Risk of Road Traffic Accidents in Patients Discharged Following Treatment for Psychotropic Drug Overdose: a Self-Controlled Case Series Study in Australia

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Abstract:

Background: Use of psychotropic drugs is known to impair driving and increase the risk of road traffic accidents. They are also the most common drugs taken in overdose in hospital-treated episodes of self-poisoning. Most of these patients are discharged within 48 hours, while they still have possible subclinical drug-effects.

Objective: Using a self-controlled case series design, we aimed to determine whether patients with psychotropic drug overdose are at a higher risk of a traffic accident in the period following discharge compared to a control period not associated with hospital-treated drug overdose.

Methodology: Using the New South Wales (NSW) Admitted Patient Data Collection (APDC) as the primary source, we retrieved 40845 hospital separation records dated between 1 July 2000 and 30 June 2008 (8-years) in patients aged 18–80 years admitted to a hospital in NSW following an intentional self-poisoning with a psychotropic drug (coded X61 or X62 as the ICD-10 external cause of injury). Of these, 33459 hospital separations (of 24284 patients) were considered eligible as they were discharged directly into the community where they could have driven a motor vehicle. We selected three separate post-admission periods (3 days, 1 week and 4 weeks), subtracted the number of inpatient days from each and calculated three separate post-discharge periods (immediate, intermediate and extended, respectively) for each episode of poisoning. The control period was the duration of the study period where the individual was 18 years or older, excluding the total person days in the post-discharge period/s and the index inpatient period/s. The APDC dataset was linked to the NSW Roads and Traffic Authority CrashLink dataset to identify any accidents in which each patient was involved as a motor-vehicle driver during the follow-up period. Incidence rate ratio (IRR) for

matched post-discharge and control periods was found using random effects Poisson regression.

Results: 72% of the subjects were discharged within 2 days following their admission with self-poisoning. Compared to the corresponding control periods the risk of a traffic accident was 3.5-times (IRR=3.49; 95%CI 1.66, 7.33; p=0.001) during the immediate, 1.9 (IRR=1.88; 95%CI 1.09, 3.25; p=0.023) during the intermediate, and 1.6 (IRR=1.65; 95%CI 1.27, 2.15; p=0.0002) during the extended post-discharge period.

Conclusions: Self-poisoning with psychotropic drugs is associated with a markedly increased risk of a traffic accident during the first few days following discharge. These findings raise clinical and medico-legal implications concerning fitness-to-drive during this period. The risk reduces with time but remains significantly elevated after 4 weeks post-overdose. Further research is necessary to find out the factors contributing to this ongoing risk.

Background

Psychotropic drugs[a] could impair driving and be associated with increased risk of road traffic accidents.[1-3] Pharmacoepidemiological studies in particular have focused on accident risk associated with therapeutic use of medications including benzodiazepines,[4-9] antidepressants[5, 8-11] and opioids [5, 8, 11, 12]. However, psychotropic drugs are also among the most common substances taken in overdose, accounting for around 100000 hospital-treated overdoses per-year in the US (2006),[13] 46000 in the UK (mid 2009–mid 2010)[14] and 20000 in Australia (mid 2007–mid 2008).[15] Most of these patients are discharged from hospitals relatively early with an average length of hospital stay of 1 day in the UK[14] and 1-2 days in Australia.[15] Therefore, many patients who are deemed 'clinically' recovered might be returning to the community while still having residual effects of the drugs on which they overdosed.

However, no study so far has examined whether patients with psychotropic drug overdose are more prone to major adverse outcomes such as traffic accidents during the period following their discharge from hospital. In the present study, we aimed to assess whether patients treated in hospitals in NSW for self-poisoning with psychotropic drugs are more prone to traffic accidents during the period following discharge from hospitals. Using a self-controlled case series approach,[16, 17] we compared the traffic accident rates of a group of patients overdosed with psychotropic drugs in the period following the overdose with the rate in a control period where they were not affected by the overdose.

Methods

Data Sources

We used a record-linkage approach based on two population databases in New South Wales (NSW), Australia.

1. NSW Admitted Patient Data Collection (APDC):

APDC includes records for all separations (i.e. discharges, transfers and deaths) in all NSW public and private hospitals and day procedure centres. The database records include a range of demographic data items (e.g. sex, date of birth, residential address), administrative items (e.g. admission and separation dates and times, mode of separation) and coded health information (e.g. principal diagnosis (ICD-10 version 4), external cause of injury (ICD-10 version 4) and any complications that occurred and procedures performed during the admission). ICD-10 coding is assigned routinely for all hospital admissions in the NSW by Clinical Coders employed by the NSW Ministry of Health. The APDC does not record individual drugs taken in self-poisoning.

2. NSW Roads and Traffic Authority Traffic Accident (CrashLink) Database:

The CrashLink database held by the NSW Roads and Traffic Authority maintains the records of traffic accidents that occur in NSW. An accident is entered in the database if it a) is reported to the police, b) occurred on a road open to the public, c) involved at least one moving road vehicle and d) involved at least one person being killed or injured or at least one motor vehicle being towed away. Therefore, minor non-injurious accidents are generally not entered into the database.

The CrashLink database records a range of data items pertaining to each vehicle controller (i.e. drivers of motor vehicles including motor cycles) involved in an accident, including demographic data items (e.g. sex, date of birth, postcode of residence) and items related to the accident (e.g. date and time of accident, road conditions, casualties). The CrashLink Dataset for the 8-year period from 1 July 2000 to 30 June 2008 consisted of 664225 motor vehicle controller records.

Data Extraction and Linkage

Using the APDC as the primary data source, we retrieved all hospital separations following an intentional self-poisoning with a psychotropic drug [coded X61 (antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified) or X62 (narcotics and hallucinogens, not elsewhere classified) as the ICD-10 version 4 external cause of injury] from a NSW hospital during an 8-year period from 1 July 2000 to 30 June 2008 (i.e. the study period), where the patient was aged 18–80 years on the day of separation. This dataset consisted of 40845 hospital separations involved 27087 patients. Of these, 7386 separations were either transfers to other inpatient institutions or in-hospital deaths and thus were excluded. The remaining 33459 separations involved 24284 individuals who were treated for intentional self-poisoning with psychotropic drugs and discharged to the community within the study period (Figure 1). Using demographic data items, the APDC data for these eligible individuals was linked to the CrashLink database to retrieve the accident records (if any) for each individual within the study period.

Ethical considerations

The primary APDC and CrashLink dataset linkage was conducted by NSW Centre for Health Record Linkage (CHeReL), independently of the researchers. Personally identifiable data items were removed from APDC and CrashLink records in the process and researchers were provided with de-identified data where each subject was assigned with a project person number. Ethics clearance for the study was granted by the NSW Population and Health Services Research Ethics Committee.

Data Analysis

Because this was the first study of its kind, we did not have previous estimates for the period where individuals could be at risk of driving impairment following a psychotropic drug overdose. Therefore, we defined three post-admission periods (3 days, 1 week and 4 weeks), subtracted the number of inpatient days (because the patients did not drive during this period) from each post-admission period and calculated three post-discharge risk periods (viz. immediate, intermediate and extended, respectively) of different lengths for each episode of overdose. Given the wide variation of the half-lives (and the doses) of drugs taken by the patients in the study, we assumed it is biologically plausible that any effect of drug overdose could last for up to 3 days to 1 week, but not up to 4 weeks. When the same patient was hospitalised for psychotropic drug overdose more than once within the study period, the total person-days were calculated for each post-discharge period by adding the separate post-discharge periods (illustrated in Figure 2). The control period for each subject was the total duration where the individual was 18 years or older during the follow-up period, excluding the total person-days included in the post-discharge period/s and the preceding inpatient days. The traffic accidents within each post-discharge period and corresponding control period were counted for each participant after combining the APDC and CrashLink datasets.

The data were analysed with random-effects Poisson regression models to calculate the Incidence rate ratio (IRR) between each post-discharge period (viz. immediate, intermediate and extended) and corresponding control period. For each analysis, the records where length of hospital stay was longer than the defined post-admission period (i.e. 3 days, 1 week or 4 weeks) were excluded owing to the underlying assumption that a patient is no longer affected by drug exposure after the end of that period.

Because we defined 3 post-discharge periods and performed three IRR comparisons for the same cohort, we used a modified Bonferroni correction procedure – the step-wise Hochberg approach[18] – to test statistical significance. The procedure ranks the p-values (three p-values in this study) and tests the first (lowest p-value) at 0.05/3. If it is significant the procedure then tests the next one at 0.05/2, if it is significant the next one at 0.05/1. If one of the p-values is not significant, all those below it on the ranking are non-significant.

Data were analysed using STATA version 11 (StataCorp, College Station, Texas).

Results

Sixty percent of the subjects were females. The mean (SD) of age was 37.5 (13.3) years, and 75% of the subjects were 45 years or younger. Of the 33459 hospital admissions 9175 were repeat admissions. Twenty percent of the patients were discharged on the same day, and 72% were discharged within 2 days following admission. There were 2825 traffic accidents where an individual in the group was involved as a driver during the study period.

The number of accidents and the computed incident rate ratios (IRRs) for each post-discharge period vs. control period are shown in Table I. Numbers of subjects included in the analyses were different depending on the selected post-discharge period (Table I, column 2), because those who were still inpatients at the end of the selected post-admission period (3, 1 week or 4 weeks) were excluded from the cohort eligible for that analysis. According to the Hochberg step-wise approach for multiple comparisons, 4-week period that gave rise to the lowest p-value was tested first at 0.017, followed by the 3-day period at 0.025 and the 7 day period at 0.05 cut-off.. All three IRRs were significant in these comparisons.18381 patients were discharged within 3 days following admission. In this group the accident rate in the post-discharge period within first 3 days following admission was 3.5 times (IRR 3.49; 95% CI 1.66, 7.33; p = 0.001) that in the corresponding control period. 21751 patients were

discharged in the first week following admission. The IRR of accidents between post-discharge and control periods in this group was 1.9 (IRR 1.88; 95% CI 1.09, 3.25; p = 0.023). 23940 patients were discharged within the first 4 weeks following admission and the accident risk remained significantly elevated[b] during the post-discharge period within this 4-week period (IRR 1.65; 95% CI: 1.27, 2.15, p = 0.0002).

Discussion

To our knowledge, this is the first study that examined whether patients treated in hospital for intentional self-poisoning with psychotropic drugs are more prone to traffic accidents as motor vehicle drivers in the period following discharge from hospital. The results show that 72% of those patients are discharged with in 2 days following admission. Their traffic accident risk during the first 1-3 days following discharge is 3.5 times their baseline accident risk. The risk reduces with time but remains significantly elevated after 4 weeks post-overdose.

Although our data are from mid-2000 to mid-2008, they are still clinically relevant, if not more so now than in 2008, because the length of hospital stay after an overdose has not changed and hospital admissions following psychotropic drug overdose has increased in Australia[15] and other high-income countries.[13, 19] We obtained data from NSW population-wide databases and thus case selection was not affected by sampling biases. The records have been entered prospectively into each source database using standard disease classification criteria and traffic accident definition criteria so that entries were not influenced by recall bias or other response bias. We eliminated confounding by unmeasured between-subject factors by using a self-controlled case-series design where each subject acted as their own control. Further, selection of a long control period increased the power of the study and eliminated the influence of random fluctuations of accident risk within the study period. We

assumed that the risk of accidents did not change with time over the 8-year study period, which may not be the case in the presence of certain time-dependent intra-individual risk factors such as age and severity of any underlying psychiatric illnesses. However, the control period included both pre- and post-overdose periods within the study duration, thus minimising the influence of any time-variant risk factors. The linked dataset in the present study – particularly the accident counts – was too small to perform stratified subgroup analyses based on different demographic factors such as age and sex.

We did not have data on the percentage of drivers in the group or the driving habits of individual subjects. However, the accident rate in the study group during the control period (4.1-4.4 per 100000 person-days, Table I) was very similar to the rate in general population in NSW: 664,225 reported accidents in NSW during the 8-year study period from an average population of 5 million[20] people between 18-80 years of age is equivalent to an accident rate of 4.5 per 100000 person-days. Eighty-three percent of the population older than 17 years held a driver's licence in NSW in 2005.[21] The above accident rates are an underrepresentation of all traffic accidents that occurred in NSW during the study period because an accident is reported to the New South Wales (NSW) Roads and Traffic Authority and entered into the CrashLink database only if it fulfils all of the criteria listed above under Methods. For example, non-injurious accidents with minor property damage are not reported to the Roads and Traffic Authority.

As this is the first study that examined driving impairment following acute psychotropic drug overdose, and included overdoses with different drugs, we did not have an empirical basis to define a single 'at risk' period for the individuals discharged from hospitals. Therefore, employing a more inclusive approach we defined three 'at-risk' periods post-overdose (3 days, 1 week and 4 weeks), and adjusted the level of statistical significance for multiple comparisons. Among the patients discharged within 3 days following admission,

the accident risk within 1-3 days following discharge was 3.5 times that of their baseline risk. Given that the accident rate in the control period in the group is similar to that of the general population in NSW, the results signify a genuine increase in risk. A 3.5-fold rise in accident risk is equivalent to that associated with a blood alcohol level of 0.09 g/dl,[22, 23] nearly double the legal limit (0.05g/dl) in NSW. The risk diminished with time as expected, but remained significantly elevated even after 4 weeks. The IRR of 1.65 observed after 4 weeks is equivalent to that observed with a blood alcohol level of 0.06 [23] to 0.07 g/dl[24] which is still above the legal limit in NSW and other states in Australia and other countries.

A high accident risk observed in first 3 days post-overdose seems compatible with drug-effects. Although the APDC dataset does not specify the psychotropic drugs taken in overdose, the majority of the ingested drugs are expected to be CNS-depressants (viz. benzodiazepines, barbiturates, antipsychotics, opioids and sedating antidepressants) as they accounted for around 80% of the psychotropic drug overdoses in patients hospitalised from 1 July 2000 to 30 June 2008 in Australia.[15] Increased accident risk at 4 weeks cannot be explained simply by acute effects of drugs taken in the overdose episode. Aggravation of underlying psychiatric illnesses, increased stress around the period following deliberate self-harm, and/or change in psychiatric medications during post-overdose psychiatric consultations are some possible causes that could make these individuals more prone to traffic accidents, but we do not have data to test these speculations.

Some patient characteristics (e.g. tolerance due to chronic use/abuse of the drug taken in overdose), drug factors (e.g. drug class, dose, half-life of the drug) and their complex interactions can modify the severity and the duration of intoxication. Information on these factors was not available in the source databases of this study. Even when such meticulous documentation is available in a database, epidemiological modelling of an infrequent

outcome like traffic accidents based on all these factors would require extensively large datasets to have reasonable statistical power.

Conclusions

Our findings suggest important clinical and medico-legal implications in relation to post-discharge management of patients with intentional-self poisoning of psychotropic drugs. We believe that clinicians should warn those patients who are discharged within 1–2 days after overdose (which constitute 72% of these patients) that they are 3-4 times more likely to encounter a traffic accident if they drive during the first couple of days following discharge, and should advise them not to drive during that period. Our results also suggest that the accident risk remains elevated at medico-legally significant levels even at 4 weeks after the day of admission. However, applying driving restrictions for this extended period for each patient with psychotropic drug overdose would be a rather contentious issue until more robust evidence identifies the specific factors that increase the 4-week accident risk in patients following psychotropic drug overdose. Future research should aim at larger population-based studies that enable such fine-grained analysis. At the same time it is worth exploring the feasibility of administering clinical tests of fitness-to-drive to patients at the time of discharge and perhaps before resuming driving, with the aim of assessing the risk on an individual basis.

Footnotes:

[a]Although opioids may not be classified under psychotropic drugs in a strict sense, they are included under the term ‘psychotropic drugs’ in the present paper to avoid verbosity. However, the distinction is made when necessary.

[b]In order to eliminate the effect of accidents occurred during first 3 days on the risk calculated for the 4-week post overdose period we also defined a post-discharge period between 3 to 28 days (i.e. a period mutually exclusive from 3-day post-overdose period) and recalculated the IRR. Fifty-one accidents occurred during this period and the IRR remained significantly elevated (IRR 1.53, 95% CI: 1.16, 2.02, p = 0.003) indicating that this is a genuine increase in accident risk, independent of the excess accidents occurred during the immediate post-discharge period.

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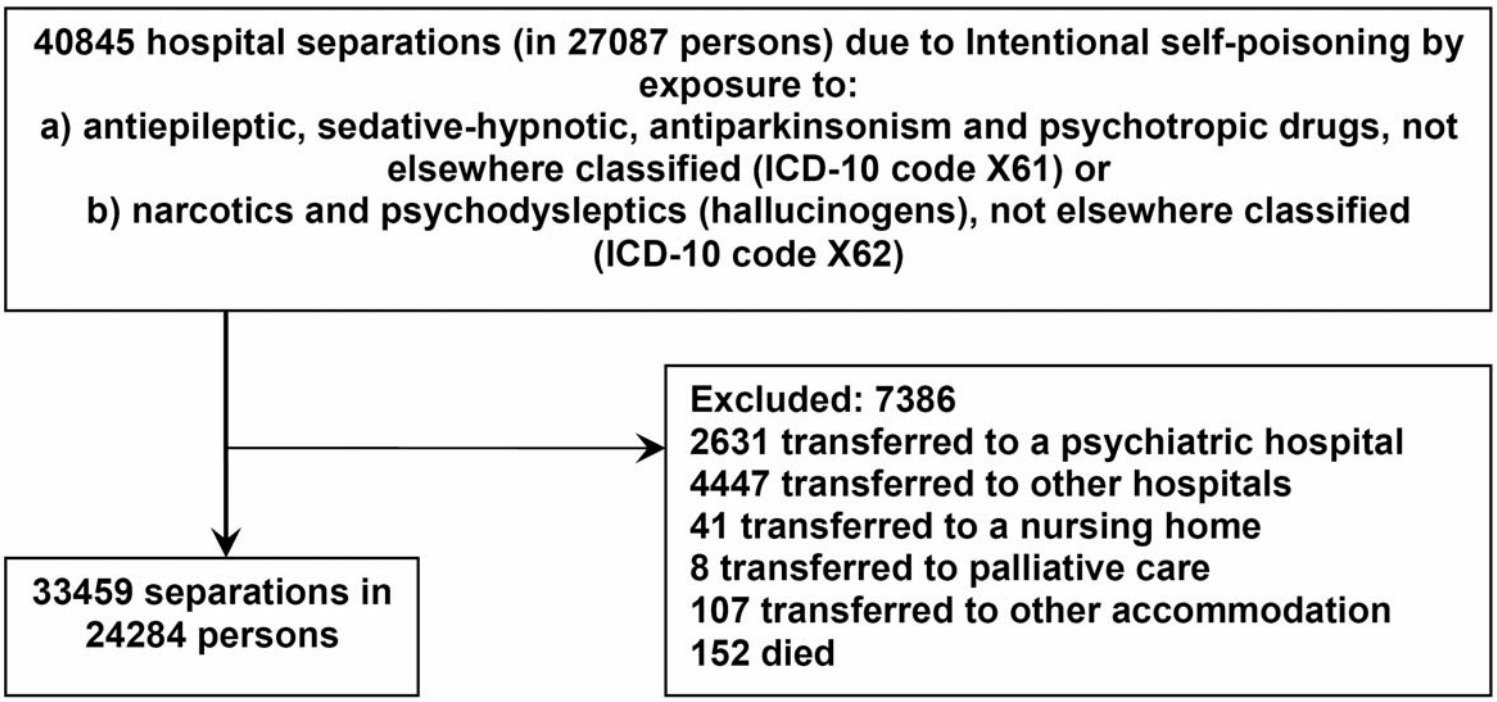
Table I: Incidence rate ratios (IRR) for traffic accidents between post-discharge periods and control periods.

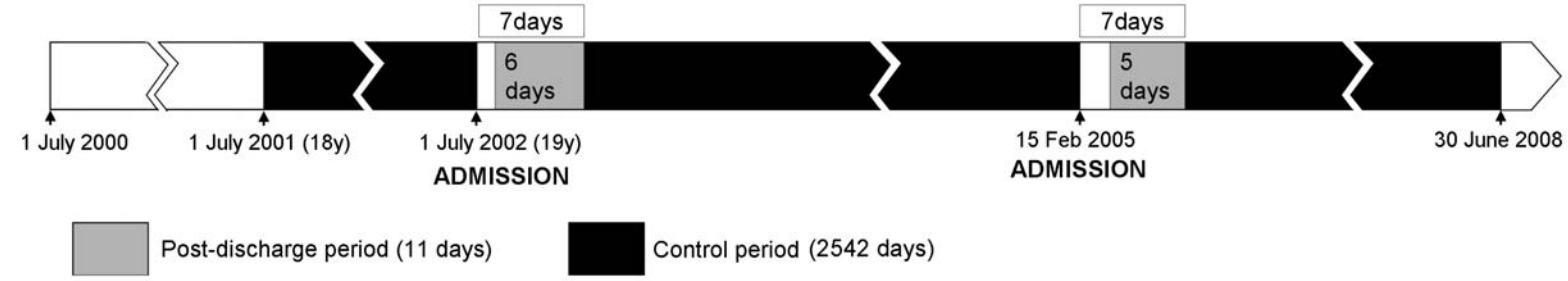
Defined post-discharge period (duration post-admission)	Number of subjects included	Post-discharge period			Control period			IRR	95% Confidence interval	p value
		Crashes	Total person-days	Accidents / 100,000 person days	Crashes	Total person-days	Accidents / 100,000 person days			
Immediate (3 days)	18381	7	44176	15.8	2271	51169460	4.4	3.49	1.66 – 7.33	0.001
Intermediate (1 wk)	21751	13	155490	8.4	2617	60565832	4.3	1.88	1.09 – 3.25	0.023
Extended (4 wks)	23940	58	824606	7.0	2733	66096087	4.1	1.65	1.27 – 2.15	0.0002

Figure captions

Figure 1: Selection of the sample.

Figure 2: Total post-discharge period and control period based on 1-week post-admission period in a hypothetical subject admitted twice during the study period, the first occurring on 1 July 2002 at the age of 19 years. When calculations are repeated for the same subject, a) based on 3-day post-admission period: post-discharge period = 3 days and control period = 2550 days; b) based on 4-week post-admission period: post-discharge period = 53 days, control period = 2500 days.


40845 hospital separations (in 27087 persons) due to Intentional self-poisoning by exposure to:
a) antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified (ICD-10 code X61) or
b) narcotics and psychodysleptics (hallucinogens), not elsewhere classified (ICD-10 code X62)
Excluded: 7386
2631 transferred to a psychiatric hospital
4447 transferred to other hospitals
41 transferred to a nursing home
8 transferred to palliative care
107 transferred to other accommodation
152 died
33459 separations in 24284 persons


7days
6
days
7days
5
days
1 July 2000
1 July 2001 (18y)
1 July 2002 (19y)
ADMISSION
15 Feb 2005
ADMISSION
30 June 2008
Post-discharge period (11 days)
Control period (2542 days)