

## **Publication**

Acute Calcineurin Inhibitor Overdose: Analysis of Cases Reported to a National Poison Center Between 1995 and 2011

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Transplant recipients and other patients requiring immunosuppression with calcineurin inhibitors or their household contacts may be exposed to overdose. This study investigated the circumstances, pharmacokinetics and outcomes of overdose with cyclosporine and tacrolimus reported to the Swiss Toxicological Information Centre between 1995 and 2011. Of 145,396 reports by healthcare professionals, 28 (0.02%) concerned enteral or parenteral overdose with these calcineurin inhibitors. Thirteen (46%) were iatrogenic errors, 12 (43%) were with suicidal intent and 3 (11%) were accidental. latrogenic overdoses usually involved noncapsule drug formulations. Acute enteral overdoses caused symptoms in a dosedependent fashion but were generally well tolerated; the mean multiple of patient's usual dose was 20.8  $\pm$  28.8 for symptomatic versus 4.4  $\pm$  3.4 for asymptomatic cases (p = 0.037). The most common symptoms were nausea, headache, somnolence, confusion, hypertension and renal impairment. In contrast, acute intravenous overdoses were often poorly tolerated and resulted in one fatality due to cerebral edema after a cyclosporine overdose. Enteral decontamination measures were performed in six cases involving oral ingestion and appeared to reduce drug absorption, as shown by pharmacokinetic calculations. In the one case where it was used, pharmacoenhancement appeared to accelerate tacrolimus clearance after intravenous overdose.

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