Multiple drugs

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Various toxicities: case report

A 17-year-old girl did to exhibit improvement during treatment with lurasidone for schizophrenia. Additionally, she developed extrapyramidal symptoms (akathisia, restlessness, muscle stiffness and gagging) during treatment with risperidone, increased mania during treatment with sertraline, altered mental status leading to delirium during treatment with risperidone and diphenhydramine, sialorrhoea during treatment with clozapine, dry mouth during treatment with haloperidol and clozapine, and catatonia during treatment with risperidone and olanzapine [*not all routes, time to reactions onsets and outcomes stated*].

The girl with a history of schizophrenia and major depressive disorder, was involuntarily admitted to an inpatient child and adolescent psychiatry unit for disorganised behaviour, aggression, agitation, psychosis and manic symptoms. Her mother reported that she had become increasingly psychotic and aggressive in the 3 weeks before the admission. As a result, the dose of lurasidone was increased from 40mg daily to 60mg daily 3 days before the admission. Her parents did not notice an improvement with the increase in lurasidone dose and reported that she had not slept since the dose was increased. Her mother reported on day of admission that her child was acting erratically, paranoid and constantly talking with an "imaginary friend.'' She was reported to be screaming and aggressive with her parents, ultimately biting her father. Parents called the police; when police arrived, she appeared to be incoherent, unresponsive to questions, and began to scream and shake. She was subsequently taken by ambulance to a community mental health center where she was given intramuscular doses of haloperidol 5mg, lorazepam and diphenhydramine 50mg, before transfer to a behavioural health hospital for further evaluation. On interview, she was euphoric, laughing inappropriately, and appeared to be talking to herself. She frequently stopped midsentence and stared blankly at the wall before being redirected. She was easily distracted by the surrounding noise. She demonstrated delusions of pregnancy, and repeatedly gave conflicting answers to questions. She was visibly paranoid, asking whether the social workers were talking about her, and whether anyone could hear her conversation with the interviewer. She was unaware of why her parents called the ambulance. She reported that she had been inconsistently taking her medications, last taking them the day before, as they made her "gurgle.'' She endorsed low mood, poor sleep, reduced concentration within the past several weeks, and intermittent suicidal ideation over the past several months. She reported having suicidal thoughts as recently as the day before admission, at which time she made two superficial cuts on her left wrist in what she reported was an attempt to kill herself. She denied any previous suicide attempts. She also denied current suicidal or homicidal ideation, intent or plan. She later became aggressive and started banging on a door in the unit, requiring additional doses of lorazepam and diphenhydramine intramuscularly on admission. Her past psychiatric history was significant for paranoia and auditory hallucinations (at the age of 13 years). She had been hospitalised three additional times at various institutions with similar symptoms and suicidal ideation. Her mother reported that her child began to verbalise suicidal thoughts 2.5 years ago, and had not acted on these thoughts in the past. Her mother also reported that her child began to display increased aggression and manic symptoms, such as poor sleep, pacing, rapid speech, irritability, and mood swings during her most recent exacerbations of psychotic symptoms within the past 2 years. Per mother, her child had a history of running away from home. Before admission to the inpatient child and adolescent psychiatry unit, she had been in treatment with an outpatient therapist and psychiatric physician assistant at a community mental health center. She had been diagnosed with major depressive disorder and schizophrenia in the past. Her medical history was also significant for migraine headaches, which had been diagnosed at the age of 13 years and spontaneously resolved a few months later. Brain MRI at time of diagnosis was normal. She also had myopia requiring corrective lenses. She had no history of general medical hospitalisations, head injury or seizures. Growth and development were on target. There were no known allergies. She denied ever taking any non-psychiatric medications other than naproxen as needed for pain, corroborated by mother. On admission, her medication regimen incl uded clonidine for aggression, sertraline 100mg daily for depressive symptoms, and lurasidone 60mg daily for psychotic symptoms. Her mother reported that sertraline had worked well for depressive symptoms. On admission to the inpatient child and adolescent psychiatry unit, a working diagnosis of psychosis and mania was made. Laboratory studies, including a comprehensive metabolic panel, complete blood count, urinalysis, and thyroid stimulating hormone (TSH), were within the normal limits. Urine drug screen, urine pregnancy test, and COVID-19 PCR were negative. Her mother was contacted for collateral information and provided consent for psychiatric medication. She was treated for a urinary tract infection; however, there was no clear correlation with psychosis, which was prominent before and after treatment with antibiotics [*specific drug not stated*]. On admission, risperidone 1mg twice daily was started for psychotic symptoms. Clonidine and sertraline 100mg daily were continued. She developed extrapyramidal symptoms (akathisia, restlessness, muscle stiffness and gagging) within 2 days of starting risperidone. Benztropine was initiated due to concern for extrapyramidal symptoms (EPS). Benztropine was replaced with diphenhydramine 25mg daily and 50mg at bedtime for EPS, as she also reported significant insomnia [*aetiology not stated*]. After a switch from benztropine to diphenhydramine, she developed altered mental status, suggesting a possible medication-induced delirium. She continued to manifest euphoria with labile affect and inappropriate laughter. She was also sexually preoccupied, appeared to be talking to herself, and demonstrated bizarre behaviour such as walking around the unit while disrobing. Risperidone was titrated upward to 2mg BID; however, she continued to display psychotic symptoms and agitation with increasing doses, requiring emergency treatment medications [*specific drug not stated*]. Sertraline 100mg daily was then tapered to discontinuation for potential contribution to increased mania. Additional collateral information obtained from mother and observations by the treatment team prompted a change in working diagnosis to schizoaffective disorder, bipolar type. She was then started on valproate-semisodium [divalproex-ER] which was gradually increased and risperidone was gradually increased to 3mg twice a day. She subsequently demonstrated significant improvement in psychotic and manic symptoms. However, serum valproic acid level was found to be supratherapeutic at 142 mg/L. As a result, the dose of valproate-semisodium was decreased, following which her psychotic and manic symptoms worsened. She described paranoid delusions, endorsed auditory hallucinations, displayed inappropriate laughter, and required daily as needed lorazepam for anxiety. Risperidone was further increased to 3mg daily and 4mg at bedtime. She continued to display psychotic symptoms, including paranoia regarding her medications, somatic preoccupations and bizarre behaviour. Valproate-semisodium was discontinued due to poor efficacy at the reduced dose. Lithium was initiated for mood stabilisation. Psychotic and manic symptoms continued to worsen, and she became increasingly agitated, urinating on the floor and banging on doors. Complete blood count, comprehensive metabolic panel, urinalysis, TSH, B12 level and folate level were all within normal limits. Brain MRI was also within the normal limits. Risperidone dose was gradually decreased and diphenhydramine was discontinued for possible contributions to her altered mental status. Her mental status later stabilised. Clozapine was initiated at 25mg at bedtime and metformin was started as prophylaxis for weight gain. The dose of risperidone was gradually decreased to discontinuation with cross-taper of increasing doses of clozapine. During cross-taper of antipsychotics, she became catatonic. She was unresponsive to questions, staring for >1 minute, posturing with hands behi nd her head for several minutes, and not able to follow commands. She scored a 12 on the Bush–Francis catatonia scale. It was found that she had received 5mg of IM olanzapine the night before developing catatonic symptoms. It was concluded that she developed catatonia secondary to

risperidone and olanzapine. The catatonia responded to a lorazepam challenge, with resolution of the symptoms on initiation of lorazepam, which was eventually tapered to discontinuation before discharge. Lithium was further increased, and clozapine was titrated slowly upward as tolerated. As clozapine was increased to 100mg twice a day, her psychotic symptoms began to improve significantly. Adverse effects of intermittent sialorrhoea (episodes of hypersalivation were transient) and dry mouth were noted at this dose. Also, haloperidol was considered to have contributed to dry mouth. She no longer endorsed auditory or visual hallucinations, and reported that her thought process felt more clear. She continued to demonstrate delusional thought content at times, but in combination with increased moments of lucidity and insight. She also reported improved mood and began interacting appropriately with her peers.

The girl was discharged on hospital day 42. Medications at discharge included clozapine 100mg daily and 125mg at bedtime, lithium, clonidine and metformin. She was discharged with referrals for outpatient psychotherapy and medication management to a community mental health center.

Miller M, et al. Overcoming complications in management of a difficult-to-treat adolescent with schizoaffective disorder. Journal of Child and Adolescent Psychopharmacology 30: 526-530, No. 8, Oct 2020. Available from: URL: http://doi.org/10.1089/cap.2020.29190.bjc 803520672