Current Treatments for Dementia and Future Prospects

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Dementia

Cognitive

- Memory
- orientation
- language
- other cognitive abilities
    - planning
    - organising
    - problem solving
- praxis

Non-cognitive (BPSD)

- behavioural symptoms
    - agitation
    - Wandering
    - apathy
- psychotic symptoms
    - delusions
    - hallucinations
- affective
    - depression

Treatment of cognitive symptoms

Available drugs

- Acetylcholinesterase inhibitors (ACHIs)
  - donepezil (Aricept)
  - rivastigmine (Exelon)
  - galantamine (Reminyl)
- NMDA agonist
  - memantine

A problem…..

- Evidence is confusing
  - 5 outcomes
  - 4 drugs
  - 3 diseases
  - 2 stages

Efficacy of AChIs

Drug	Dose	Number needed to treat	Adverse effects
donepezil	10mg	4	+
rivastigmine	6mg bd	5	+++
galantamine	12mg bd	7	+

- Sustained effects up to 240 weeks
  - Improved over baseline for 38 weeks
  - Benefit over placebo sustained

- mild-moderate dementia
  - Delays functional decline in by 5 months (NNT 7)
  - No effect on Quality of life

- moderate-severe dementia (MMSE 5-17)
  - Improve global state, preserves ADLs, and reduce carer stress

Memantine

- Moderate to severe AD.
  - Marginal improvements on cognition and ADL
- Mild to moderate AD.
  - Marginal improvement on cognition
    - ADAS-cog 0.99 (0.21 to 1.78)
  - no significant effect on behaviour or activities of daily living
- Few side effects

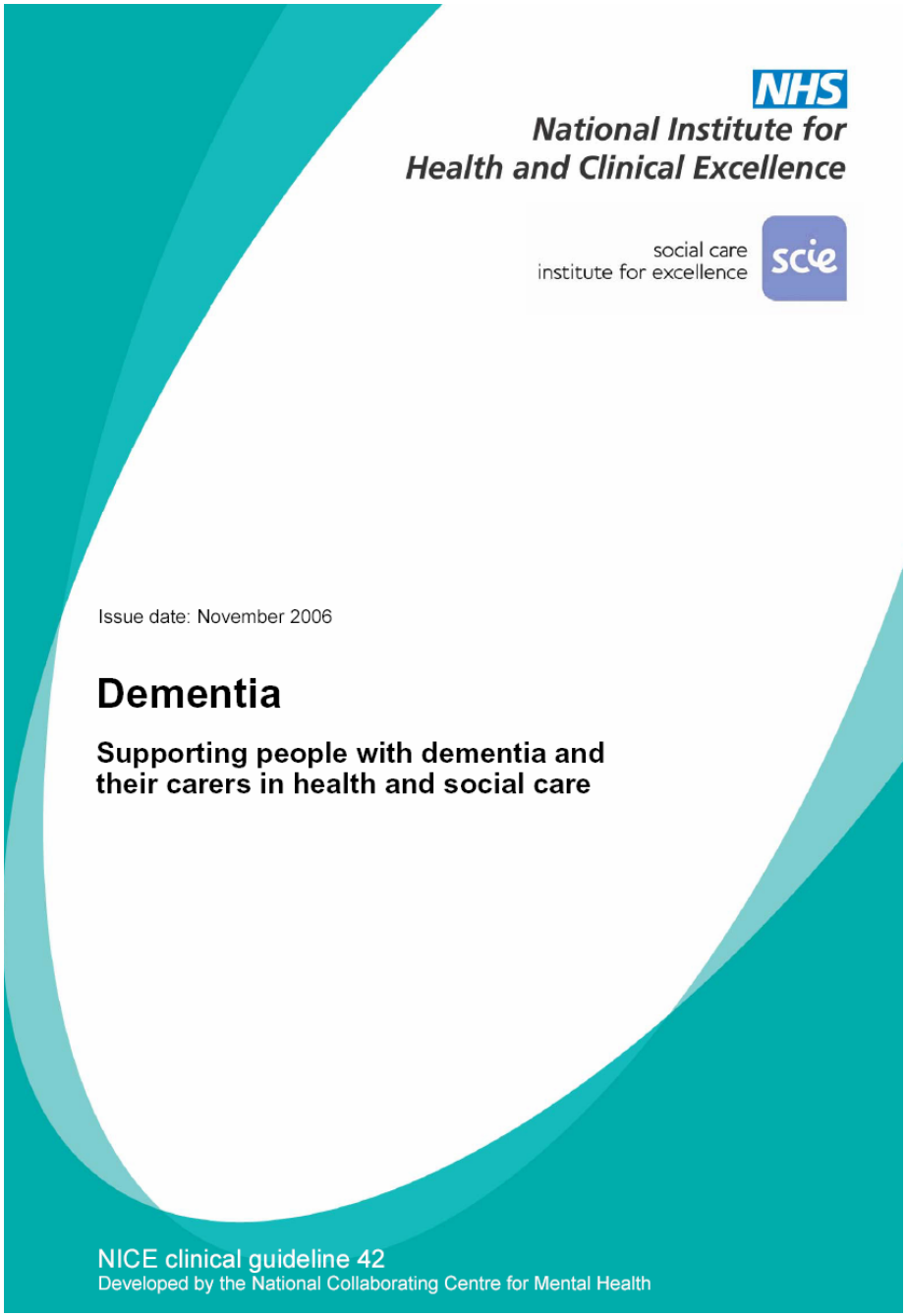
Other treatments for dementia

current evidence-base

drug	Alzheimer's	vascular
oestrogen	+/-	+/-
Vitamin E	-	-
Ginkgo biloba	+/-	?
NSAIDS	?	?
Statins	?	?

Non-drug treatments

- Reminiscence therapy
- Music therapy
- Reality orientation
- Exercise
- Cognitive training


NHS
National Institute for
Health and Clinical Excellence
social care
institute for excellence
scie
Issue date: November 2006
Dementia
Supporting people with dementia and
their carers in health and social care
NICE clinical guideline 42
Developed by the National Collaborating Centre for Mental Health

NICE recommendations

- Alzheimer’s disease only
- MMSE 10-20 (but caveats)
- Specialist initiation
- Least expensive drug
- Review (MMSE, function and behaviour) 6-monthly (can be by GP)
- Continue while MMSE remains 10+

Problems with NICE

- Alzheimer's disease only
  - Evidence for other dementias is mounting
- Not recommended for mild dementia
- Decision based on QALYs
  - QoL does not improve with ACHIs
- Overlooks individual impact
- Stopping if MMSE < 10 is problematic

Proportion with AD receiving ACHIs

Country	percentage
Italy	84%
Spain	76%
Japan	68%
US	64%
France	61%
Germany	55%

Source: Alzheimer Europe 2007

Proportion with AD receiving ACHIs

Country	Drug treatment rate
Italy	84%
Spain	76%
Japan	68%
US	64%
France	61%
Germany	55%
UK	**33%**

Source: Alzheimer Europe 2007

Prescribing Observatory for Mental Health

- 2007 audit of 19 Trusts (54 PCTs)
  - 1897 patients

Prescribing Observatory for Mental Health

- 2007 audit of 19 Trusts (54 PCTs)
  - 1897 patients
- **13% of eligible people received ACHIs**
  - 67% donepezil
  - 20% galantamine
  - 9% rivastigmine
- 50% prescribed in primary care

Why are ACHIs not used?

- NICE guidance is too restrictive?
- Cost considerations?
- Lack of shared care?
- Concerns about evidence?

Unanswered questions

- Can we predict who will respond?
- How long do the drugs work for?
- Is one CI better than another?
- Is earlier treatment relatively better?
- Do ACHIs work in other types of dementia?
- If one doesn’t work, is it worth trying another?

Recommendations

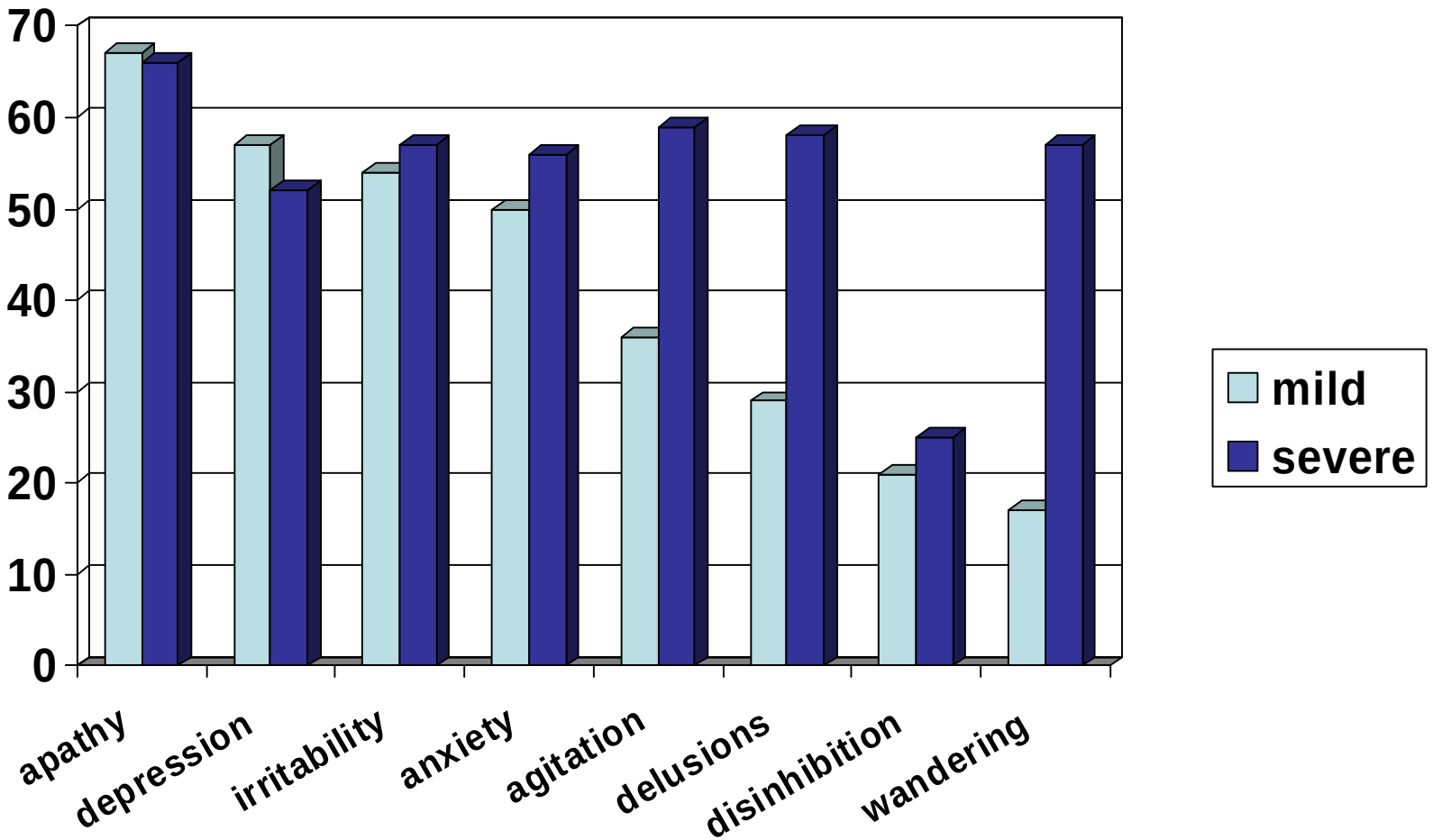
- Do not let drugs dominate dementia care
  - Maintain holistic approach
- All patients with AD/VaD should have trial of donepezil or galantamine
- Review after 3-6 months and stop if not effective
- Do not rely on MMSE or NICE to guide decisions on treatment

Behavioural and Psychological Symptoms of Dementia (BPSD)

Extract from: Alzheimer A. **Über eine eigenartige Erkrankung der Hirnrinde** *Allgemeine Zeitschrift fur Psychiatrie und Psychisch-gerichtliche Medizin*. 1907

“One of the first disease symptoms of a 51-year-old woman was a strong feeling of jealousy towards her husband. Very soon she showed rapidly increasing memory impairments; she could not find her way about her home, she dragged objects to and fro, hid herself, or sometimes thought that people were out to kill her, then she would start to scream loudly.”

“From time to time she was completely delirious, dragging her blankets and sheets to and fro, calling for her husband and daughter, and seeming to have auditory hallucinations. Often she would scream for hours and hours in a horrible voice.”


70
60
50
40
30
20
10
0
apathy
depression
irritability
anxiety
agitation
delusions
disinhibition
wandering
mild
severe

BPSD consequences

- Associated with greater functional impairment
- Very distressing for individual
- Very distressing for carers
- Institutional care
- Overmedication
- Elder abuse
- Associated with increased mortality

Treatment options

- Identify cause
- Wait and see?
- Education and counselling
- Prophylaxis
- Environmental modification
- Direct behavioural approaches
- Medication

BPSD Drug Treatment

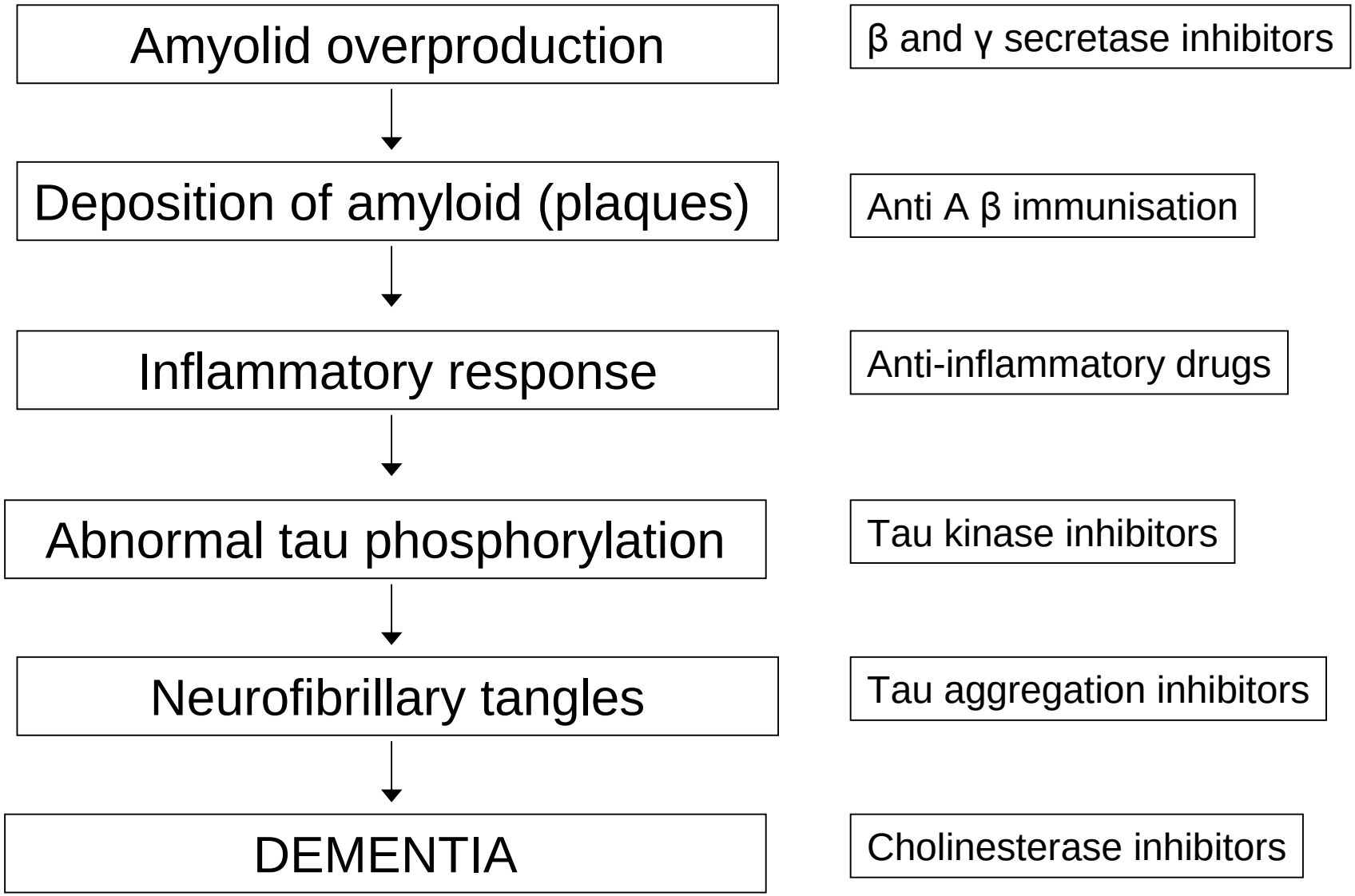
- Risperidone and haloperidol are effective
  - Significant increased risk of stroke and death
- ACHIs- probably not effective
  - More studies needed
- Benzodiazepines- probably effective
  - More studies needed
- Carbamazepine- probably effective
  - More studies needed

BPSD management

- Drug treatment
  - Last resort
  - Should target *specific* symptoms
  - Specialist initiation
  - Regular review

The future

- Over 40 drugs in development
- Around 20 have potential disease modifying action


Amyolid overproduction
β and γ secretase inhibitors
Deposition of amyloid (plaques)
Anti A β immunisation
Inflammatory response
Anti-inflammatory drugs
Abnormal tau phosphorylation
Tau kinase inhibitors
Neurofibrillary tangles
Tau aggregation inhibitors
DEMENTIA
Cholinesterase inhibitors

conclusions

- Drug treatments must not become focus of management
- Good evidence for ACHIs in Alzheimer's disease and Vascular dementia
  - donepezil and galantamine safe and well tolerated
- Drug treatment of BPSD is last resort
- Several exciting developments awaited

Thank You