

# LAMOTRIGINE AND KETAMINE

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The other day, I was called to the ED to assist in chemically controlling one of our psychiatric usual suspects who had been admitted with her customary friday night OD. This time she had ingested an unknown amount of the Lamotrigine she was on for a bipolar disorder.

## **Our patient**

Most lamotrigin ODs experience minor clinical effects like drowsiness or tachycardia. Our patient was, on the contrary, extremely agitated with choreatic/ataxic flailing movements of her extremities. It is a known <sup>[1]</sup>, but uncommon presentation of Lamotrigine toxicity.

At my arrival two nurses and two paramedics were pretty much sitting on the patient. For her own safety and to at all manage the situation, the patient urgently needed to be sedated. We opted for an intubation and then sedation in the ICU over night. For no particular reason, other than that there were too many unknowns in this scenario, I decided to use ketamine for induction.

## **The not so rapid sequence induction**

After three minutes of forced pre-oxygenation we decided to push the ketamine.

She was given boluses of 50mg. Our plan was then to push the succinylcholine and intubate whenever we achieved dissociative anaesthesia.

*Well...dissociative anaesthesia never happened.*

*The patient, weighing 60kgs was administered a total of 300mgs of IV Ketamine without even flinching.*

There was no anaesthesia, no sedation, actually no change whatsoever in her behaviour. The nurse anaesthetist noted how the patient was possibly more agitated than before.

After waiting for ten minutes we had enough. We administered 120mg of propofol, the patients promptly went comatose, we pushed the sux and uneventfully intubated the patient (Proving our IV lines were good).

The next day our patient was extubated and could confirm that she had overdosed on lamotrigine alone. Serum lamotrigine concentrations arrived a few days later.

191,9 micromol/L, well above the therapeutic reference values of 10-60.

### **Ketamine and Lamotrigin don't match**

300mg of Ketamine had been pushed and the patient didn't even flinch. She weighed approximately 60kgs, meaning she was given 5mg/kg intravenously. We know how some patients require higher doses to achieve dissociative anaesthesia but I never had to give more than 4mg/kg IV.

We suspected lamotrigine somehow had attenuated the expected ketamine effect and decided to look into it.

The only reference google came up with was from a forum for *people of a low moral fiber*. In the comments section for the thread called 'Exit from planet K' I read the following:

*'I am a bipolar and have been abusing K for a year shooting huge amounts almost daily and just couldn't stop until the day I started taking a mood stabilizer called "Lamotrigine" which blocked Ketamine effects completely'*

So it would seem those people of a *low moral fibre* know something I don't. Lamotrigine does attenuate or block ketamine effects.

I decided to ignore the next comment as it didn't make sense to me. It was just crazy talk:

*'My pet monkey used to use silly amounts of ketamine nasally and felt trapped within this addiction until one day for an unknown reason my monkey just stopped.'*

### **Lamotrigine attenuates Ketamine**

Next I made a quick pubmed search. I could only find two studies that were immediately relevant. Both of them seem to give clues as to why our patient was resistant to ketamine.

In short they describe how ketamine's dissociative effects is not likely to be mediated by NMDA-antagonism. Rather they are mediated by ketamine increasing glutamate production and this increased glutamate acting on non-NMDA-recetors.

Lamotrigine is an anti-convulsant, that works partly by decreasing glutamate release. In theory lamotrigine directly counteracts the increased non-NMDA

glutamnergic transmission of ketamine.

Could it explain why our patient wasn't affected by the high intravenous dose of ketamine she was given?

1. <http://www.ncbi.nlm.nih.gov/pubmed/15353576>
2. <http://www.scancrit.com/wp-content/uploads/2012/06/Abstract1.jpg>
3. <http://www.scancrit.com/wp-content/uploads/2012/06/Abstract1.jpg>