Drug and Alcohol Dependence 165 (2016) 126–131

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Non-physiological mechanisms influencing disulfiram treatment of alcohol use disorder: A grounded theory study

Giles Newton-Howes[a,*], William M.M. Levack[b], Sam McBride[c], Moira Gilmor[c], Rachel Tester[d]

[a] Department of Psychological Medicine, University of Otago, Mein Street, Wellington, New Zealand
[b] Rehabilitation Teaching and Research Unit, Department of Medicine, University of Otago, Mein Street, Wellington, New Zealand
[c] Community Alcohol & Drug Service, Capital & Coast District Health Board, Wellington, New Zealand
[d] Department of Psychological Medicine, University of Otago, Wellington, New Zealand

ARTICLE INFO

Article history:
Received 2 May 2016
Received in revised form 25 May 2016
Accepted 28 May 2016
Available online 4 June 2016

Keywords:
Alcohol use disorder
Grounded theory
Qualitative research
Disulfiram
Antabuse

ABSTRACT

Background: The mechanism of action of disulfiram is not clear and recent systematic reviews have reached differing conclusions. The purpose of this research was to develop a conceptual model of the mechanisms that underpin the effective use of disulfiram in management of alcohol used disorder.
Methods: Grounded theory was used, based on anonymized transcripts of in-depth interviews with 14 individual clients who experienced taking disulfiram for alcohol use disorder within the context of a specialized clinic setting from New Zealand.
Results: The central concept was that of abstinence being a psychosocial construction, with the taking of disulfiram, being a physical manifestation of the decision not to drink. The main subthemes included the importance of participants believing in the potential for disulfiram producing a negative reaction, the increased autonomy achieved by disulfiram removing the need to ruminate on drinking decisions, and the importance of external structure, routine, and social contact with others to support ongoing engagement with disulfiram therapy.
Conclusions: The physiological effects of disulfiram, in particular its adverse reaction when combined with alcohol, explains only part of its effect on problem drinking behaviour. The act of taking a disulfiram pill is also partly symbolic of making an absolute decision not to drink for a short period, allowing people with alcohol use disorder to explore other options for managing life without alcohol. Drug trials involving disulfiram need to treat it not simply as pharmaceutical but as part of a complex psychosocial intervention conducted within a supportive social context.

1. Introduction

Alcohol use disorder (AUD) is a chronic relapsing condition in which patients develop compulsive use of alcohol associated with craving, sensitivity to triggers and dyscontrol. In New Zealand (the country of origin for this paper) 4% of people will experience AUD every year (Wells et al., 2006), with the lifetime prevalence estimate to be in excess of 20% (Oakley Browne et al., 2006). Māori, the indigenous people of New Zealand, are at threefold increased risk (Oakley Browne et al., 2006), a finding replicated internationally with indigenous populations (Calabria et al., 2010; Whitbeck et al., 2008). There are major negative personal (Rehm et al., 2009) and societal problems associated with AUD (Sellman and Adamson, 2012), which cost the country more than $4.5 billion dollars per year (Slack et al., 2009). The significant negative issues associated with AUD in New Zealand are reflected in many Western countries (Rehm et al., 2009), representing a significant public health and individual burden.

Despite the magnitude of the problem and associated harms, there is generally low uptake of medication to better manage AUD. It has been argued that use of medication-assisted treatment is lower than it should be (Roman et al., 2011). In New Zealand, only two pharmacotherapies for AUD are fully subsidized: disulfiram – also known by its more commonly known trade name, Antabuse – and naltrexone. Disulfiram has been touted as a powerful negative reinforcer to support abstinence. It acts physiologically by disrupting hepatic metabolism of alcohol leading to accumulation of acetaldehyde, causing a noxious reaction if alcohol is consumed

* Corresponding author.
E-mail address: Giles.newton-howes@otago.ac.nz (G. Newton-Howes).

http://dx.doi.org/10.1016/j.drugalcdep.2016.05.027
0376-8716/

in a dose dependent fashion. This can range from mild flushing to severe physiological instability and, in extreme cases, death. This potential for serious harm has resulted in some arguing for the cessation of disulfiram prescription (Thorens et al., 2010).

Further restricting uptake of disulfiram is uncertainty about its effectiveness, highlighted recently by two well conducted meta-analyses with conflicting conclusions. In the first meta-analysis, a US group undertook a comprehensive review of all pharmacotherapy for adults with AUD in outpatient settings (Jonas et al., 2014). This review only included double-blinded randomised controlled trials with interventions that ran over a minimum 12 week period. The authors screened over 6000 records identifying 123 studies of which four reported on the effectiveness of disulfiram. On the basis of these four studies, the authors concluded that: "Evidence from well controlled trials of disulfiram does not adequately support an association with preventing return to any drinking or improvement in other alcohol consumption outcomes" (Jonas et al., 2014, p. 1891).

In the second meta-analysis, a French group conducted a systematic review just of studies involving disulfiram, but extended their selection criteria to include open-label (i.e., non-blinded) as well as blinded RCTs (Skinner et al., 2014). These authors found 22 relevant RCTs, six of which were double-blinded. They reported that while double-blinded RCTs found no difference between disulfiram and placebo interventions, open-label studies were associated with significantly greater reduction in drinking behaviour when compared to a control intervention (Hedge's g = 0.70; 95% confidence interval = 0.46–0.93; indicative of a moderate to large effect size). The authors argued that as not drinking on disulfiram renders the drug essentially a placebo (i.e., producing no physiological effect), and knowledge of content of the pill was part of the drug's effectiveness, blinded trials are inappropriate for studying the effectiveness of the drug. This is different from trials where an active drug is given and physiological consequences always occur when the drug is effective. It may be that disulfiram is effective for reasons other than its physiological mechanism of action (Skinner et al., 2014).

Recent reviews have also highlighted the importance of good supervision and the impact of psychological, social and cultural elements on disulfiram effectiveness (Jørgensen et al., 2011). Patient self-management, reducing the dose of disulfiram to consume alcohol or increasing the dose to increase the reinforcing effects, is the corollary of this. It has been posited that the key mode of action of disulfiram may in fact be unrelated to the likelihood of it producing a pharmacological aversive reaction (Krampe and Ehrenreich, 2010). Rather, disulfiram is proposed to act as a bridge between dependent alcohol use and the development of psychosocial strategies to aide long-term abstinence (Krampe and Ehrenreich, 2010). As yet, however, there is little empirical evidence for this view. Furthermore, there is currently no consensus regarding what might be the essential elements of good supervision or good psychosocial support in disulfiram programs, or how supervision and psychosocial support might achieve their effects (Roman et al., 2011). Most published information on the non-pharmacological aspects of the delivery of disulfiram has relied on expert opinion. Allen and Litten (1992) described four methods for increasing compliance with disulfiram including implants, incentives, patient contracts and providing patient information (Allen and Litten, 1992), although only contracting has been considered in any depth in the literature (Azrin et al., 1982; O'Farrell and Bayog, 1986). Brewer et al. (2000) stated that the effectiveness of disulfiram relies upon three reinforcing factors: an aversive reaction, the symbolism of surrendering control, and the involvement of others in therapy and monitoring. They provided a detailed approach to supervision consisting of involvement of a monitor, an external agency to ensure adherence, and a structured agreement (Brewer et al., 2000). Again, they provide no empirical basis for their theory. There is only one published qualitative study on patient experiences of disulfiram treatment (Machin, 1994), but this study provided little information about the non-pharmacological factors influencing effectiveness and insufficient information to guide the future development of service or prescribing practices.

The lack of data on patients' views regarding supervision and the components that determine the success of disulfiram treatment is striking. We therefore undertook a qualitative study in order to address this gap. The aim of this study was to use patient experiences to examine factors that enhanced or impaired the utility of disulfiram in treatment of severe AUD. We also aimed to use this data to develop ideas about the possible mechanisms of effect by which disulfiram might achieve improved recovery outcomes. We chose grounded theory as a research method as it emphasises the inductive development of theoretical frameworks from lived experiences (Charmaz, 2006). It is from the development of such a framework that better clinical trials can be designed to examine the effectiveness of disulfiram.

2. Materials and methods

2.1. Research design

This study employed grounded theory (Charmaz, 2006) to investigate the experiences of those with AUD in order to understand their experience of addiction and the place of disulfiram in their recovery. Data collection involved audio-recording and transcription of individual, in-depth interviews. Grounded theory has been recognised as suitable for theory development in healthcare research for almost five decades (Gerhardt, 1990; Glaser and Strauss, 1967). Ethical approval for this study was provided by the University of Otago Human Ethics Committee (Health).

2.2. Participants

Participants were recruited from the Antabuse clinic, a specialist service within the Wellington Community Alcohol and Drug Service (CADS) in New Zealand during the months of January–November 2015. This is a publically funded service for those with moderate to severe problems with addictions. In this Antabuse clinic patients were encouraged to take disulfiram, typically supervised in community pharmacy settings or occasionally by family members. The clinic is nurse led with psychiatrist oversight and consists of monthly monitoring to ensure co-ordination of blood tests and clinical review. The clinic was designed to complement rather than replace usual treatment. Pharmacists received no specific training in supervision of disulfiram clients though were encouraged to communicate any concerns (including non-compliance) to clinical staff.

To be included in the study, participants were required to be adults enrolled in the CADS service for disulfiram treatment for alcohol dependence. Participants had to be accepted by the service, be able to give informed consent, and speak English to be included in the study.

Initially, we used purposeful sampling to maximise diversity in the participant group to ensure a range of views from men and women, people of different ages, people with different durations of AUD, and from different ethnic backgrounds. We endeavoured to oversample Māori as AUD is a particular problem for Māori in New Zealand (Wells et al., 2006). As the study progressed, and in line with grounded theory methods, we employed theoretical sampling in order to recruit people with who we could examine and challenge emerging concepts and ideas from the initial data in more depth (Draucker et al., 2007).