Management of Weight Gain in Taiwanese Patients with Schizophrenia Treated with Second Generation Antipsychotics: A Review of Existing Data

Chaucer C.H. Lin[1,2], Ya-Mei Bai[3,4],Mong-Liang Lu[5], Chao-Cheng Lin[6]

1 Medical Division, Eli Lilly Taiwan, Taipei, Taiwan. 2 Department of Psychiatry, Buddhist Tzu Chi General Hospital and University, Hualien, Taiwan. 3 Department of Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan. 4 Department of Psychiatry, College of Medicine, National Yang-Ming University, Taipei, Taiwan. 5 Department of Psychiatry, Wan-Fang Hospital and School of Medicine, Taipei Medical University, Taipei, Taiwan. 6 Department of Psychiatry, National Taiwan University Hospital and National Taiwan University College of Medicine, Taiwan.

ABSTRACT

Background: Second generation antipsychotics (SGAs) have been widely used for the treatment of schizophrenia and other psychotic disorders. Weight gain and changes in metabolic parameters, including glucose and lipids, have been reported during treatment with SGAs. This review is focused on the existing data for weight gain during treatment with SGAs and its management in Taiwanese patients, as an effort to overview this issue in the Taiwanese population is not yet noted. Our aim is to obtain further insights when prescribing SGAs and to help patients to deal with the potential risk of weight gain and changes in metabolic parameters they may encounter during SGA treatment. **Methods:** A literature search for studies published online by the time of start of this report (May 5th, 2011) using the keywords "weight gain", "metabolic", "second generation antipsychotics", "olanzapine", "clozapine", "Taiwan" or "management" yielded approximately 45 articles from PubMed, out of which 33 reports were on weight gain and metabolic changes during treatment with SGAs in Taiwan. Twelve of these were on the management of weight gain and changes in metabolic parameters, which is the focus of this review. **Results:** The weight gain was more pronounced in patients with lower initial body weight, younger age and greater treatment response. Decreased levels of ghrelin and adiponectin might be associated with the weight gain in SGA-treated patients. About one-third of patients with schizophrenia treated with antipsychotics had metabolic changes. Pharmacological interventions like switching to an alternate SGA with a lower risk of weight gain or co-treatment with fluvoxamine, topiramate or metformin have been shown to reduce weight gain. Non-pharmacological interventions like close metabolic monitoring, dietary control, exercise and weight control programs have been found to be successful in weight reduction. **Conclusion:** Weight gain during treatment with SGAs in schizophrenic patients in Taiwan can be successfully managed by pharmacological or non-pharmacological interventions, which is compatible with international studies.

INTRODUCTION

Second Generation Antipsychotics (SGAs)[1]

- Good efficacy for negative symptoms
- Favorable effects on cognitive function
- Low risk of extrapyramidal adverse events at effective clinical doses
- Low rate of relapse/treatment failure

Fig 1: Potential Metabolic-related Adverse Events During Treatment with SGAs

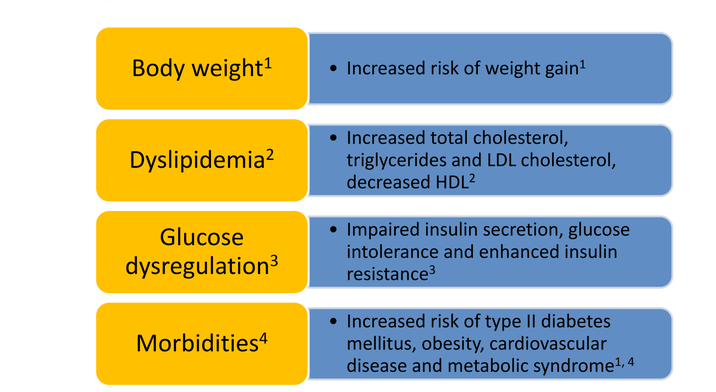
Body weight[1]	• Increased risk of weight gain[1]
Dyslipidemia[2]	• Increased total cholesterol, triglycerides and LDL cholesterol, decreased HDL[2]
Glucose dysregulation[3]	• Impaired insulin secretion, glucose intolerance and enhanced insulin resistance[3]
Morbidities[4]	• Increased risk of type II diabetes mellitus, obesity, cardiovascular disease and metabolic syndrome[1, 4]

Objective

To review the existing data on treatment-emergent weight gain and its management in Taiwanese patients

METHODOLOGY

Fig 2: Summary of Studies Reviewed



ECG: electrocardiogram

RESULTS

Table 1: Obesity in Schizophrenic Outpatients Receiving SGAs in Taiwan[5]

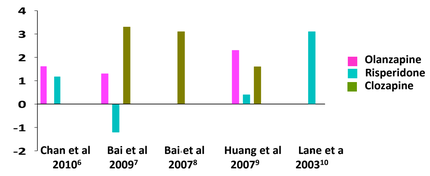
- Prevalence of obesity (26.4 < BMI < 28.6) with SGAs: 37.9%
- Prevalence of severe obesity (BMI ≥ 28.6) with SGAs: 24.1%

	Patients, n (%)				
BMI	Olanzapine (n = 26)	Risperidone (n = 17)	Quetiapine (n = 6)	Clozapine (n = 6)	Zotepine (n = 3)
< 24.2	9 (34.6)	6 (35.3)	4 (66.7)	3 (50.0)	1 (33.3)
24.2–26.4	5 (19.2)	5 (29.4)	1 (16.7)	0 (0.0)	2 (66.7)
26.4–28.6	2 (7.7)	3 (17.6)	1 (16.7)	2 (33.3)	0 (0.0)
≥ 28.6	10 (38.5)	3 (17.6)	0 (0.0)	1 (16.7)	0 (0.0)

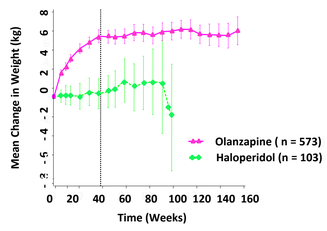
BMI: body mass index

Fig 3: SGAs and Weight Gain

A. Treatment-emergent Weight Gain with SGAs in Taiwanese Studies



B. Weight Gain May Plateau After 39 Weeks in Olanzapine-treated Patients with Schizophrenia[11]



C. Early Identification of Patients with Schizophrenia at Risk for Substantial Weight Gain on Olanzapine[12]

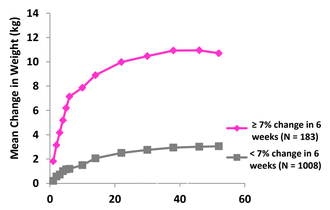
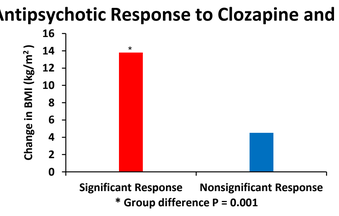
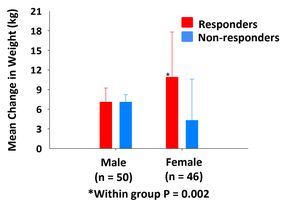


Fig 4: Predictors of Weight Gain

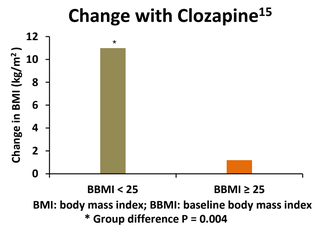
A. Initial Antipsychotic Response to Clozapine and Long-term Weight Gain[13]



B. Comparison of Change in Weight with Response to Clozapine[14]



C. Effect of Baseline BMI on Course of BMI Change with Clozapine[15]



Weight Gain Risk Factor Checklist Upon Initiation of Antipsychotics[16]

At baseline

- Younger age
- Male gender
- Low baseline body mass index
- Non-Caucasian race
- Poor patient insight
- Eat until feeling full
- Poor eating habits
- Increased appetite
- High energy intake
- Diagnosis of undifferentiated schizophrenia
- Other medical comorbidities
- Low social activity
- Low physical activity
- Supervised housing conditions

At 3rd week after treatment initiation

- Improved clinical response at the 3rd week of treatment
- Did your patient gain weight at the 3rd week of treatment ≥ 2 kg

Fig 5: Management of Treatment-emergent Weight Gain

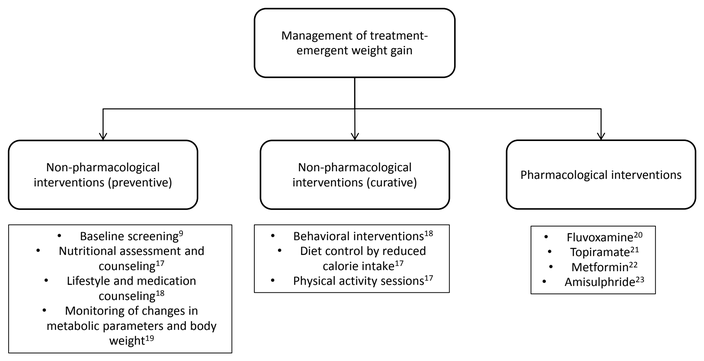
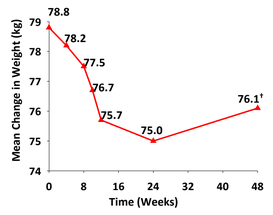


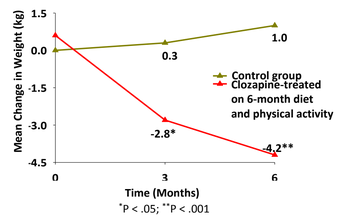
Fig 6: Non-pharmacological Interventions

A. 10-week Weight Control Program[17]



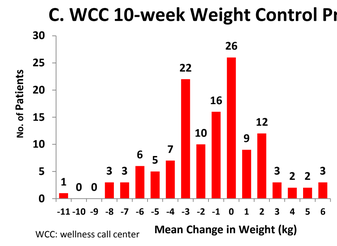
For all values n = 26; †n = 16

B. 6-month Diet and Physical Activity Program[19]



*P < .05; **P < .001

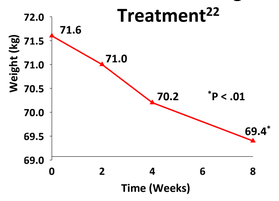
C. WCC 10-week Weight Control Program[24]



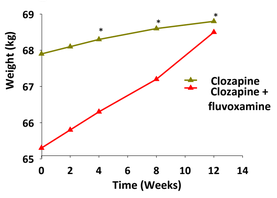
WCC: wellness call center

Fig 7: Pharmacological Interventions

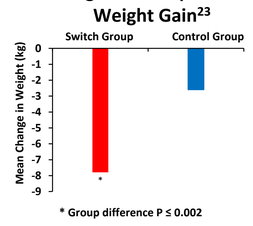
A. Metformin Use to Address Changes in Metabolic Parameters During Olanzapine Treatment[22]



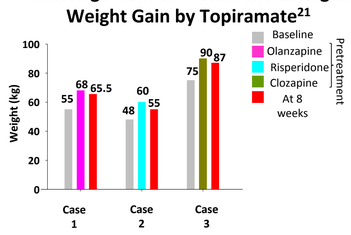
B. Fluvoxamine Inhibits Clozapine-related Weight Gain[20]



C. Switching to Amisulpride Reduced Weight Gain[23]



D. Management of Treatment-emergent Weight Gain by Topiramate[21]



Limitations

- Non-pharmacological interventions
  - High-cost and safety issues[17,19]
  - Long-term adherence required[19]
  - Lack of motivation[19]
  - Suppression of appetite for long-term difficult[19]
- Pharmacological interventions
  - Economic burden of adding another drug[20]
  - Risk of adverse events[20]
  - Risk of potential drug interactions[20]
  - Chances of disease relapse[23]

CONCLUSIONS

- Patients treated with any antipsychotic agents, including olanzapine, should be observed for weight gain, lipid alterations, signs and symptoms of hyperglycemia and patients with diabetes mellitus or with risk factors for diabetes mellitus should be monitored regularly for worsening of glucose control and alterations should be managed as clinically appropriate
- Appropriate clinical monitoring is advisable in accordance with utilised antipsychotic guidelines
- Weight gain is associated with SGAs as evidenced by Taiwanese studies
- Weight gain in Taiwanese patients with schizophrenia treated with SGAs can be successfully managed by non-pharmacological and pharmacological interventions
- The results of the Taiwanese studies are in agreement with global studies

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