

# 實證醫學病例討論

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精神科

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## Case presentation- Chief Problem

- Suicide attempt by strangulation (3/3)

## Case presentation- Present illness(1)

- A 61 years old woman of major depressive disorder. She had been admitted to our ward third and followed up in OPD with good medical adherence. She was just discharged from our ward on 2009/03/02. Last hospitalization, she suffered from depressed mood, loss of interest, fatigue, excessive anxiety to trivial things, poor appetite, poor memory, poor concentration, indecisiveness, guilty feeling (to her family), hopeless and recurrent thought of death, she also has transient suicide idea/gesture, such as using knife toward her neck.
- After discharged on 3/2, she had suicide attempt on 3/3 PM10:00 (拿毛巾.絲巾.纜線勒脖子). She had suicidal gesture almost everyday but was stable with other family's company(只要家人在旁,病患都很穩定,但一不留神,病患就會有勒頸的行爲). She states that she felt hopeless about her disease.

## Case presentation- Present illness(2)

- Tracing back to her history, patient's personality was changed since last February, and she had been admitted to neurology ward during last June due to acute conscious disturbance. Guilty feeling, self-talking, anxiety mood, insomnia (no sleeping for less than week), less oral intake (less than one week) were told. Several foci of ischemic-gliotic change in bilateral frontal subcortical white matter via brain MRI, vascular dementia was suspect. After treatment, depression was not improved, so she visited psychiatry OPD, major depressive disorder was impressed. She has regular medication control and three times admission due to worsening of depression.
- She ever attempted to suicide by strangulation, but was saved by family. And she attempted suicide by 絲巾 hang on the window due to unwilling to be admitted before. This time due to suicide gesture almost everyday after last discharge, she was admitted to our ward again for further treatment.

# Past History&Personal History

1. Diabetes Mellitus : hyperglycemia since last May
2. Hypertension (+)
3. Cardiac disease (-)
4. suspect prior ischemia stroke
5. Smoking:(-) Alcohol:(-)
- 6 Liver/Kidney disease: (-)/(-)
7. Gouty arthritis (-)
8. Drug allergy(-)

Cigarette Smoking : denied

Alcohol : denied

Occupation history : housewife

Contact history : nil

Travel history : nil

生育史 : three children

Psychosocial stressors: 擔心孩子的發展

Pre-morbid personality: 強勢，主導家中決定

# Physical examination

- Consciousness: clear
- Conjunctiva: not pale
- Sclera: not icteric
- Neck: supple, no lymphadenopathy, with bruises over the neck due to strangulation
- Thyroid: no goiter
- Chest: symmetric expansion
- Breathing sound: bilaterally clear
- Heart sound: regular heart beat
- Abdomen: soft, no tenderness
- Liver and spleen: impalpable
- Bowel sound: normoactive
- Extremities: freely movable, no pitting edema

# Neurological examination

- Cons.: E4V5M6, alert and awakeful
- Cranial nerves: grossly normal
- Muscle power: all full
- Deep tendon reflex: bilaterally symmetric
- Cerebellar signs: normal

# Mental status examination(1)

## 1. Appearance:

Body build: moderate

Facial expression: **flatten**

Personal care and hygiene: kempt

Dressing and grooming: kempt

Attitude: cooperative

## 2. Psychomotor activity and behavior:

Gait: steady

Activity: **hypoactivity**

Behavior: suicidal gesture

destructive/violence behavior(-)

Tic, gesture and twitches: nil

## 3. Affect:

Mood: **mixed with depression and anxiety**

Affective expression: **restricted**

Appropriateness: appropriate

# Mental status examination(2)

## 4.Speech:

Overall quantity and quality:

hypotalktive, coherent and relevant

Rate of production: **slow**

Productivity: **passive**

## 5.Cognition:

Stream of thought: fluent

Content of thought: no detectable delusion

**suicidal idea(+)**

**negative thoughts(+)**

**hopeless(+)**

**guilty feeling(+)**

## 6.Perception: denied of AH/VH

## 7.Insight: intellectual

# Impression

- Axis I: Major depressive disorder, recurrent, severe without psychotic features
- Axis II: No diagnosis
- Axis III: **Hyperlipidemia** , Herpes
- Axis IV: Intrafamily problems
- Axis V: GAF= 21-30

# Medication history

- Smilon (Mirtazapine) #1+Risperdal 1mg
- Smilon (Mirtazapine) +Deanxit +Risperdal
- Smilon (Mirtazapine) #1+Dogmatyl\*低\* 50mg (Sulpiride) #1
- Efexor XR 75mg 4#
- Efexor XR 75mg 4#+Lithium
- Efexor XR 75mg (Venlafaxine)x3#+Wellbutrin SR 150mg(Bupropion)1#

# Thinking

- As our usual clinical practice, antidepressant is a standard treatment for major depressive disorder
- However, some patients do not respond to antidepressant monotherapy (full dose and full course) , nor even combined therapy with another antidepressant or mood stabilizer → we call them “treatment refractory” or “treatment resistance” depression
- What other treatment strategies can we try?

# Asking

- Beside combining psychotherapy, rehabilitation, what else can we do?
- Focus on pharmacotherapy → How about add on antipsychotics for augmentation therapy?

P: treatment resistance major depressive disorder

I: augmentation or adjunctive treatment with antipsychotics

C: antidepressant only or antidepressant+antipsychotics

O: response rate

# Acquire

- 高雄醫學大學圖書館首頁→電子館藏系統→實證醫學→Pubmed

- Key words & Search strategy:

**Search (major depressi\* [title]) AND (augment\* OR adjunct\*)  
AND (antipsychotic\* OR olanzapine OR quetiapine OR  
aripiprazole OR ziprasidone OR clozapine OR risperidone)  
AND (refractory OR resistance [text])**

- 17 results (8 results after 2007)
- Exclude the medication which may cause side effect of metabolic syndrome (such as quetiapine, olanzapine, clozapine)
- Choose 1 of them after appraisal

# appraisal

- The Efficacy and Safety of Aripiprazole as Adjunctive Therapy in Major Depressive Disorder --A Second Multicenter, Randomized, Double-Blind, Placebo-Controlled Study
- Ronald N. Marcus, MD,\* Robert D. McQuade, PhD,y William H. Carson, MD,y Delphine Hennicken, MS,z Maurizio Fava, MD,x Jeffrey S. Simon, MD,k Madhukar H. Trivedi, MD,{ Michael E. Thase, MD,\*\* and Robert M. Berman, MD\*
- (J Clin Psychopharmacol 2008;28:156–165)

## Question

- How effective and safe is aripiprazole as an adjunctive treatment for major depressive disorder (MDD) in people who have failed to respond to one or more antidepressants?

# Patients

- 381 adult outpatients (aged 18–65 years) with a DSM-IV diagnosis of MDD, who had inadequate response to an 8–week single blind antidepressant trial, and had previously experienced inadequate response to between one and three antidepressants (assessed using the Antidepressant Treatment Response Questionnaire).

# Setting

- 36 sites in the USA; September 2004 to December 2006

## Intervention

- Adjunctive aripiprazole (starting dose 5 mg/day, which could be adjusted to a maximum of 20 mg/day as tolerated by week 4) or placebo for 6 weeks. Type of antidepressant or dosage was not changed during this period.

# Outcomes

- Change in symptoms from baseline (Montgomery-Åsberg Depression Rating Scale (MADRS)); adverse events.

## Patient follow-up

- 85% completed treatment (97% analysed for efficacy using last observation carried forward).

# METHODS

- Design: Randomised controlled trial.
- Allocation: Unclear.
- Blinding: Double blind.
- Follow-up period: Six weeks (treatment period only).

# MAIN RESULTS

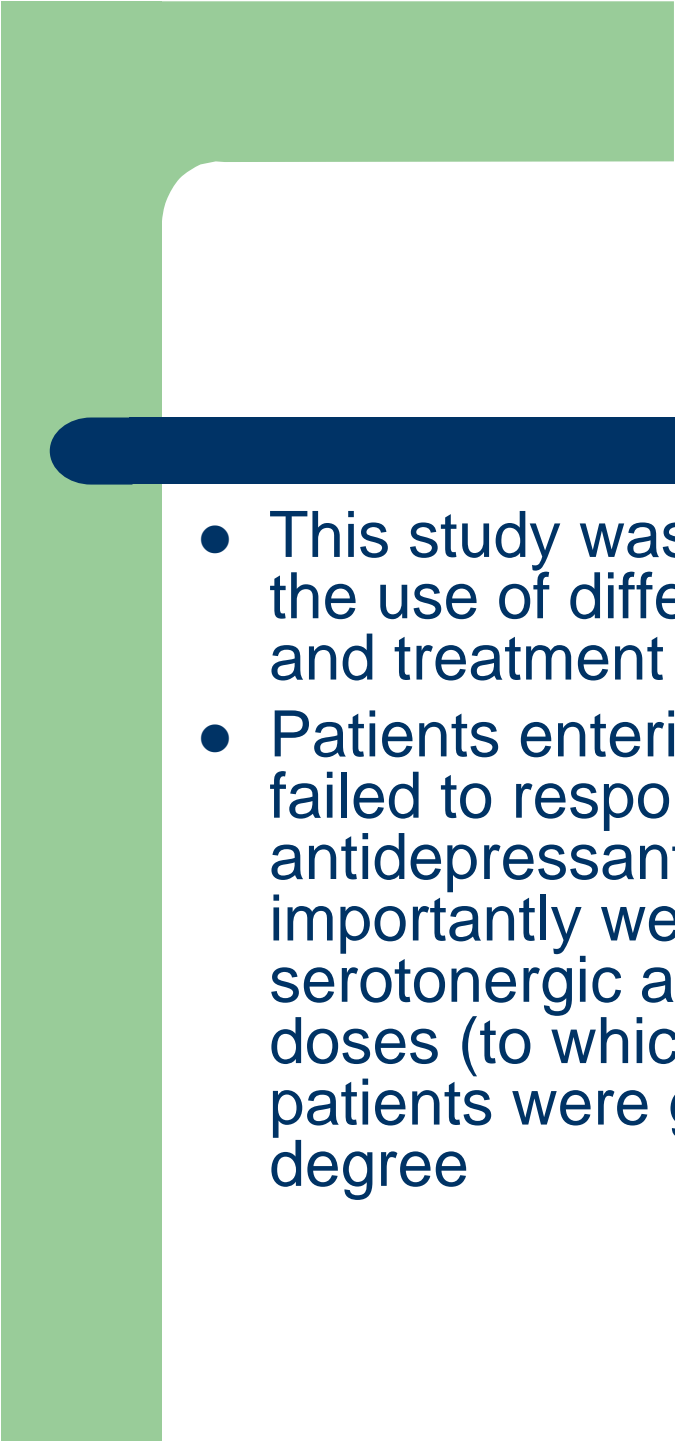

- The average dose of aripiprazole in the last week of treatment was 11 mg daily. When added to current antidepressant treatment, aripiprazole significantly improved symptoms of depression compared with placebo over 6 weeks (mean change in MADRS score: 28.5 with aripiprazole v 25.7 with placebo;  $p=0.001$ ). Adverse events that were more common with aripiprazole than placebo included: akathisia (25.9% vs 4.2%), fatigue (10.1% vs 3.7%), restlessness (9.5% vs 0.5%), insomnia (7.4% vs 1.6%), tremor (6.3% vs 2.6%) and constipation (5.3% vs 2.6%; significance of differences not reported). Discontinuation due to adverse effects occurred in 3.7% of the aripiprazole group, compared to 1.1% in the placebo group (significance not reported).

# CONCLUSIONS

- Adjunctive aripiprazole improves symptoms in people with major depressive disorder that have not responded to standard antidepressant treatment.

# COMMENTARY

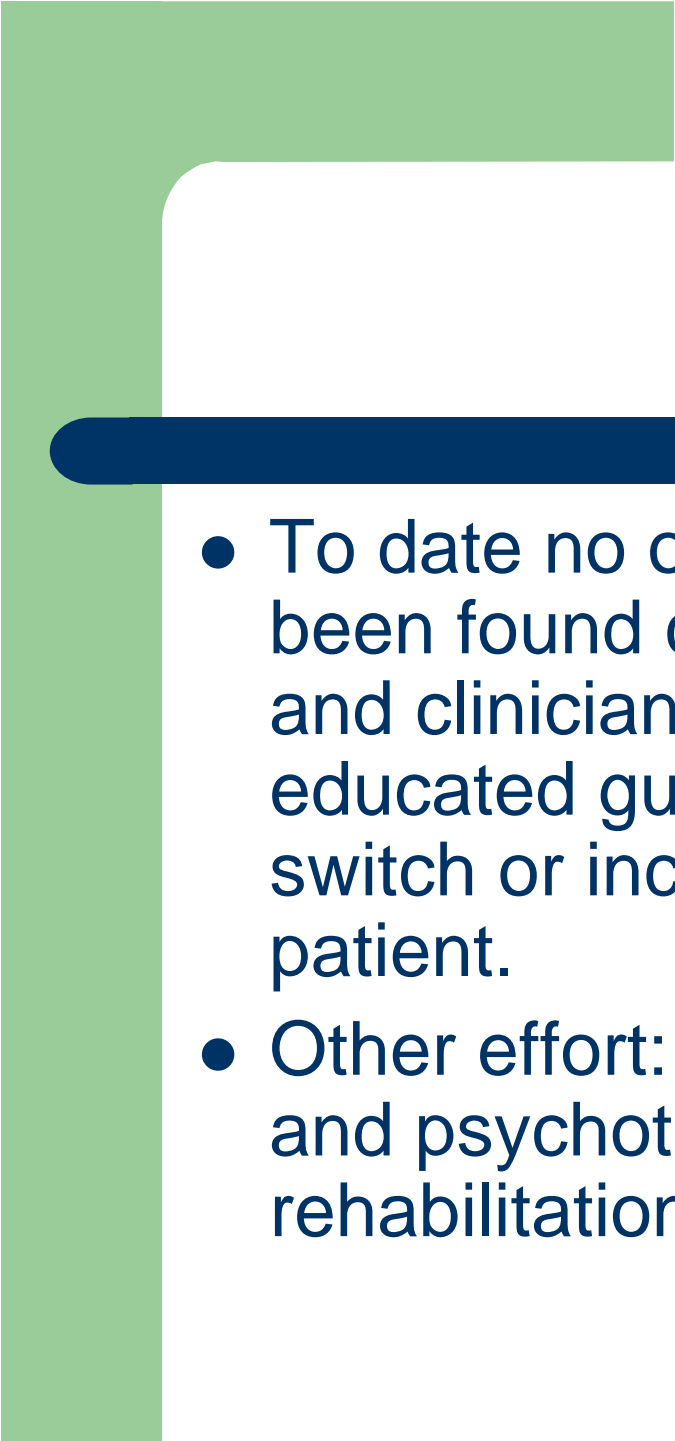

- Only about 40% of depressed patients enter remission after taking an SSRI
- The psychopharmacological management of treatment resistant patients is really challenging.
- Switch?(take time), Combination? Augmentation?
- RCTs that provide information on novel strategies are welcome.

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- This study was designed including tweaks such as the use of different instruments to define study entry and treatment response.
  - Patients entering the study → assessed as having failed to respond to at least one prior adequate antidepressant trial (dose and duration), but importantly were then given a prospective trial of a serotonergic antidepressant in moderately high doses (to which 40% responded) → ensure that patients were genuinely treatment resistant to some degree

- Aripiprazole proved more effective than placebo in improving symptoms and disability, with higher remission rates.

But....

- The effect size was small, and remission rates remained low (25% after 6 weeks of aripiprazole).
- Rates of akathisia (25%) were high and often required dose reduction.
- Only short-term efficacy was demonstrated, whereas treatment resistant depression is a long-term and recurrent illness.

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- To date no one augmentation strategy has been found consistently superior to others, and clinicians will continue to rely on educated guesses as to whether to augment, switch or increase dosing in an individual patient.
  - Other effort: combining pharmacotherapy and psychotherapy, and then rehabilitation...make it complicated

## Apply (Practice)

- After admission, Abilify(Aripiprazole) was administered for augmentation treatment (Efexor(SNRI)75mgx3#+Abilify 10mg1#)
- By our practice, the patient can tolerate the medication. No obvious side effect was complained.
- After 1 week after admission, patient's suicidal idea decreased. Persistent depressed mood and anxiety was observed. We will keep observe patient's symptoms, by using specific rating scale (ex: MADRS) to evaluate the response rate is needed.



Thanks for your attention!