The Chinese University of Hong Kong
The Nethersole School of Nursing
CADENZA Training Programme

CTP 004 – Dementia: Preventive and Supportive Care

Web-based Course for Professional Social and Health Care Workers

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Chapter 3
Medical treatment for dementia and preventive care

Content

- Medical treatment
  - Role of medical treatment in dementia
  - An overview of medical treatment in dementia
- Preventive care
  - Modifiable risk factors in dementia
  - Strategies for primary prevention of dementia

Medical treatment

Role of medical treatment in dementia

Incurable ≠ untreatable

- Control symptoms (physical, cognitive, behavioural and psychological symptoms of dementia BPSD)
- Treating underlying, reversible cause of dementia
- Delay the progression of some of the underlying irreversible diseases
- Treatment of co-morbid conditions
- Evaluate the indications/contraindications of other therapeutic intervention
  - Review of medication to discontinue drugs with negative effect on patient's condition

Overview of medical treatment

Medical treatment

- Antidementia drugs
- Treatment of BPSD
- Treatment of other medical problems

Antidementia drugs

- Dementia produces specific abnormalities in memory and cognition
- Antidementia drugs target at symptomatic relief/slowing the progress of dementia
- Include:
  - Cholinesterase inhibitors
  - N-Methyl-D-Aspartate (NMDA) receptor antagonist
  - Anti-aggregants and other drugs

Cholinesterase inhibitors (ChEIs)

- Cholinergic hypothesis: symptoms is caused by neuronal death – ê acetylcholine level
  - Acetylcholine: a neurotransmitter which is chemicals that are used to relay, amplify and modulate signals between neurons
- Cholinesterase inhibitors
  - Also named "Cognitive enhancer"
  - Tacrine
  - Donepezil
  - Rivastigmine
  - Galantamine
- Inhibit chemical (acetylcholinesterase) which breaks down acetylcholine

Jones, 2000

Cholinesterase inhibitors (ChEIs)

- Indication: mild to moderate Alzheimer's disease (AD)
  - Mini-Mental State Examination (MMSE) score 10-26
- Therapeutic effects: Improve cognitive function, activities of daily living, may also improve behavioural symptoms
- Side effects
  - Gastrointestinal (GI) symptoms
    - Nausea, vomiting & diarrhoea
  - Sweating
  - Bradycardia
  - Headache
  - Dizziness
  - Insomnia
  - Loss of appetite
  - Liver function abnormalities (Tacrine)

Jones, 2000

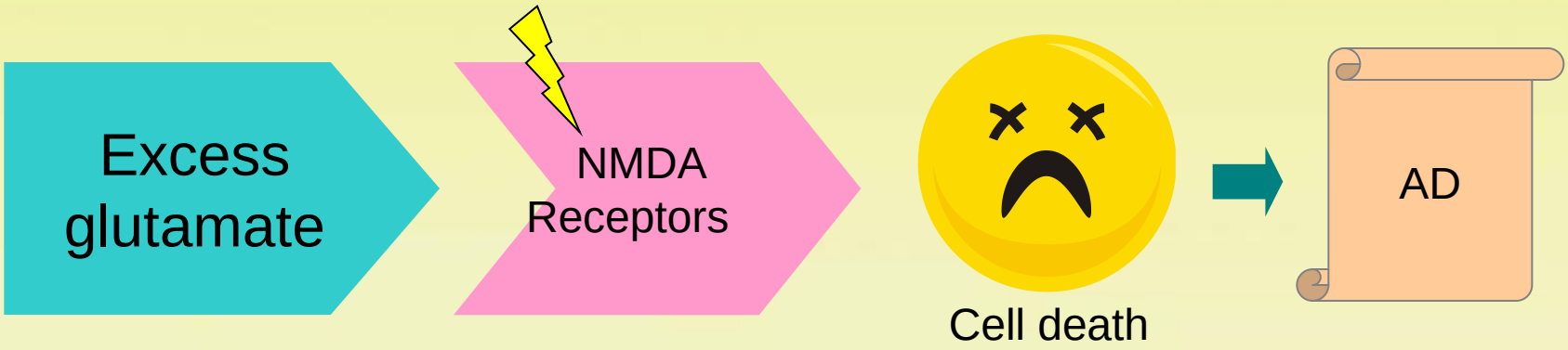
Cholinesterase inhibitors (ChEIs)

Specific implication in ChEIs administration

- Monitor for clinical improvement
  - Monitor therapeutic effectiveness, as noted on any improvement in MMSE
- Monitor closely for signs and symptoms of GI ulceration and bleeding
  - e.g. Coffee-grounds emesis, tarry stools, epigastric pain
- Monitor ambulation as dizziness is a common adverse effect

NMDA receptor antagonist

- **Memantine**
- Regulating the activity of glutamate, a chemical involved in information processing, storage and retrieval
- Excess glutamate è over-stimulates NMDA receptors è cell death – contribute to the symptoms and pathogenesis of AD



(Alzheimer's Association, 2007)

NMDA receptor antagonist

- Indication: moderate to severe AD
- Therapeutic effects:
  - Reduction in functional and cognitive deterioration
  - Positive effect on the behavioural disturbances
- Side effects:
  - Transient ischaemic attack (TIA), vertigo, ataxia, aggressive reaction
  - headache, constipation, confusion and dizziness
- Specific implication in memantine administration
  - Assess for and report sign and symptoms of focal neurologic deficits (e.g. TIA, ataxia, vertigo)

Jones, 2000

Efficacy of ChEIs and memantine in non-alzheimer dementias

	Vascular dementia (VaD)	Dementia with Lewy bodies (DLB)	Frontotemporal dementia (FTD)
ChEIs	+	+	+/-
Memantine	+/-	+/-	+/-

+: some evidences support

+/-: insufficient evidence

(Arit & Jahn, 2006; Waldemar et al., 2007)

Anti-aggregants

- Aspirin
  - Low dose + long term:
    - Prevent blood clot formation in people at high risk for developing blood clots
    - Widely use in treatment of myocardial infarction, stroke
- Indication: dementia patient with vascular risk factor (vascular dementia)
- Therapeutic effect:
  - Improve cerebral perfusion (Rands et al., 2000)
  - Improve cognitive function
- Side effects: GI bleeding, tinnitus, hearing loss

Anti-aggregants

- Specific implication in aspirin administration
  - Monitor for salicylate toxicity
    - Sensation of fullness in the ears, tinnitus, decreased or muffled hearing
  - Monitor for loss of tolerance to aspirin
    - Profuse rhinorrhea (running nose), erythema (redness of the skin), nausea, vomiting, intestinal cramps, diarrhea
    - Occur 15 minutes to 3 hours after ingestion
  - Observe and report signs of bleeding
    - e.g. bleeding gums, bloody or black stools, bloody urine

Other drugs used in AD

- Gingko biloba
  - Some evidences of improvement in cognition and function
  - Inconsistent results from modern trials
  - A recent largest and longest study reported that gingko biloba showed no evidence of reducing the overall incidence of dementia (DeKosky et al., 2008)
- Non-steroidal anti-inflammatory drugs (NSAID)
  - Suggested to be protective against AD
  - Not found to be effective in slowing the progression of AD
- Vitamin E
  - Delay progression in patient with AD
  - Insufficient evidence for the efficacy in treatment of AD

Jones, 2000; Waldemar et al., 2006

Other drugs used in AD

- Selegiline
  - May improve cognitive and behavioural symptoms
  - Insufficient evidence to recommend it use
  - Avoid use in DLB è precipitate hallucinations
- Oestrogens
  - Symptomatic benefits or reduce the risk of AD
  - Not indicated for cognitive improvement or maintenance for women with AD
- Statins
  - Reduce risk of AD amongst those with diseases such as hypertension and ischaemic heart disease
  - No good evidence to recommend it use

Jones, 2000; Waldemar et al., 2006

Pharmacological treatment of BPSD - **Neuroleptics**

- Indication: Psychotic disorders and agitation
- e.g.Thioridazine, haloperidol, sulpiride
- Therapeutic effects:
  - Reduce excitement, agitation and psychotic manifestations
- Side effects
  - Extrapyramidal reactions: parkinsonism symptoms (e.g. dystonia, akathisia)
  - Hypotension

Pharmacological treatment of BPSD - **Neuroleptics**

- Specific implication in neuroleptics administration
  - Monitor for extrapyramidal reactions
    - Occur frequently during first few days of treatment
    - Symptoms are dose related
    - Controlled by dosage reduction or concomitant administration of antiparkinson drugs
    - Avoid use in patient with DLB
  - Orthostatic hypotension may occur in early therapy
    - Make position changes slowly, especially from lying down to upright posture

Pharmacological treatment of BPSD – Atypical antipsychotics

- Indication: Psychotic disorders and agitation
- e.g. Risperidone, olanzapine, quetiapine, clozapine
- Therapeutic effects:
  - Reduce psychotic behaviour
- Side effects
  - Extrapyramidal reactions (high dose)
  - é risk of stroke in elderly (Risperidone)
  - Hyperglycemia, diabetes mellitus

Pharmacological treatment of BPSD – Atypical antipsychotics

- Specific implication in atypical antipsychotics administration
  - Monitor diabetics for loss of glycaemic control
  - Monitor closely of the neurologic status

Pharmacological treatment of BPSD - antidepressants

- Indication: Depression
  - e.g. amitriptyline, citalopram, trazodone
- Therapeutic effects:
  - Antidepression
  - Increase sleep time, decreases number and duration of awakenings in depressed patient (Trazodone)
- Side effects
  - Agitation, insomnia, postural hypotension, drowsiness

Pharmacological treatment of BPSD - antidepressants

- Specific implication in antidepressants administration
  - Check patient for symptoms of hypotension /drowsiness and reduce danger of fall
  - Watch closely for worsening of depression or emergence of suicide ideation

Pharmacological treatment of BPSD - Anxiolytics

- Indications: Anxiety disorders
- E.g. Diazepam, Lorazepam
- Therapeutic effects:
  - Antiolytic, anticonvulsant, sedative and hypnotic
- Side effects
  - Drowsiness, vertigo, weakness and unsteadiness, confusion

Pharmacological treatment of BPSD - Anxiolytics

- Specific implication in anxiolytics administration
  - Supervise ambulation of older adult for at least 8 hours after injection to prevent falling and injury
  - Preventive precautions for suicidal tendencies that may be present in anxiety states accompanied by depression

Pharmacological treatment of BPSD - Hypnotics

- Indication: sleep disorder – insomnia
- e.g. chloral hydrate, Benzodiazepine such as triazolam, zolpidem
- Therapeutic effects:
  - Hypnotics, decrease sleep latency and number of nocturnal awakenings, increase duration of sleep
- Side effects:
  - Drowsiness, "rebound insomnia", confusion, fall
  - Depression (Zolpidem)

Pharmacological treatment of BPSD - Hypnotics

- Specific implication in Hypnotics administration
  - Monitor the sign of developing tolerance or adaptation due to long-term use
  - Monitor the symptoms of overdose:
    - Slurred speech, confusion, coma, etc
  - Monitor patients for depression, cognitive or motor function

Pharmacological treatment of BPSD

- ChEIs
  - Rivastigmine
    - reduced apathy, anxiety, hallucinations, delusions and irritability in DLB (McKeith et al., 2000)
  - Galantamine
    - reduced neuropsychiatic features in mild to moderate AD patient (Loy & Schneider, 2006)
  - May also need to be used in conjunction with other agents (e.g. neuroleptic). (Waldemar et al., 2007)

Treatment of other medical problems in dementia

- Reversible dementia
  - Hypothyroidism
  - Vitamin B12 deficiency
  - Folate deficiency
  - Neurosyphilis
  - Normal pressure hydrocephalus
  - Frontal meningioma
  - Hyperparathyroidism
- Other conditions (especially in vascular dementia)
  - Diabetes mellitus
  - Hypertension
  - Hyperlipidemia
  - Coronary artery disease

Problem in medication compliance

- People with dementia may not able to handle medication independently
- Practical difficulties in drug compliance:
  - Refusal
  - Cognitive dysfunction: forget to take medication in correct time, correct name and correct dose
  - Polypharmacy
  - Side effects

Methods to handle problems in medication compliance

- Explain to older people the importance of drug compliance
- Used of reminder:
  - Posting checklists
  - Labeled pill containers specifying when, where and how medications are to be taken
- Place medication in a fixed place visible to the older people
- Assess the ability of the older people to take pills by him/herself

Methods to handle problems in medication compliance

- Assist old people to arrange drug, especially in case of multiple medication
- Assess whether patient refuse taking the drug is due to unpleasant taste or any side effect after taking the drug
- Monitor any side effect and report to doctor immediately
- Direct supervision of medication administration

Preventive care

Risk assessment for dementia

- Modifiable risk factors
  - Vascular
  - Lifestyle
  - Sociodemographic
  - Other

Vascular risk factors

- Blood pressure (BP)
  - High systolic pressure > 180mmHg è 50% é risk (Fratiglioni et al., 2007)
    - use of antihypertensive drugs ê risk (Forette et al., 1998)
  - Low diastolic blood pressure (<65mmHg) è 40% é risk (Qiu et al., 2003a)
    - May due to hypoperfusion

Vascular risk factors

- Heart failure
  - 80% é risk of dementia and AD (Qiu et al., 2006)
  - Additive effect with low diastolic (BP)
- Hyperlipidemia
  - Midlife elevation of total serum cholesterol level è é risk of AD (Patterson et al., 2007)

Vascular risk factors

- Diabetes
  - é the risk of all-cause dementia in mid-life and in old people (Schnaider Beeri et al., 2004; Xu et al., 2004)
- Stroke
  - Presence of clinical strokes/silent infarctions on neuroimaging é risk of all-cause dementia (Honig et al., 2003)

Lifestyle

- Diet
  - High intake of total fat é risk of dementia (Kalmijn et al., 1997)
    - Mediterranean-style diet is associated with a ê risk of AD
    - Regular consumption of fish and seafood is associated with ê risk of dementia (Patterson et al., 2007)

Life style

- Smoking
  - Early case control studies suggested that smoking ê risk of dementia
  - Longitudinal studies identified significantly é risk of all-cause dementia (Almeida et al., 2002; Launer et al., 1999)
- Wine
  - Epidemiologic study in France: Consumption of moderate amount of red wine (250-500 mL/day) ê risk of dementia (Larrieu et al., 2004)
  - Insufficient evidence from randomized controlled trials (RCT)

Life style

- Activities
  - Regular physical activities ê risk of dementia (Laurin et al., 2001; Lindsay et al., 2002)
  - Daily mental activities associated with ê risk of dementia in the Kungsholmen study (Wang et al., 2002)
    - Reading books/newspapers
    - Writing/studying
    - Working crossword puzzles
    - Painting or drawing
  - Mah-jong playing was reported to improve cognitive performance in persons with dementia (Cheng et al., 2006)
    - Lack of controlled trial

Sociodemographic

- 60% é risk among elderly with poor or limited social network (Fratiglioni et al., 2000)
  - Frequent participation in social activities associated with ê risk of dementia (Wang et al., 2002)
- Manual labour é risk of dementia (Qiu et al., 2003b)
- Longer periods of education ê risk of dementia (Kukull et al., 2002)

Other factors

- Head injury
  - Head trauma with unconsciousness was associated with an é risk of dementia (Plassman et al., 2000)
- Exposure to toxins
  - Pesticides, fertilizers: é risk of VaD (Hébert et al., 2000)
  - Defoliants and fumigants: é risk of AD (Tyas et al., 2001)

Preventive strategies for dementia (Good evidence)

- Good control of blood pressure
  - Both in adult and late life
  - Monitor antihypertensive treatment to prevent too low levels of diastolic BP
  - Also reduce risk of stroke
  - Target BP systolic ≤ 140mmHg

(Fratiglioni et al., 2007)

Preventive strategies for dementia (insufficient evidence)

- Proper treatment for diabetes, hyperlipidemia, heart failure and stroke
  - No convincing evidence relating treatment to the above conditions to the prevention of dementia
  - Many other reasons for treatment of these conditions
    - Health
    - Prevent complications
    - ê mortality

Preventive strategies for dementia (insufficient evidence)

- Diet
  - Potential advantages of
    - Increase consumption of fish
    - Reduced consumption of dietary fat
    - Moderate consumption of wine
    - Adequate vitamin B12 and Folate

    for prevention of dementia
- Smoking
  - Not only for the potential risk
  - Well-known risk factors for many vascular diseases, include hypertension

Preventive strategies for dementia (insufficient evidence)

- Active and socially integrated life in old age
  - Participate in mentally, socially and physically stimulating activities may postpone the onset of dementia (Fratiglioni et al., 2007)
  - Attending the theater, concerts, or art exhibitions; traveling; playing cards/games and mahjong; or participating in social groups or a pension organization (Cheng et al., 2006; Wang et al., 2002)

Preventive strategies for dementia (insufficient evidence)

- Reduce the risk of serious head injuries
- Protective clothing during administration of pesticides, fumigants, fertilizers and defoliants
- Avoid use of medication like NSAID, vitamins E, estrogens and statin for specific purpose of ê risk of dementia
  - High dose vitamin E (≥ 400 units/day) associated with excess mortality

(Fratiglioni et al., 2007)

Curry can prevent dementia?

- Researchers at UCLA have shown that the curry pigment curcumin slows the formation of, and even destroys, accumulated plaque deposits in mouse brains

Yang et al., 2005

Summary

- Medical management involves different aspect
  - Control symptoms
  - Treatment of co-morbid condition/reversible cause of dementia
  - Monitoring side effect of drugs
  - Management of other condition during medical care
- Prevention of dementia by
  - Identification and management of modifiable risk factors
  - Special attention for controlling BP!!

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