CASE REPORT PEER REVIEWED | OPEN ACCESS

Urinary retention by mirtazapine: A case report

Madhav Gajananrao Raje

ABSTRACT

Introduction: Mirtazapine is considered to be safest and versatile antidepressant. However, sedation is known to be dose dependent side effect. 7.5 mg/day mirtazapine induces more sedation than 15 mg/day mirtazapine. There is no other side effect of mirtazapine which is reported to be dose dependent. Case Report: Here is a case, where dose dependent urinary retention is detected. A 38-year-old married female reported with array of recurring symptoms like dysphoria, insomnia, loss of appetite, burning all over, uneasiness, increased frequency of micturation and stool, irritability, frustration, weeping often. She was symptomatic since last five to six years, despite regular psychiatric treatment. Her earlier psychiatrist had expressed inability to treat recurrence and intensity of her symptoms. She was kept on mirtazapine 7.5 mg per day to begin with. She responded favorably. To gain more relief dose of mirtazapine was increased to 15 mg/day. Within one to two days she complained of inability to pass urine. Her complaint was specific that she was not able to empty her bladder completely. After completing the act of micturation she used to experience much discomfort in pelvic region. Further investigations revealed significant urinary retention. Lowering of dose brought her relief immediately. Conclusion: Mirtazapine with dose of 7.5 mg per day effectively could treat recurring symptoms of a female patient. But increase in dose up to 15 mg/day caused significant side effect of urinary retention against the conventional belief of rise in dose of mirtazapine would increase the relief.

Keywords: Dose dependant side effect, Mirtazapine, Rare adverse effect, Urinary retention

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INTRODUCTION

Common side effects of mirtazapine are weight gain and sedation. Its antagonistic action on 5HT3 and H1 receptors [1, 2] is attributed for this side effect. Other common side effects of mirtazapine are (head to toe) giddiness, confusion, swelling over face/feet, eye pain, red eye, difficulty in breathing, dry mouth, rash/itching, tightness in chest, gastrointestinal disturbances like nausea/vomiting, constipation, weakness, loss of libido, weight gain, arthralgia, uneasiness, urinary retention, etc. Most of the time side effects disappear after couple of days [2], despite continued medication.

Urinary retention is not one of the commonly reported side effects, though occasionally it is observed in psychiatry practice [3]. Data available on epidemiology of female urinary retention is also not adequate [3,

4]. Urinary retention in female is more uncommon. Antidepressant like mirtazapine which belong to Norepinephrine specific serotonin receptor inhibitor (NaSSA) class may rarely cause urinary retention. However, dose dependant phenomenon of this side effect is not known.

Unlike sedation [2]; dose dependant urinary retention is not yet been reported. Hence, case of urinary retention by higher dose of mirtazapine is worth to be noticed.

CASE REPORT

A 38-year-old mother of two children, weighing 65 kg, a part-time laborer, with caring and supporting nuclear family presented with array of changing symptoms. Symptoms were, all day long dysphoria, lack of sleep, loss of appetite, burning all over body, indigestion, body ache, chest pain, uneasiness, increased frequency of micturation and stool, headache, frustration to the extent of weeping at times, irritability. She was experiencing these symptoms with fluctuating intensity, since five to six years. She had over-concern for her health issues fulfilling the criteria of Hypochondriasis. Occasionally, she experiences intense uneasiness, fear of dying, palpitation. History suggestive of obsessive compulsive features, hypochondriasis, phobia, and dysthymia was noticed in detail psychiatric interview. Detailed psychiatric interview diagnosed her as suffering from obsessive compulsive spectrum disorder (OCSD), dysthymia, and benzodiazepine dependence.

Past history revealed that she was taking treatment from psychiatrist for more than two years. She was prescribed clonazepam, etizolam, and olanzapine regularly for more than two years. But her symptoms used to recur quite often. Her symptoms were mostly uneasiness, changing somatic complaints like chest pain, headache, backache, increased frequency of micturation. She also complained of lack of sleep, irritability, nervousness repeatedly. As a result of these varying symptoms she used to get impatient and intolerant. She used to express her frustration, lack of relief to her doctor. Hence she used to visit her doctor every now and then, even much before her next appointment. After more than a year her treating psychiatrist expressed his frustration of offering her total relief. She remembers him telling her to seek another psychiatrist's help. According to her past history and clinical picture she was categorized a 'difficult patient to treat'.

Blood investigations of the patient revealed hemoglobin 11.6 g/dl, serum prolactin 7.5 ng/ml, urea 22.72 mg/dl, creatinine 0.73 mg/dl, Na 136 mEq/L, K 3.2 mEq/L.

In view of persistent symptoms, especially of Insomnia, anxiety, hypochondriac thoughts, she was put on sertraline, clonidine, and diazepam. Psycho education clubbed with supportive psychotherapy was offered simultaneously (APA 2004 guidelines assert). Her insomnia and dysphoria as a result of lack of sleep was treated in the first consultation by paradoxical intervention (a psychotherapeutic module) effectively.

The patient responded partially, i.e. symptoms like insomnia, uneasiness, reduced. But symptoms like loss of appetite, frequency of micturition, burning over chest, headache, dysphoria, hypochondriac thoughts did not improve for almost two to three weeks. Her increased frequency of micturation and amenorrhea did not improve over a month's period, so was referred to gynecologist. Gynecologist found nothing significant on clinical and sonography examination and prescribed alkalizer to alleviate symptoms. Micturation related symptoms recovered after six weeks, on its own.

She was kept on sertraline 100 mg, diazepam 10 mg, and gabapentin 300 mg, per day for 11 weeks (clonidine which was prescribed for sedation and anxiety was withdrawn after two weeks). There was partial improvement. But, symptoms like disturbed sleep, delay in passing urine, body ache, giddiness, fear of going out, etc. fluctuated significantly and persisted even after treatment for 11 weeks. So sertraline (SSRI) was gradually tapered off and mirtazapine was introduced. Her anxiety responded favorably and within two to three days [3] in response to the beginning dose of 7.5 mg once a day mirtazapine at night. Diazepam, gabapentin were continued in earlier doses. However her pain did not respond, so dose of mirtazapine was increased to 15 mg/day after six weeks. Within one to two days of starting 15 mg/day mirtazapine, she started complaining of increased frequency of micturition, discomfort and fullness in lower abdomen, associated with passing small amount of urine every time. This increased frequency of micturition disturbed her sleep, bowel movements too.

Looking at the patient heightened symptomatic picture, she was referred to gynecologist again. On sonography; this time, gynecologist noticed significant post void residual urine (more than 100 ml). On the basis of clinical judgment, instead of referring her to urologist, dose of mirtazapine was reduced to 7.5 mg immediately. Next day she reported relief. On subsequent days, she reported improved bowel movements, improved feel of evacuation and symptoms related to passing urine reduced completely. She was asymptomatic with 7.5 mg of mirtazapine once day (OD) at night, with gabapentin 300 mg once a day, diazepam 5 mg OD in the next follow up even after four months.

DISCUSSION

Core mechanism of action of antidepressants, may be TCA or SSRI, is potentiating serotonergic transmission. That means, both NE reuptake inhibitors and serotonin reuptake inhibitors work to enhance serotonergic function. However, mirtazapine is a receptor blocking drug rather than uptake inhibitor and enzyme inhibitor unlike other antidepressants. Hence it is called Noradrenergic and specific serotonergic antidepressant (NaSSA). It blocks alpha 2 adrenergic receptors (auto and hetero), 5HT receptors which are presynaptic, there by facilitates

increased release of Noradrenalin and serotonin. It also blocks the 5HT-2 and 5HT-3 receptors which are post-synaptic. Thus it spares action on 5HT1, resulting in specific serotonin release activity. It is a partial agonist of 5HT-1, resulting in increase in transmission through 5HT-1. At lower dose, mirtazapine has more affinity with histamine receptors, thus causes sedation. But at higher doses it does not block histamine receptor, so causes less sedation [2, 5]. At higher doses, mirtazapine increases noradrenergic transmission.

Pharmacokinetics of mirtazapine is age and gender dependent [5]. Female and elderly show higher plasma levels. It is rapidly absorbed when taken orally [2]. Plasma concentration is achieved within one to two hours. 50% of drug's bioavailability is achieved within two to three hours, since mirtazapine is metabolized through first intestinal and hepatic bypass mechanism. Hence, unlike other antidepressants mirtazapine start therapeutic effect within first week [3]. Male under 48 years, require more dose than female to have equivalent plasma concentration. Meaning young female absorb mirtazapine faster and maximum pl. concentration is reached earlier than male. Half-life of mirtazapine is 37 hours and 26 hours in case of female and male respectively [6].

Reasons behind selection of mirtazapine: Overwhelming anxiety, psychic element of anxiety, repeated somatic complaints, disturbed sleep and experience of partial relief even with poly-pharmacy were the reasons behind selection of mirtazapine [7, 8].

Mirtazapine is also reckoned to reduce obsessive compulsive symptoms hence replacing SSRI by mirtazapine could not have accelerated OCSD symptoms. Additionally; issues of poly-pharmacy and issue of treating 'difficult patient' could have been dealt with by mirtazapine [7]. So, Mirtazapine was the real answer to many questions.

Effect of mirtazapine is found different at 7.5 mg than that of at 15 mg. At 7.5 mg mirtazapine shows agonistic effect on histamine receptors (H1) and antagonistic effect on alpha 2 adrenergic receptors. Apha 2 c receptor is situated on adrenal medulla. It causes inhibition of catecholamine. Antagonistic action of mirtazapine on alpha 2 c causes release of noradrenalin. This increased surge of noradrenaline has attributed urinary retention in this case. At higher doses like 15 mg a day, it sans partial effect on H1 receptors, but has significant effect on serotonergic and noradrenergic receptors. So noradrenaline release increases [8]. It is because of this increased release of noradrenaline, constriction of sphincters, i.e., of bladder and bowel might have taken place in this patient. Thus, constriction of sphincters has caused symptomatic urinary retention. Despite starting dose of mirtazapine is usually 15 mg per day [2], it is found that 7.5 mg per day dose of mirtazapine not only relieved symptoms in this case but maintained recovery as well.

CONCLUSION

Increase in the dose of mirtazapine up to 15 mg per day from 7.5 mg/day caused urinary retention in an adult female. Adverse effect of mirtazapine occurred within one to three days. Urinary retention was reverted back within a day on reducing the dose. 7.5 mg of mirtazapine is an adequate dose to treat dysthymia in this case. 7.5 mg of mirtazapine effectively avoided polypharmacy and maintained good clinical long lasting outcome.

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Author Contribution

Madhav Gajananrao Raje – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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