

## CASE REPORT

## A Case Series on the Use of Atypical Long Acting Injectable as First-line Antipsychotic Treatment in Malaysia: Who Benefits and How?

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### Abstract

**Introduction:** The use of long acting injectable (LAI) antipsychotics is mainly reserved as the second line treatment when all efforts to ensure patients' adherence to regular oral medication failed. We aim to describe the common clinical features of patients with schizophrenia who benefited from the use of LAI early in the course of illness. **Methods:** We report four patients with first presentation of schizophrenia, all of whom were started with atypical LAI antipsychotics without prior history of oral antipsychotic. **Results:** In all of the cases, short acting major tranquilizers were not administered in the acute phase of psychosis because the patients were not agitated. Beside absence of agitation, other common clinical features observed in the four patients were prominent delusion (rather than hallucination), obstinate refusal of oral medication, good pre-morbid functioning and very poor insight. Interestingly, following the remission of the acute psychotic phase, all showed marked improvement in their insight and had better than expected therapeutic alliance. **Discussion:** LAI may improve the doctor-patient therapeutic alliance due to its minimal side effects and by ways of increasing the patients' sense of control and allowing psychoeducation to take place when the patient is ready. We conclude that LAI may be used as the first line antipsychotic treatment in the acute psychotic phase in patients who are non-agitated but have prominent symptom of delusions with poor insight.

**Keywords:** Antipsychotics, Depot Preparation, Acute Psychosis

### Introduction

Long acting injectable (LAI) antipsychotics have long been recognized to benefit the management of chronic psychotic disorders like schizophrenia. Primarily, LAI were developed to address the issue of treatment

non-adherence for maintenance therapy of psychotic disorders<sup>1</sup>. For this reason, LAI are usually considered for use in the later course of illness whereby poor compliance is a recurring factor that hinders remission and recovery<sup>2</sup>.

As recommended by the 2009 NICE guidelines<sup>3</sup>, oral antipsychotic medication should be offered first for the newly diagnosed patients with schizophrenia, before LAI. LAI should be considered after an acute episode and/ or “where avoiding covert non-adherence to antipsychotic medication is a clinical priority within the treatment plan”<sup>4</sup>.

In the acute phase of psychosis, parenteral short acting antipsychotics are commonly administered to control the patients’ agitation and disturbed behaviour. More recently, with the advent of atypical antipsychotics in depot preparation such as intramuscular (IM) aripiprazole, IM risperidone and IM paliperidone, administration of LAIs in the early phase of the illness may have potential benefits due to their advantage of lesser side effects compared to the typical antipsychotics on top of improved delivery of medication as less monitoring is required<sup>5</sup>. It may have the capacity for better efficacy for symptom improvement and relapse prevention, thus preserving better functioning and quality of life<sup>6</sup>.

In this case series, we described the common clinical features of patients with psychosis who achieved remission after the administration of LAI as the first antipsychotic treatment. We report four patients, all of whom were drug naïve before they were administered LAI following a first presentation. We hypothesized that early administration of LAI atypical antipsychotic might actually improve the patient-doctor relationship in patients with certain clinical presentation.

### Case 1

Ms A, a 45 year-old lady, divorcee and beauty salon owner, had delusion of love with a superstar singer who had an untimely death, just prior to the onset of her illness.

She believed that the singer was alive and in hiding as he sent her signals of love through telephone messages and internet. She also had persecutory delusion as she believed that the singer conspired against her to cause her having financial problems with her business. She made reports against the late singer to the embassy of the country of the singer’s origin. At the time, she also faced business problems. Her family member observed that she started to make errors in her business and started to become preoccupied with peculiar talk about the superstar. Her pre-morbid functioning was good. She has a strong family history of schizophrenia.

She was brought to see a private psychiatrist who started her on IM risperidone and referred her to our hospital for psychiatric admission. In the ward, she was calm and cooperative despite having very poor insight. Initially, she refused oral antipsychotics. In the second week of her admission, she started to show improvement as she became less convinced in her delusional beliefs. She became aware of her abnormal symptoms and agreed to take daily oral risperidone. The depot injection was discontinued as the patient preferred to take the oral medication. She was compliant with the medication and regularly came for her follow-up clinic since her discharge.

### Case 2

Ms B, a 51 year old lady, divorcee and stationery shop owner, had an insidious onset of persecutory delusion of a few years toward her ex-husband and in-laws. She also persistently believed that her ex-husband was having extra-marital affair leading to their divorce. Her psychosis markedly worsened in the following years whereby her persecutory delusion later was extended against her children. She also had delusion of love as she believed that one of her

regular client was sending her messages of love. A month prior to her first psychiatric admission, she developed delusion of control in that she would only eat, drink and pass urine at certain times of the day as the rules were enforced to her by an external force. Physical examination and investigation showed she was weak and dehydrated with hypokalaemia. She was admitted to psychiatric ward, where she continued to refuse meals and oral medication. After rehydration, she was administered IM risperidone. She started to show improvement on day 6 of admission: she reported that the 'control' was lifted and started to eat. She became aware of her symptoms and also receptive to treatment. After the second dose of IM risperidone (after 2 weeks from the 1<sup>st</sup> dose) she complained of oligomenorrhea (secondary to hyperprolactinaemia, serum prolactin was 364iu/L). The treatment was then switched to IM paliperidone but oligomenorrhea persisted. Her treatment was then switched to oral olanzapine 5 mg daily. She had since discharged and been on regular psychiatric outpatient follow-up.

### Case 3

Ms C, a 36 year-old single lady, a business owner, presented with one year history of persecutory delusion towards her siblings following a failed business venture. She strongly believed that her siblings were jealous of her and sabotaged her to take over her business. She believed that she was secretly monitored by CCTV for over one year. She also strongly believed that a special microchip to monitor her thoughts was inserted into her ear by the treating psychiatrist when she was brought by her family members to the clinic. She refused to take any medication as she believed the psychiatrist was part of the conspiracy team. She however attended her clinic follow up regularly in the hope to have the chip

removed. She denied any hallucination or other psychotic symptoms. Her persecutory delusion persisted and she became more preoccupied with the microchip to the extent of requesting the veterinary surgeon to remove it. She was admitted to the ward involuntarily after a physical brawl with her siblings. She agreed to take depot injection of paliperidone as a bargain for her short stay in the ward. Her progress was noted in that she was no longer preoccupied about the microchip after the second administration of LAI in the following month even though she believed the chip was still in place. She agreed the medication has calmed her by reducing the unnecessary thoughts in her mind. She is currently in her sixth month of monthly LAI treatment and just started working as a cashier.

### Case 4

Ms D, a 35 year-old single lady, a university graduate and unemployed, had a prodromal illness of vague psychotic symptoms which started when she was a university student. Her illness became full blown a few years later as she presented with persecutory delusion related to her belief of having a non-existent business venture in the Middle East. There was inappropriate behaviour of talking to herself, reciting Quran or turning the radio loudly (possibly to alleviate auditory hallucinations), as well as neglect of self hygiene. She was brought for psychiatric treatment and prescribed with different types of oral atypical antipsychotics, which she never took. She was finally hospitalized for aggressive behaviour. In the ward, she refused all forms of treatment except for gastritis as she insisted that was her only problem. With her family's permission, she was started on risperidone depot injection. She improved and was discharged. Nevertheless, delivering the two-weekly risperidone injections remained a challenge as she

continued to resist the frequent injection. Her treatment was changed to monthly paliperidone injection when it became available in our setting in 2011. She progress well into remission as she became more cooperative with improved insight.

## Discussion

In this case series, we described four patients with first episode of schizophrenia whom were prescribed atypical LAI as the first antipsychotic treatment. They reported favourable outcomes in their symptoms remission and treatment compliance. The common indication for starting the LAI in these patients was to prevent treatment non-adherence, which was anticipated even in the early phase of their illnesses<sup>3</sup>.

We observed that all four patients shared a few common clinical features: 1) an obstinate refusal to treatment 2) absence of agitation 3) prominent delusion(s) 4) good pre-morbid functioning and 5) poor insight. Even though two out of four of the patients eventually chose to be on oral maintenance treatment, all the patients eventually agreed on their accord to be on regular medication.

In this case series, all four patients were administered the atypical LAI which was either risperidone or paliperidone. The first patient was on risperidone and later switched to paliperidone. As her insight improved, she chose to be on oral risperidone. The treatment for the second case was switched from risperidone to paliperidone and subsequently to oral olanzapine due to hyperprolactinaemia. Case 3 and case 4 continued to be well on monthly paliperidone. Both risperidone and paliperidone shared a common mechanism i.e. dopamine D2 and serotonin 5-HT<sub>2A</sub> antagonist with difference in the affinity to the respective receptors<sup>7,8</sup>. While the atypical antipsychotic has remarkably less extrapyramidal side effects, a proportion of

patients experienced significant metabolic side effects and hyperprolactinaemia, particularly in the long term<sup>9</sup>.

Interestingly, the therapeutic alliance between the patient and the doctor was better than expected. Hypothetically, early administration of LAI might have an added advantage of improving the patient-doctor therapeutic alliance as the treating team was spared the daily struggle of coaxing and monitoring the patient's medication intake since the patient obstinately refused oral medications. Meanwhile, the patients' receptiveness to his or her illness may be improved as the psychosis is reduced with LAI administration. The patients might feel in control as they were given the autonomy to take the oral medication when they were ready. This in turn, improves the effectiveness of psychoeducation; which is an integral part of psychiatric management in our setting.

Long term management of schizophrenia aims for full functioning patients' recovery, achievable by good compliance of maintenance therapy. In realizing this, the route of administration of antipsychotic may play a bigger role than previously thought of. Controlled trial of LAI as first line antipsychotic in combination with psychosocial measure like psychoeducation for indicated patients may provide a more conclusive evidence.

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