extent as in younger people[21].
Recently, it has been observed that reduction in renal function may significantly affecting not only renally excreted drugs but also drugs undergoing extensive metabolism in the liver[22,23]
A decreased in liver cytochrome P450 activity secondarily to reduce gene expression, have been observed in renal failure[24]. Therefore, the age-associated reduction in renal function might potentially affected drug metabolism in the liver.

II. CONCLUSION

The changes in pharmacokinetics occurs due to age-related physiological perturbations. These changes contribute to alter dose requirement in older person's.

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