Quetiapine-related deaths and emergencies in Victoria, Australia (2006-16)

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Introduction & Aims: Quetiapine is a short-acting antipsychotic used in the treatment of schizophrenia and bipolar disorder. Increasing evidence of potentially risky off-label use, in addition to misuse for its sedative and hedonic effects, has raised concerns with regards to overdose. This study aimed to examine Victorian coroners' cases and calls to the Victorian Poisons Information Centre (VPIC) over the last decade, to examine the trends and characteristics of quetiapine-related harm.

Methods: Fatal cases were identified from the Victorian Institute of Forensic Medicine's case management system. All deaths occurring between 1 January 2006 and 31 December 2016 were collected where quetiapine was detected following toxicological analysis. Information from calls made to the VPIC during the same period was also collected. The VPIC provides over-the-phone community information regarding poisoning, overdose, and envenomation. Details of these calls are maintained in a database which was interrogated for this study. Prescription data was also collected from the Pharmaceutical Benefits Scheme's Australian Statistics on Medicines.

Results & Discussion: There were 359 quetiapine-related deaths occurring over the 11 years, with a 544% increase between 2006 (n=9) and 2016 (n=58). There were more males (56.5%) with an average age of 42 (range 15 – 79) years old. Intentional self-harm and unintentional deaths accounted for 25.1% and 17.8% of the cohort, respectively. In the remaining cases, intent was undetermined. Blood quetiapine concentrations ranged from 0.01-667mg/L, with a median of 0.14mg/L. Other drugs co-detected in blood with quetiapine commonly included alcohol, benzodiazepines and pharmaceutical opioids, as well as 6-acetylmorphine (heroin metabolite) and methylamphetamine. During 2006-2016, calls to the VPIC concerning quetiapine increased 5.5 fold; from 126 calls in 2006 to 751 calls in 2016. Many of these involved polypharmacy; specifically antidepressants (41%) or benzodiazepines (40%). Calls typically related to overdose (77%), followed by therapeutic error (11.7%), misuse (5%), accidents (5.6%), or miscellaneous concerns (<1%). Females were most represented among quetiapine overdose calls (68%), with the 25mg (n=474) and 100mg (n=407) immediate release formulations most commonly implicated. Quetiapine prescriptions in Australia also increased over time; defined daily doses per 100 population showed a 225-fold increase between 2000 (0.012) and 2015 (2.7).

Conclusions: This study demonstrated an increasing trend in quetiapine-related deaths and non-fatal overdose in Victoria over the past decade. This correlates with an increase in quetiapine prescriptions, which may be related to the extra indications added since initial market release. This indicates the need for increased monitoring of quetiapine-treated patients, particularly in the setting of polypharmacy.

Keywords: quetiapine; fatalities; overdose; prescription drugs; antipsychotic