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Short communication

National trends in alcohol pharmacotherapy: Findings from an Australian claims database

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ABSTRACT

Background: Although the efficacy of alcohol pharmacotherapy has been widely investigated, little is known about real-world prescription patterns. Population-based dispensing data can provide an understanding of prescription patterns and characteristics of treatment in nonexperimental settings.
Methods: A retrospective cohort study of patients (aged 15–84) treated with acamprosate or naltrexone between July 2009 and June 2013 was conducted using dispensing claims from the Australian Pharmaceutical benefits Scheme Database. Only individuals with prescriptions from September 2009 onwards were included.
Results: We identified 61,904 individuals (40% female, 32% in 35–44 age bracket,) with a total number of 198,247 dispensings. There were 23,452 naltrexone-treated and 38,452 acamprosate-treated patients. For naltrexone, 42% of initial dispenses were followed by a second dispense with only 25% receiving at least 3 months of treatment. For acamprosate, 28% of dispenses were followed by a third dispense with only 15% receiving at least 3 months of treatment. Patients in older age groups were more likely to be dispensed a repeat script than those in younger age groups (e.g., for the 75–84 vs 15–24 age bracket OR's = 2.27 and 2.98 for naltrexone and acamprosate respectively).
Conclusion: Current national guidelines in Australia recommend alcohol pharmacotherapy for a minimum period of 3 months yet only 15–25% are receive this duration of treatment. Naltrexone-treated patients were more likely to return for a second and third dispense than acamprosate-treated patients. Prevalence and prescribing patterns change with age.

1. Introduction

World-wide, harmful use of alcohol is responsible for 5.9% of all deaths and is a causal factor in more than 200 disease and injury conditions (WHO, 2015). In Australia, alcohol misuse accounts for an annual economic burden estimated at $30 billion including harms to drinkers and harms to others (Laslett et al., 2010) and is a major cause of drug-related death, twice that of tobacco when expressed as potential years of life lost (Collins and Lapsley, 2008). Alcohol-use disorders are highly prevalent in Australia yet fewer than one-third of those affected will seek treatment (Teesson et al., 2010).

Acamprosate and naltrexone are the most commonly used 'anti-craving' pharmacotherapies for the treatment of alcohol dependence internationally. Since 2000, the Australian government has subsidised treatment with acamprosate and naltrexone on the Pharmaceutical Benefits Scheme (PBS), establishing a continuing clinical role for these medicines. National treatment guidelines recommend naltrexone and acamprosate as first-line therapy with at least a 90 day treatment period (Morley et al., 2009). Naltrexone is an orally active non-specific opioid antagonist with a moderate, but statistically reliable effect in reducing heavy drinking, as demonstrated in meta-analyses of randomised controlled trials (RCTs; Jonas et al., 2014; Rösner et al., 2010). Acamprosate is a synthetic GABA analogue thought to restore N-methyl-D-aspartate (NMDA) receptor tone following increased neuronal hyperexcitability during alcohol withdrawal (Rammes et al., 2001) and, while not consistently observed (e.g., Anton et al., 2006; Chick et al., 2000; Morley et al., 2006), meta-analyses of pooled RCT data sug-

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gest some efficacy for controlling alcohol consumption (Jonas et al., 2014).

However, while randomised controlled trials have high internal validity whereby group differences can be causally linked to treatment, it is not guaranteed that treatments will be as effective in other contexts such as those found in clinical practice (Buri et al., 2007). Compliance with medicines prescribed to treat substance abuse is recognised as a challenge (Kranzler et al., 1996). Between 25–50% of subjects enrolled in many clinical trials for alcohol dependence fail to complete the 12 weeks of recommended therapy, with most dropouts taking place within the first 6 weeks. Adherence with naltrexone has been found to be associated with improved treatment effect (Volpicelli et al., 1997) suggesting that naltrexone is an active agent whereby good compliance is central to effectiveness. Thus, given low adherence to treatment in general in this population the benefits of alcohol pharmacotherapy in real-world clinical practice have been questioned (Bouza et al., 2004). Indeed, a retrospective analysis of paid health insurance claims in the United States for naltrexone indicated that most patients do not complete a full course of treatment (Harris and Thomas, 2004).

The aim of the current study was thus to characterise patterns and costs of alcohol pharmacotherapy in Australia. We conducted a population-based evaluation of the 'anti-craving' alcohol pharmacotherapies, naltrexone and acamprosate, dispensed in Australia between 2009 and 2013. Information regarding pharmacotherapy dispensing rates, adherence rate and prevalence of usage can provide insight into real-world clinical practice.

2. Methods

We conducted a restrospective cohort study of all patients dispensed acamprosate and/or naltrexone under the PBS between July 2009 and May 2013. The Australian PBS is a government medicine reimbursement system subsidising a range of prescribed medicines (Mellish et al., 2015). For medicines costing more than the relevant beneficiary co-payment, additional costs are paid by the government. The Department of Human Services maintains a database of all PBS-subsidised claims, amounting to approximately 280 million dispensings a year. The dispensing of a PBS medicine is only not recorded in the database if the government does not contribute to the cost of the medicine. Acamprosate and naltrexone are above the general beneficiary co-payment threshold such that the claims database represents a complete capture of the total population prescribed acamprosate or naltrexone in the Australian community (and private hospitals) under the PBS. Both medications are dispensed in a 30 day supply package. We extracted data for naltrexone and acamprosate dispenses, date of supply, gender and age group. The Australian Government, Department of Human Services External Request Committee granted data access approval.

To allow for consistency in our database, we included a two month wash out period which excluded prescription data from the first two months of our cohort window. This prevented the inclusion of patients that may have been receiving medications on a continual basis before the period of observation. The index dispense for each patient was the first original prescription of either acamprosate or naltrexone that appeared in the dataset for that period. A treatment episode was defined as the period between the index dispense and the estimated end date of the last prescription calculated as 31 days from that last dispense date.

We calculated the rate of a second and a third dispense (3 months treatment duration) from the index dispense date, defined as a dispensing for the same medication within 31 days from the estimated end date of the previous prescription. Thus, a gap of 31 days between the end of a prescription and the beginning of the following one was allowed (60 days since date of prescription). If more than one 30 day supply was dispensed simultaneously to the same individual it was considered to be a repeat (only a small number of cases). The median days on medication was computed as the duration between the index date and the estimated end date of the last prescription. Concurrent use was defined as a co-dispense for the alternative alcohol pharmacotherapy within 31 days from the estimated end date of the last prescription. Switching was defined as the absence of a refill prescription for naltrexone or acamprosate in addition to a dispensing for the alternate alcohol pharmacotherapy more than 31 days since the estimated end date of the last prescription.

Descriptive statistics were used to determine socio-demographics (age group, gender) and prescription patterns (frequency and patterns of dispensing, concurrent use and switching). Chi-squared tests were employed to examine the association between categorical variables and prescription pattern. All data were analysed using SPSS 22.0 and all tests were two tailed with a significance level at $P < 0.05$.

Table 1
Number of patients with at least one index dispense for alcohol pharmacotherapy in Australia, 2009–2013 for gender and age.

	Naltrexone	Acamprosate	OR (95% CI)
Total	23452	38452	
Gender, % (n)			
Male	59 (13823)	60 (23241)	0.94 (0.91–0.97)**
Female	41 (9629)	40 (15211)	
Age, % (n)			
15–24	4 (104)	4 (1538)	1.01 (0.09–0.13)***
25–34	20 (4725)	19 (7175)	1.01 (1.06–1.15)***
35–44	32 (7386)	31 (11727)	1.05 (1.01–1.09)*
45–54	26 (5973)	26 (10157)	0.95 (0.92–0.99)*
55–64	14 (3197)	15 (5651)	0.92 (0.87–0.96)**
65–74	4 (997)	5 (1911)	0.85 (0.79–0.92)***
75–84	1 (13)	1 (293)	0.07 (0.04–0.13)***

Notes: The index dispense was the first original prescription of either acamprosate or naltrexone that appeared in the dataset for that period (to prevent including patients receiving medications on a continual basis before the period of observation we excluded prescriptions before September 2009). OR = Odds ratio for naltrexone versus acamprosate, CI = confidence interval.

* $p < 0.01$.
** $p < 0.001$.
*** $p < 0.0001$.

3. Results

A total of 61,904 individuals and 198,247 dispensed scripts were included in the analysis (2009–2013). The number of individuals dispensed alcohol pharmacotherapy over a representative 12 month period (2011–2012) was 23, 206, or 23.21 per 1000.

Dispense patterns are depicted in Tables 1 and 2. For naltrexone, we identified 73,024 dispenses and 23,452 patients with a median of 2 dispenses per patient and a median treatment duration of 1 month. In terms of repeat dispenses, 42% (9934) of index dispenses were followed by a second dispense and 25% (5764) were followed by a third dispense. Thus, 57% of naltrexone-treated patients completed only one month of treatment. For acamprosate, we identified 125,223 dispenses and 38,452 patients with a median of 1 dispense per patient and a median treatment duration of 1 month. In terms of repeat dispenses, whereby 28% (10,839) of index dispenses were followed by a second dispense and 15% (5666) followed up with a third dispense. Thus, 72% of acamprosate-treated patients completed only one month of treatment. Naltrexone users were more likely to return for a second dispense than acamprosate users (OR = 1.86, $\chi_1^2 = 1294.68$, $p < 0.0001$, 95% CI: 1.80–1.93) and also more likely to return for three dispenses (OR = 1.89, 95% CI: 1.81–1.97, $p < 0.0001$).