ANTIPSYCHOTIC MEDICATION USE AND FRACTURE: A POPULATION-BASED CASE-CONTROL STUDY

Behnaz Azimi Manavi*[1], Amanda L Stuart[1], Julie A Pasco[1,2,3], Jason M Hodge[1,2], D Kavindi Weerasinghe[1], Rasika M Samarasinghe[1], Lana J Williams[1,2]

[1]Deakin University, IMPACT – the Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Geelong, Australia
[2]Barwon Health, Geelong, Australia
[3]Department of Medicine-Western Health, The University of Melbourne, St Albans, Australia

*Contact information: bazimimanavi@deakin.edu.au

Introduction

- Antipsychotic medication initially emerged to control symptoms of psychosis (Hálfdánarson, 2017, eur neuropsychopharmacol).
- Antipsychotic use is increasing globally. The number of prescriptions filled for one or more antipsychotics increased from 261,000 in 2005 to 422,000 in 2021 in Australia (Health, 2022, AIHW).
- Common side effects of antipsychotic use include weight gain, diabetes, cognitive impairment, falls and sedation (Stroup, 2018, World Psychiatry).
- More recently, antipsychotic use has been associated with an increased risk of osteoporosis (Graham, 2011, Expert Opin Drug Saf).
- Thus, we aimed to determine whether antipsychotic use is associated with fracture risk in a population-based sample of men and women.

Methods

Participants

- Cases and controls were recruited from the Barwon Statistical Division (BSD), situated in south-eastern Australia.

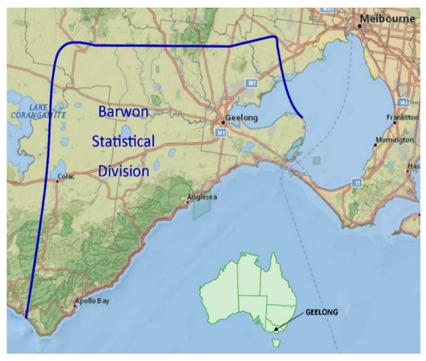

Figure: Barwon Statistical Division (BSD), the study region

Cases

- 1,458 participants (48.2% men) aged 20+ years with a confirmed radiological report of fracture between June 1st 2012 and May 31st 2013. Cases were drawn from the Predictors and Outcomes of incident FRACtures (Stuart, 2019, J Public Health Res).

Controls

- 1,795 participants (53.5% men) were drawn from the Geelong Osteoporosis Study (Pasco, 2012, Int J Epidemiol) who had not experienced a fracture between June 1st 2012 to May 31st 2013.

Data

Outcome

- Radiologically confirmed fracture.

Exposures

- Exposure to antipsychotic and other medication use prior to fracture and lifestyle factors were documented by self-report.

Statistics

- Differences between cases and controls were analysed using t-tests for parametric data, Kruskal Wallis for non-parametric data and Chi-Square for categorical data. Multivariable binary logistic regression was used to explore the associations between antipsychotic use and fracture following adjustment for possible confounders.

Results

- Characteristics of the cases and controls according to sex are in the Table.
- For women, exposure to antipsychotics was documented for 20 of 755 (2.6%) cases and 10 of 834 (1.2%) controls (p=0.034). For men, exposure to antipsychotics was documented for 13 of 703 (1.8%) cases and 5 of 961 (0.5%) controls (p=0.010).
- Following adjustment for age, antipsychotic use was associated with a 2.4-fold increased risk of fracture in women **(OR 2.42, 95%CI 1.11 - 5.24, p=0.025)** and a 3.5-fold increased risk of fracture in men **(OR 3.49, 95%CI 1.20 - 10.14, p=0.021)**.
- Further adjustment for lifestyle factors, past fracture, falls and other medication use did not explain the findings and patterns persisted after exclusion of minor fractures and self-reported schizophrenia.

Table: Characteristics of fracture cases and controls for men and women, results displayed as median (interquartile range) or n (%).

	Men			Women		
	Cases n=703	Controls n=961	P	Cases n=755	Controls n=834	P
Age (yrs)	48.5 (31.8-62.7)	59.5 (45.9-73.4)	<0.001	61.7 (49.2-76.7)	56.3 (42.5-69.7)	<0.001
Weight (kg)	82.0 (75.0-92.0)	82.7 (74.6- 92.8)	0.594	68.0 (60.0-78.0)	71.7 (62.3-83.8)	<0.001
Height (cm)	178.0 (172.7-183.0)	174.8 (170.1-179.6)	<0.001	162.0 (157.0-168.0)	161.7 (157.6-166.1)	0.193
Smoking (current)	152 (21.8%)	108 (11.3%)	<0.001	95 (12.8%)	91 (11.1%)	0.295
Mobility (active)	522 (75.3%)	677 (71.0%)	0.050	449 (60.1%)	578 (70.8%)	<0.001
Frequent alcohol consumption	222 (31.6%)	394 (41.0%)	<0.001	180 (23.8%)	186 (22.3%)	0.467
Prior adult fracture	246 (36.5%)	318 (34.2%)	0.340	276 (37.7%)	155 (18.7%)	<0.001
Faller (past 12 months)	111 (16.0%)	172 (18.1%)	0.274	177 (23.7%)	224 (27.1%)	0.123
Schizophrenia (lifetime)	7 (1.0%)	3 (0.3%)	0.107	2 (0.3%)	1 (0.1%)	0.607
Medication (prior to #)						
Antipsychotics	13 (1.8%)	5 (0.5%)	0.010	20 (2.6%)	10 (1.2%)	0.034
Other psychotropics	106 (15.1%)	87 (9.1%)	<0.001	202 (26.8%)	179 (21.5%)	0.014
Adrenal steroid hormones	15 (2.1%)	10 (1.0%)	0.070	31 (4.1%)	23 (2.8%)	0.139
Gonadal hormones	9 (1.3%)	3 (0.3%)	0.036	37 (4.9%)	32 (3.8%)	0.299
Thyroid hormones	7 (1.0%)	10 (1.0%)	0.928	58 (7.7%)	61 (7.3%)	0.781
Anti-fracture agents	18 (2.6%)	17 (1.8%)	0.266	58 (7.7%)	28 (3.4%)	<0.001
Calcium/vitamin D	50 (7.1%)	62 (6.5%)	0.595	219 (29.0%)	190 (22.8%)	0.005

Discussion & Conclusion

- Our results indicate that antipsychotic use is independently associated with increased risk of fracture.
- Antipsychotic-induced hyperprolactinemia and/or side-effects such as hypotension or sedation (Stroup, 2018, World Psychiatry).
- leading to increased falls risk may explain the findings. Furthermore, the use of antipsychotics has been associated with decreased bone mineral density leading to weaker bones (Crews, 2012, Hum Psychopharmacol) and a higher probability that a fall will result in a fracture.
- While future research exploring underlying mechanisms is needed, regular monitoring of bone health in antipsychotic users should be considered.

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