

DRUG DISEASE INTERACTIONS IN HEART FAILURE

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INTRODUCTION

- Cardiovascular disease is the greatest cause of morbidity and mortality in the elderly representing a major health burden
- Dramatic increase of congestive heart failure (CHF) in the elderly (prevalent rate :10 per 1000 subjects over 65 years of age) in the Westernised countries
- Elderly subjects represent the targeted population for cardiovascular drugs

Heart disease and stroke statistics: 2005 update. Dallas (TX) . American Heart Association 2004

- Controlled randomized trials for the oldest old in order to provide standardized protocols for safe drugs administration and drug overall costs
- Altered homeostatic and homeostenotic capacity, heterogeneity, environment, age-related changes relevant to drug pharmacology of the oldest old
- The frail elderly with comorbidity, polipharmacy, enhanced disability and high risk of drug-drug interactions, drug-disease interactions and adverse drug reaction (25% ADR prevalent rate)

AGE - RELATED CHANGES IN PHARMACOLOGY

Altered pharmacokinetics due to :

- Impaired absorption (decreased absorptive surface, decreased splanic blood flow, increase gastric Ph)
- Impaired distribution (decreased total body water, decreased lean body mass, increased body fat, altered protein binding and albumin levels)
- Altered liver and kidney clearance (reduced organ mass and blood flow with impaired metabolism and excretion)

Altered pharmacodynamics due to:

- Altered tissue sensitivity (altered receptor number and affinity, impaired second messenger functioning , cellular and nuclear responses)

Mangoni et al. Drug Aging 2005

DISEASE - RELATED CHANGES IN PHARMACOLOGY

- Cardiac and vascular stiffening (altered diastolic relaxation performance, remodeling and vascular resistance , enhanced calcification of conduction system and impaired cardiac output)
- Blunted Beta adrenoreceptor response (impaired orthostatic activation)
- increased fluid retention (altered cardiac pre load, afterload, aedema, systemic congestion)

Raza J.A et al .Intern. J. of Cardiol 2002

NON CARDIAC DRUG INTERACTIONS IN CHF

- NSAIDs
- Corticosteroids
- High sodium drugs and sodium salts
- Beta agonists
- Trycyclic antidepressants
- Anticholinergics
- Intraconazole
- Clozapine
- Herbal remedies

Amabile CM et al. Arch Intern Med 2004

CARDIAC DRUG INTERACTIONS IN CHF

- Beta blockers
- Calcium channel blockers
- Loop diuretics
- Digoxin
- Antiarrhythmics

Aronow W.S. et al. Cardiology 2007

THE FRAIL ELDERLY

Comorbidity

- Drug disease interactions
- Failure to thrive
- End stage heart failure

Polipharmacy

- Drug-drug interactions
- Adverse drug reactions

Rockwood k et al. J. Geront A Biol Sci Med. Sci 2005

STATE OF ART ON THE ISSUE

- The updated De Beers criteria for potentially Inappropriate Medication Use in Older Adults provide plan interventions for drug related costs and appropriate prescriptions?
- Few controlled randomized trials for the frail and old to assess targeted patient outcomes
- Empirical use of cardiovascular drugs based on studies of young or younger old subjects, personal experience and common sense (Narrative Medicine)

?Fick D et al . Arch Med intern 2003

TAKE HOME MESSAGES

It is a multisensorial experience:

EYE : clinical judgments, literature data on controlled randomized trials, updated De Beers criteria

EAR : Narrative medicine, common sense and experience

TOUCH : technology support system available for drug interactions immediate detection

... caution and a geriatric spirit in order to fulfill the drug related problem in the elderly as emerging health care quality and safety issues for this decade

Disease oriented model	Tailored model
<ul style="list-style-type: none"> • The clinical decision is based on diagnosis, the Trapy, prognosis and prevention • Specific biological factors generate specific diseases codified by a specific therapy • Bio psyc social and enviromental factors are secondary • The expected results are modulated Healing is the main goal to obtain • on the disease 	<ul style="list-style-type: none"> • The clinical decision is modulated on priorities and patient's choices • The clinical conditions are the results of genetic factors, pathologies, environmental, bio, psyco-social factors • The treatment is addressed to improve the health and to facilitate the achievement of realistic outcomes • Syntoms and disturbances are the main target of treatment even if not strictly related to the disease • The expected results are modulated on patient's choices • The survival is the main goal to achieve
TINETTI 2006	

disease-oriented Model	tailored Model
<p>La decisione clinica è basata sulla diagnosi, sulla clinica, sulla prognosi e sulla prevenzione di una specifica patologia</p>	<p>La decisione clinica è basata sulle priorità individuate e sulle preferenze del paziente</p>
<p>A fattori biologici bene identificati corrispondono patologie specifiche che hanno ben codificati trattamenti farmacologici, mirati al meccanismo fisiopatologico sotteso alla malattia</p>	<p>Le condizioni cliniche sono il risultato complesso di un intreccio tra fattori genetici, patologici, ambientali, psicologici, mentali, sociali e altro ancora</p>
<p>fattori psico-sociali, ambientali e psicologici sono secondari</p>	<p>Il trattamento è indirizzato a fattori modificabili che contribuiscono alla salute del paziente o che impediscono il raggiungimento di obiettivi realistici</p>
<p>i risultati attesi sono ritagliati sulla patologia considerata</p>	<p>sintomi e disturbi sono bersagli primari di trattamento anche se non strettamente legati a patologie definite</p>
<p>la guarigione e la sopravvivenza sono obiettivi principali</p>	<p>i risultati attesi sono modulati in base alle preferenze della persona</p>
	<p>La sopravvivenza è uno degli obiettivi da raggiungere</p>
da M. Tinetti, 2006	

