Terlipressin and tricyclic antidepressant intoxication

Dear sir,

Veris-van Dieren *et al*. report the importance of early ECG recordings in the diagnostic process of patients who are suspect for tricyclic antidepressant (TCA) intoxication.[1] The first case describes a clinical example of pulseless electrical activity (PEA), bradycardia and immeasurable pulse in a 66-year-old woman intoxicated with tricyclic antidepressants. The patient was treated with high-dose (quantity not mentioned) inotropics and vasopressors (epinephrine and norepinephrine). Since catecholamines compete with TCAs for α_1-adrenergic receptor binding, clinicians may be forced to infuse high doses of catecholamine in TCA-overdose patients in order to maintain an adequate organ perfusion pressure. *Tables 1* and *2* show the correlation between receptor affinity of TCAs and occurrence of side effects. However, high-dose catecholamines can have detrimental side effects.[2] Earlier this year we reported[3] a similar case in which the patient was treated with 1 mg terlipressin intravenously, with excellent haemodynamic and neurological outcome.[3] Terlipressin, a vasopressin analogue with a prolonged duration of action, acts as a selective V_1-receptor agonist. Stimulation of V_1 receptors

Table 1. *Common adverse effects of TCAs*

Generic name	Adverse effects				
Tertiary amines	**Hypotension**	**Sedation**	**Anticholinergica***	**Cardiac effects**	**Seizures**
Amitriptyline	+++	+++	+++	+++	++
Clomipramine	++	++	+++	+++	+++
Doxepine	+++	+++	++	++	++
Imipramine	++	++	++	+++	++
Trimipramine	++	+++	+++	+++	++
Secondary amines					
Amoxapine	++	+	+	++	++
Desipramine	+	o/+	+	++	+
Maprotiline	++	++	++	++	+++
Nortriptyline	+	+	+	++	+

*For example, tachycardia, dry mouth, urine retention, constipation.

Table 2. *Receptor affinity of TCAs*

Generic name	Receptor affinity				
Tertiary amines	α_1	H_1	M_1	D_2	α_2
Amitriptyline	+++	++++	++++	o	+/-
Clomipramine	++	+	++	++	o
Doxepine	+++	++++	++	o	o
Imipramine	++	+	++	o	o
Trimipramine	+++	++++	++	++	+/-
Secondary amines					
Amoxapine	++	+	o	++	o
Desipramine	+	+/-	+	o	o
Maprotiline	++	+++	+	+	o
Nortriptyline	++	+	++	o	o

α_1 = alpha-1 receptor; α_2 = alpha-2 receptor; H_1 = histamine-1 receptor; M_1 =muscarine-1 receptor; D_2 = dopamine-2 receptor.

results in elevation of intracellular calcium which, in turn, contracts smooth muscle cells resulting in an α_1-adrenergic receptor-independent vasoconstriction, and increase in systemic vascular resistance (SVR) and mean arterial pressure (MAP).[4] Since vasopressin analogues 'bypass' the hampered catecholamine system in TCA overdose, it may be an alternative strategy to manage hypotension that is refractory to catecholamines in TCA intoxication.

Furthermore, based upon old literature, the authors advise the reader to be cautious with the use of sodium bicarbonate ($NaHCO_3$) in TCA intoxication. Some case reports and animal studies suggest that cardiac arrhythmias and broad QRS complexes react to aggressive treatment with $NaHCO_3$. In spite of hard scientific evidence, Vrijlandt and colleagues recommend the use of $NaHCO_3$ in TCA-intoxicated patients.[5] As mentioned before, $NaHCO_3$ can diminish direct cardiac toxicity and facilitates binding of TCA to proteins which, in turn, lowers the free fraction of TCA.

In conclusion, we suggest that terlipressin may have a potential role as an adjunct vasopressor in a shock state refractory to catecholamines in TCA-intoxicated patients and recommend the use of $NaHCO_3$.

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REFERENCES

1. Veris-van Dieren J, Valk L, van Geijlswijk I, Tjan D, van Zanten A. Coma with ECG abnormalities: consider tricyclic antidepressant intoxication. Neth J Med 2007;65(4):142-6.
2. Luckner G, Dunser MW, Jochberger S, et al. Arginine vasopressin in 316 patients with advanced vasodilatory shock. Crit Care Med 2005;33(11):2659-66.
3. Zuidema X, Dunser MW, Wenzel V, Rozendaal FW, de Jager CP. Terlipressin as an adjunct vasopressor in refractory hypotension after tricyclic antidepressant intoxication. Resuscitation. 2007 Feb;72(2):319-23.
4. Kam PC, Williams S, Yoong FF. Vasopressin and terlipressin: pharmacology and its clinical relevance. Anaesthesia 2004;59(10):993-1001.
5. Vrijlandt PJ, Bosch TM, Zijlstra JG, Tulleken JE, Ligtenberg JJ, van der Werf TS. Sodium bicarbonate infusion for intoxication with tricyclic antidepressants: recommended in spite of lack of scientific evidence. Ned Tijdschr Geneeskd 2001;145(35):1686-9.