Safety and efficacy of ketamine infusion in late onset depression, and conversion to treatment response

Sir,

Response rates to first line antidepressant therapy are abysmally low, and more so in older adults. Ketamine has been used successfully in treatment-resistant depression (TRD), and in nongeriatric population, with response rates at 24 and 72 h postinfusion being 25–85% and 14–72%, respectively. The postulated mechanism of action is through antagonism of N-methyl-D-aspartate receptors.

A 65-year-old retired civil servant, living with her husband had fourth episode of depressive illness. In the last 3 years, the illness showed increasing resistance to antidepressant medication(s) with each additional episode. The first episode remitted with escitalopram (10 mg/day), the second episode required higher dosage of escitalopram (40 mg/day), and later, augmentation with amisulpride 25 mg/day, and the third episode remitted with duloxetine (up to 60 mg/day) (as she had relapsed while on escitalopram) and amisulpride 100 mg/day. In the Inter-episode period, the patient had attended all follow-up appointments and continued with prescribed medication. In this episode, she had failed treatment with duloxetine + amisulpride, agomelatine, and agomelatine + amisulpride, respectively.

Informed consent was obtained from the patient. Ketamine infusion (0.5 mg/kg diluted in 100 ml of normal saline) was given over 40 min, under the supervision of consultant anesthetist (RSG). Ratings of mood (Hamilton rating scale for depression [HAMD]) and side effects (Clinician Administered Dissociative States Scale) were undertaken on morning of the infusion, and 1, 2, and 4 h following infusions, and on in between days of the infusion [labelled as postinfusion days in Table 1]. Four days after the 4th infusion (HAMD = 10), the patient feeling very much improved subjectively, the ketamine infusions were discontinued, with the provision that further infusions may be required if the depressive symptoms recurred. Agomelatine 50 mg/day was continued through the infusion period and in the follow-up phase.

Remission (HAMD <7) was maintained for another 1 year (HAMD administered biweekly for first 2 weeks, then weekly for 4 weeks, and then monthly) when the patient discontinued follow-up visits.

The side effects reported with the infusions were – alteration of passage of time (infusion 3, hours 1 and 2) and mild gaps in memory (infusion 4, hour 2). These symptoms disappeared in an hour of the infusion.

The case illustrates several points of interest: From the first episode 3 years ago, subsequent episodes became more difficult to treat; amisulpride worked effectively as augmentation agent in the previous episodes when co-administered with a selective serotonin reuptake inhibitor and serotonin and norepinephrine reuptake inhibitors, respectively, ketamine was well tolerated with minor and transient side effects; and the remission induced by ketamine infusions was maintained on the same antidepressant agomelatine.

Contrary to previous literature, where ketamine has been used as a “last resort in pharmacotherapy” for TRD, it was

| Infusion day | HAMD day 1 | HAMD day 2 |
|-------------|------------|------------|
| Ketamine-1 – Monday | 17 | 5 |
| Ketamine-2 – Thursday | 12 | 3 |
| Ketamine-3 – Monday | 9 | 13 |
| Ketamine-4 – Thursday | 19 | 8 |

Infusion day – 1 h before giving ketamine infusion; 1 h/2 h/4 h – Duration after completed ketamine infusion. HAMD – Hamilton rating scale for depression.
used relatively early in the course of illness. The aim was to abort the depressive episode as longer unresolved episodes lead to poor prognosis.[5]

To the best of our knowledge, this is the first report of use of ketamine in late onset depression, and illustrates therapeutic efficacy and safety of ketamine in an older adult, and conversion from treatment resistant to treatment responder on the same antidepressant.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Shrikant Srivastava, Radhey S. Gangwar, Ambrish Kumar
Department of Geriatric Mental Health, K G Medical University, Lucknow, Uttar Pradesh, India.
E-mail: shrikant@kgmu-edu.org

REFERENCES

1. aan het Rot M, Collins KA, Murrough JW, Perez AM, Reich DL, Charney DS, et al. Safety and efficacy of repeated-dose intravenous ketamine for treatment-resistant depression. Biol Psychiatry 2010;67:139-45.
2. Rao TSS, Andrade C. Innovative approaches to treatment- refractory depression: The ketamine story. Indian J Psychiatry 2010;52:97-9.
3. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56-62.
4. Bremner JD, Krystal JH, Putnam FW, Southwick SM, Marmar C, Charney DS, et al. Measurement of dissociative states with the Clinician-Administered Dissociative States Scale (CADSS). J Trauma Stress 1998;11:125-36.
5. Koenig AM, Butters MA, Begley A, Ogbagaber S, Wahed AS, Reynolds CF rd. Response to antidepressant medications in late-life depression across the spectrum of cognitive functioning. J Clin Psychiatry 2014;75:e100-7.