MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

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Pharmacovigilance and the elderly

Some proposals for improvement

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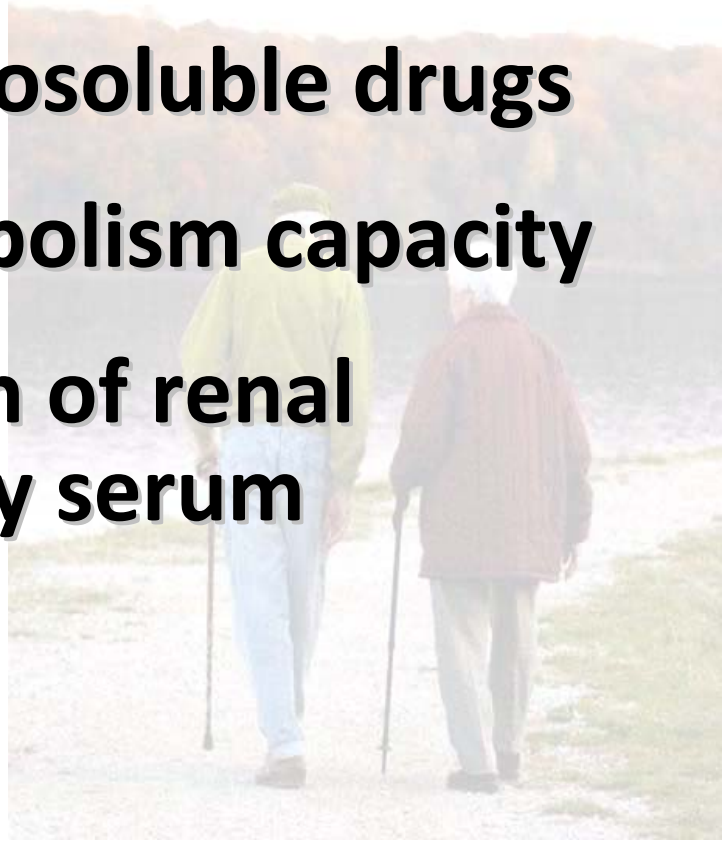
- General considerations
- Some data from the regulatory perspective
- Some proposals for improvement

Special aspects of medicines in the elderly

Pharmacokinetics

- Higher distribution of liposoluble drugs
- Decreased hepatic metabolism capacity
- Progressive deterioration of renal function (not reflected by serum creatinine)



Special aspects of medicines in the elderly

Pharmacodynamics

- Less studied and probably more relevant
- Decrease hemostatic response (postural control, termoregulation, cognitive function).
- Altered by a number of drugs: psychopharms, anticoagulants…

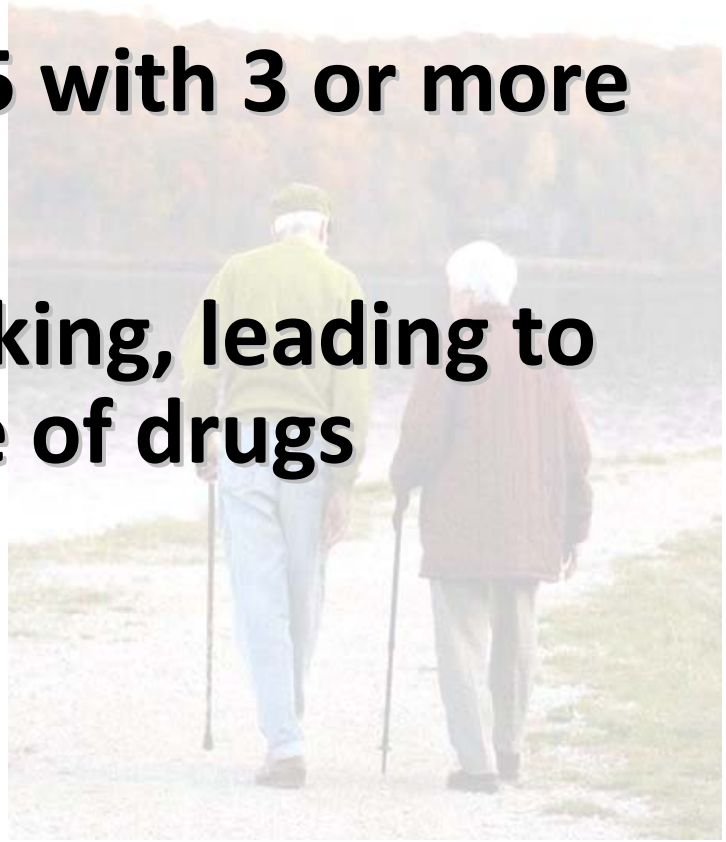
Special aspects of medicines in the elderly

- Functional status (calcium antagonists in patients with chronic constipation)
- Cognitive status specially relevant in frail patients
- Co-morbidities, which leads to polymedication and relevant drug interactions

Special aspects of medicines in the elderly

Polymedication and drug interactions

- 35% of patients above 65 with 3 or more concomitant illnesses
- Integral review often lacking, leading to duplications and cascade of drugs



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BiobadaDERM

Some data on Spanish Registries

- Registry of patients with psoriasis taking biologicals or classic therapy
- Patients being followed: 1,042
- All adverse events recorded

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BiobadaDERM

Some data on Spanish Registries

- **30% patients ineligible for pivotal CT, being age (>70 years) one of the criteria**
- **Higher risk of serious adverse reactions, being age the best predictor:**
  - **16 per 1000 patient-years (95%CI: 11-24) in eligible population**
  - **42 per 1000 patient-years (95%CI:28-62) in non-eligible population**

Accepted for publication in Archives of Dermatology

Some data on Spanish Registries

- Registry of patients with rheumatic inflammatory diseases treated with biologicals
- Patients being followed: 4,851
- All adverse events recorded

Some data on Spanish Registries

- **Age at treatment predicts reason for discontinuation of TNF antagonists:**

  "In older patients, adverse events were the most common reason for discontinuation regardless the diagnosis of the patient and TNF antagonist molecule, whereas in the younger group, the most common cause of discontinuation was inefficacy"

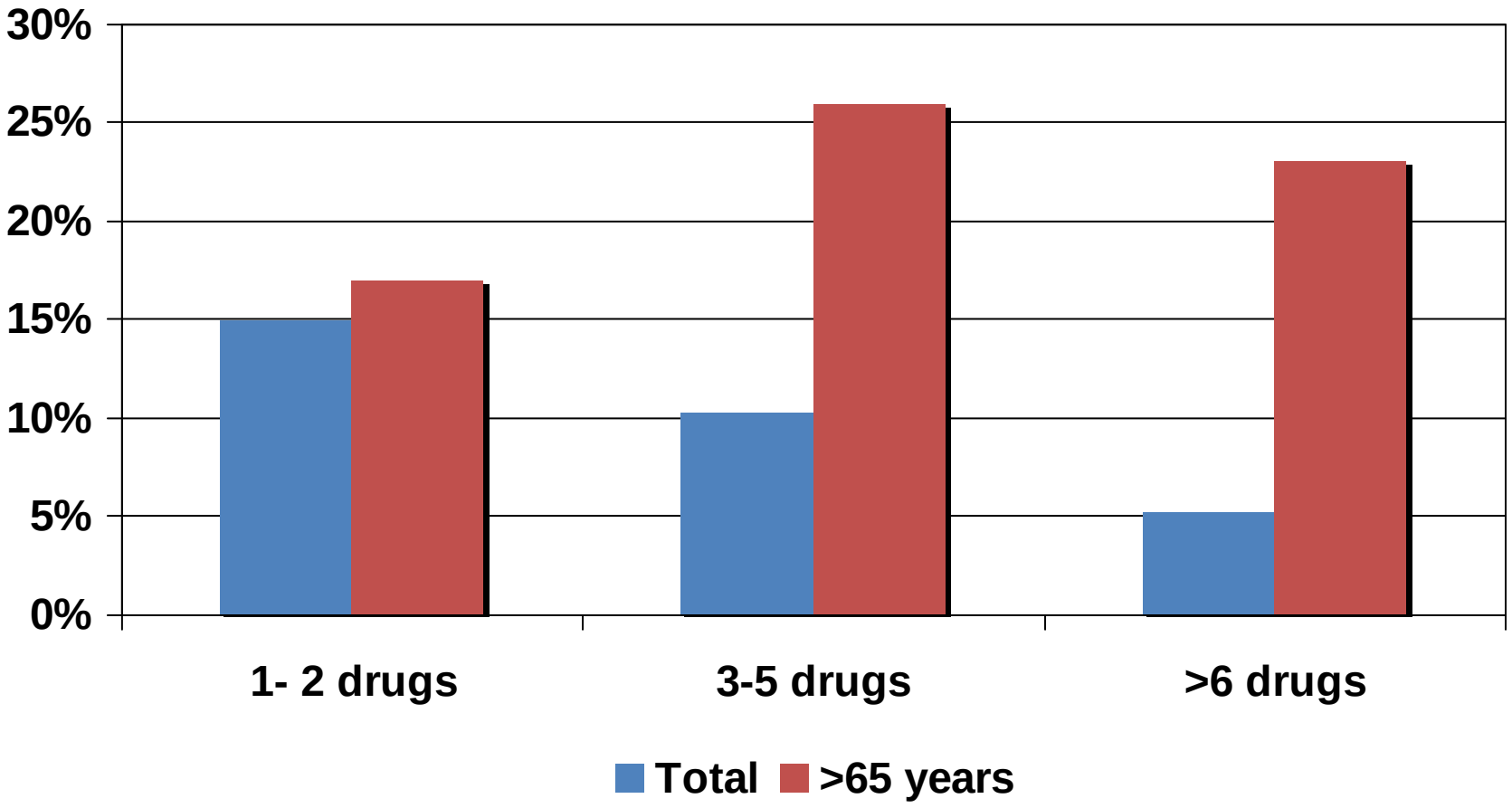
  Rheumatology 2011; 50:1990-2004

Some data on Spanish Registries

Database of electronic healthcare records

- Prevalence study on number of medications patients receive
- Analysis of prescriptions in the month previous to the cut-off date
- Information on 380,837 patients

Data on number of drugs received
BIFAP database



Current regulatory situation

- Are the elderly accurately represented in clinical trials?
- Does the marketing authorisation / SPC provide helpful information for prescribing in the elderly?
- What about risk management plans?

Clinical trials authorised by AEMPS (1993- 2009)

- **Elderly population included in 30% of the trials**
- **The percentage has increased over time from 14% of CT in 1993 to 50% of CT in 2009**

Spanish survey on SmPC

- **SPC specific information on the 100 drugs most consumed by the elderly:**
  - **52% specific pharmacokinetics information**
  - **6% specific pharmacodynamics information**
  - **81% specific posology**
  - **46% specific warings**
  - **16% specific interactions**
  - **15% specific information on ADRs**

Opportunities to improve PhV for elderlies

New European legislation

- Direct patient reporting
- Additional monitoring of certain medicines
- Signal detection using Eudravigilance
- Risk management plans
- Information in patient leaflets

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

9 November 2011
EMA/838825/2011
Human Medicines Development and Evaluation

Informal PhVWP, Warsaw:

Outcome of discussion on pharmacovigilance in older population: key points for consideration

The PhVWP, at its informal meeting in Warsaw on 6-7th October 2011, dedicated a session to pharmacovigilance in the older population, and discussed the key points for consideration outlined below, which could improve the demonstration of an appropriate benefit/risk balance in this population.

Pharmacovigilance in elderly (1)

Spontaneous reporting

- New methods for detecting signals on drug interaction in the databases
- Encourage and improve reporting of ADR (age)
- New approach to categorise seriousness of ADR (functional and cognitive impairment)
- Simplification of the recording of concomitant medication
- Facilitation of patient reporting

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Spanish Pharmacovigilance System

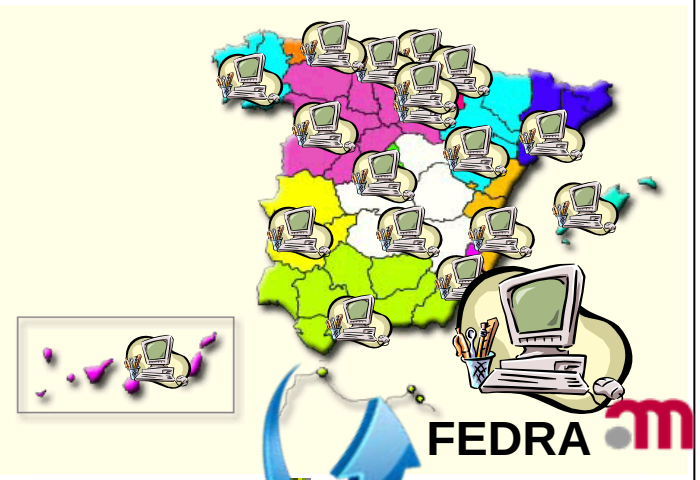
HCP

80% direct reports

Web, postal mail

Citizens

Eudravigilance



Regional Centers

Pharmacovigilance in elderly (2)

Risk Management Plans

- For indications which explicitly provides for use in the elderly, sufficient data should be included for the authorisation of the medicine
- If there is the possibility of post-marketing exposure of the older population despite their lack of representation in clinical trials, the RMP should reflect that there is no information available, and posautorisation studies requested

Pharmacovigilance in elderly (2)

Risk Management Plans

- Monitoring should be foreseen for renal impairment, frailty, fractures and other relevant aspects not covered in the CT (exclusion criteria and excluded comedications)
- Drug utilisation studies could be helpful to confirm that the age distribution of the real life population corresponds to the clinical trial population
- Specific risk minimisation material to be considered

Pharmacovigilance in elderly (3)

Post-authorisation studies

Post-authorisation clinical effectiveness studies (observational databases to be explored for this purpose)

Pharmacovigilance in elderly (4)

PIL & SmPC

- Clearer information on interactions
- Standard SmPC text for encouraging periodic medication review in chronic treatments
- Inform on data available from elderly population
- Specific information material for patients with cognitive/functional impairment