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Journal of Addiction Medicine and Therapy

Case Report

Nalmefene in Supporting Alcohol Reduction: Observations from a Clinical Cohort

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Submitted: 12 January 2015

Accepted: 19 January 2015

Published: 22 January 2015

ISSN: 2333-665X

Keywords

- Risky drinking
- Alcohol reduction
- Brief intervention
- Nalmefene

Abstract

With the support of our local clinical commissioning group, we developed a pathway of care to support risky drinkers in attaining and maintaining an alcohol reduction treatment goal. Thirty seven patients attending a nurse-led alcohol treatment clinic were provided with the opportunity to commence nalmefene as an adjunct to psychosocial support in the form of nurse delivered structured one-to-one brief intervention. At 3 and 6 month follow-up we observed a 79% retention rate with sustained levels of reduced risky drinking behavior. This is a small observational sample, but does provide some promising observations for development of care pathways that include pharmacotherapy as a treatment choice to help patients reduce their drinking. Well-designed research studies are needed to examine the utility and effectiveness of nalmefene in real life healthcare settings.

ABBREVIATIONS

AUDIT: Alcohol use Disorders Identification Test**; SADQ:** Severity of Alcohol Dependence Questionnaire**; NICE:** Health and Care Excellence; **EMA:** European Medicines Agency; **EBI:** Extended Brief Intervention; **TLFB:** Time Line Follow Back; **ASN:** Alcohol Specialist Nurse

INTRODUCTION

Alcohol consumption and its associated consequences remain a major public health challenge. Policies aimed at decreasing population level consumption through controlling alcohol availability and affordability have been shown to be effective [1,2]. However, the development of individual treatments aimed at alcohol reduction is also a crucial adjunct to this strategy. Risky drinking is far more prevalent than physiological or psychological dependence on alcohol, and significantly increases the likelihood of psychological, social and physical harm, with alcohol use causing an estimated 10% of total disability-adjusted life years lost [3]. Unfortunately, it remains the case that identification of those most vulnerable to harm from risky drinking behaviour remains inadequate [4], and stratification of individual risk based on DSM IV or ICD-10 criteria is rare in generalist clinical settings. This persists despite an international consensus for the utilisation of screening strategies across different healthcare settings [4], and effectiveness of preventive non-specialist approaches such as brief interventions [BI] [5,6]. One of the reported barriers to implementing such strategies is the professional scepticism for the effectiveness of alcohol reduction interventions [7,8] and the lack of services available for referral. The fact that treatment services have traditionally been aimed at dependent drinkers has perhaps reinforced the notion that those at the less severe end of the alcohol-problems spectrum do not require specialist intervention. This helps explain reports which state that the majority of individuals who would benefit from an alcohol intervention will never receive support [9,10]. It is paramount therefore that novel approaches are developed to both identify and provide treatment for risky drinkers.

Importantly, an improved understanding of the biological mechanisms underpinning alcohol misuse has resulted in the development and utilisation of several medications aimed at alcohol reduction and/or abstinence. The opioid receptor system modulator, nalmefene is one such pharmacotherapy. It acts as an antagonist at the mu and delta receptor and as a partial agonist at the kappa receptor [11], although affinity is variable across receptor subtypes [12]. Nalmefene is reported to reduce both craving and the rewarding effects associated with alcohol and, as

such, can be considered an anti-craving mediation which aims to reduce consumption rather than maintain abstinence [13].

In 2013, the European Medicines Agency [EMA] approved nalmefene for the reduction of alcohol consumption in adults who continue to drink heavily following structured intervention. In November 2014, the National Institute for Health and Care Excellence [NICE] published their technology appraisal for implementing nalmefene in the UK [14]. Therefore, there is a need to ensure that clinicians, particularly those in primary care, have the knowledge and opportunities to develop skills in managing this patient group.

The aim of this report is to assist primary care practitioners in identifying patients where nalmefene may provide an effective adjunct to psychosocial intervention. We have described the characteristics that we believe make these patients suitable for treatment, [consistent with NICE health technology appraisal [14] and briefly discuss some contemporary issues in this area. In presenting our outcomes we acknowledge the limitations associated with observational data collection and small sample sizes. Furthermore, we are unable to present reliable drug compliance data.

CASE PRESENTATION

These patients, who were not thought to pose a risk of acute alcohol withdrawal after a full history and physical assessment, had been referred to a nurse-led alcohol treatment clinic in an acute hospital and were otherwise unselected. The assessment was performed by an alcohol specialist nurse [ASN] and included alcohol consumption measures via quantity frequency utilising time follow back [TLFB] [15], Alcohol Use Disorder Identification Tool [AUDIT] [16] and Severity of Alcohol Dependence Questionnaire [SADQ] [17]. The presence of significant liver disease was excluded via assessment of biochemical markers of alcohol- related liver disease [gamma-glutamyl transferase, alanine transaminase, bilirubin and albumin] and/or fibroelastography of the liver. Patients were screened for opioid use [illicit or prescribed] as a positive response excluded nalmefene use.

Where an alcohol-reduction treatment goal was negotiated, the patient received psychosocial support in the form of one-to-one extended brief interventions [EBI] using a standardised protocol [18], which included a minimum of 2 interventions over 2 weeks, delivered by one of two ASNs with a duration of between 5 and 10 minutes. If this did not result in successful alcohol-reduction the patient was commenced on nalmefene 18 mg on an as-needed basis, with maximum daily dose of one tablet [19]. The patients were provided with a diary combining alcohol consumption and medication compliance, and a manufactures information booklet containing Medical Information Card. Between March and September 2014 37 [12 females] patients were prescribed nalmefene. The median age was 49 years [IQR = 17] (Figure 1). All patients had baseline alcohol assessment data and either biochemical or fibroelastography data as reported in Table 1.

This is a contemporary cohort and therefore patients are at different stages in the treatment pathway. Retention in treatment was good; 34 of the 37 patients were due three month follow-up

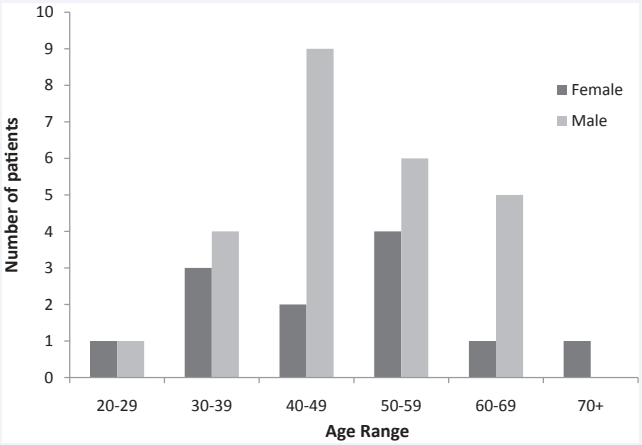

Figure 1 Distribution of cohort by age range and sex.

Table 1: Baseline characteristics for patients prescribed nalmefene.

Variable	N	Median	Interquartile range
AUDIT Score	37	21	12
Fibroelastography [kPa]	29	6.1	4.3
Gamma-glutamyl transferase	35	66	138
Alanine transaminase	35	26	35
Bilirubin	35	8	9
Albumin	35	45	6

Abbreviations: **AUDIT:** Alcohol use disorders identification test

appointments, of which 27 attended [79%]. Eleven out of the 14 patients [79%] due six month follow-up attended. This retention rate compares favourably with those reported in healthcare based brief intervention studies [20,21] At both three and six month follow-up there appeared to be a sustained improvement in alcohol risk category (Figure 2).

DISCUSSION

We have provided an analysis of a naturally occurring patient cohort. Although identified as having developed significant problems around their alcohol use, the patients at the time of assessment: a] did not present with any symptoms of physical dependence, and b] recognized the need for support and treatment, which is perhaps more significant. These patients expressed a preferred treatment goal of alcohol reduction and perceived abstinence as neither realistic nor desired, which is an important factor in this treatment pathway [22]. It could therefore be argued that both the high rates of follow-up and positive outcomes observed in this small cohort are due to a self-selecting highly motivated, treatment seeking population.

Reducing alcohol consumption to safer levels is viewed as an option to improve the global health status of patients [23], and so the use of pharmacotherapy to support reduced consumption as a treatment goal is emerging as a viable option [24]. This treatment goal can either be used as a vehicle to permanent responsible use of alcohol or as an intermediate step towards attaining abstinence [25]. Use of this novel approach to treatment

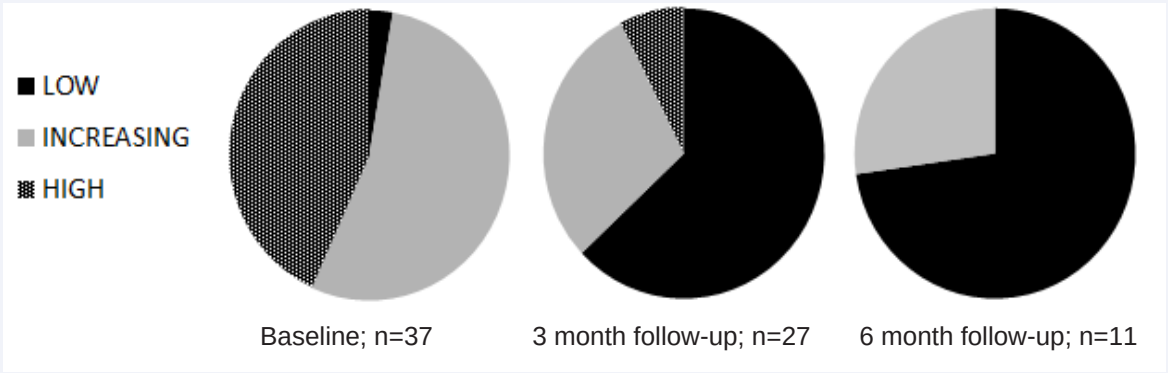

Figure 2 Alcohol consumption risk categorisation at baseline and follow-up. Risk categorisation based on AUDIT score [39].

has been cited [26] as more desirable than abstinence in several subgroups of risky drinkers. Unfortunately, our cohort is too small to draw conclusions.

It has long been understood that risk from alcohol consumption is complex and multifactorial [27]. Therefore it is not surprising that there is no single drug with universal efficacy or evidence for superiority [28,29]. Instead there are several drugs with different actions of moderate efficacy [30, 31]. Nalmefene represents a new clinical choice in an area that is under-served with treatment modalities. Importantly, it remains to be seen whether nalmefene will offer genuine clinical advantages over the established opiate antagonist naltrexone, although the latter is not currently licensed in the UK for reducing consumption. However, through careful selection of patients [32-34] nalmafene has the potential to reduce the overall burden associated with risky drinking behavior [35]. Utilizing information gained through screening may lead to better identification and stratification of patients into appropriate treatment pathways, and may ultimately aid healthcare practitioners in providing a more personalized service. The use of such a model may help to increase patient engagement, adherence and motivation, which should translate to improved attainment of treatment objectives [36].

Although our patients came from a heterogeneous population, this did not seem to influence our cohorts' willingness to engage, ability to comply or treatment outcome. Therefore, we hope that this observational study will help healthcare practitioners, particularly those in primary care, in identifying this population as an important target group in reducing overall alcohol-related harm. Moreover, we hope to have imparted confidence for practitioners to utilise alcohol reduction as a treatment option. The practitioner and patient need to work closely to understand the factors and objectives that may underlie individual treatment success, and personalise therapy accordingly [37, 38].

ACKNOWLEDGEMENTS

The authors would like to thank Liverpool Clinical Commissioning Group for their support in providing the funding to enable prescribing of Nalmefene prior to NICE Health Technology Appraisal

CONFLICT OF INTEREST

Dr Owens has received honoraria for educational support from the manufactures of Nalmefene

Dr Richardson has received honoraria for educational support from the manufactures of Nalmefene

REFERENCES

1. Boyle P, Boffetta P, Lowenfels AB, Burns H, Brawley O, Zatonski W, et al. Alcohol: Science, Policy and Public Health: Oxford University Press; 2013.
2. Brennan A, Meng Y, Holmes J, Hill-McManus D, Meier PS. Potential benefits of minimum unit pricing for alcohol versus a ban on below cost selling in England 2014: modelling study. BMJ. 2014; 349: 5452.
3. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. Lancet. 2009; 373: 2223-2233.
4. NICE. Alcohol-use disorders: preventing harmful drinking [PH24]. London: National Institute for Health and Care Excellence. 2010.
5. Babor T. Alcohol: no ordinary commodity: research and public policy: Oxford University Press. 2010.
6. Kaner EF, Beyer F, Dickinson HO, Pienaar E, Campbell F, Schlesinger C, et al. Effectiveness of brief alcohol interventions in primary care populations. Cochrane Database Syst Rev. 2007; CD004148.
7. Nehlin C, Fredriksson A, Grönbladh L, Jansson L. Three hours of training improve psychiatric staff's self-perceived knowledge and attitudes toward problem-drinking patients. Drug Alcohol Rev. 2012; 31: 544-549.
8. Soares J, de Vargas D, Formigoni ML2. [Knowledge and attitudes of nurses towards alcohol and related problems: the impact of an educational intervention]. Rev Esc Enferm USP. 2013; 47: 1178-1185.
9. Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Archives of general psychiatry. 2007; 64: 830-42.
10. Drummond C, Oyefeso A, Phillips T, Cheeta S, Deluca P, Perryman K, et al. Alcohol needs assessment research project (ANARP): The 2004 national alcohol needs assessment for England. London: Department of Health London. 2005.
11. Bart G, Schluger JH, Borg L, Ho A, Bidlack JM, Kreek MJ. Nalmefene

induced elevation in serum prolactin in normal human volunteers: partial kappa opioid agonist activity? Neuropsychopharmacology. 2005; 30: 2254-2262.

12. Emmerson PJ, Liu MR, Woods JH, Medzihradsky F. Binding affinity and selectivity of opioids at mu, delta and kappa receptors in monkey brain membranes. J Pharmacol Exp Ther. 1994; 271: 1630-1637.

13. Drobes DJ, Anton RF, Thomas SE, Voronin K. Effects of Naltrexone and Nalmefene on Subjective Response to Alcohol Among Non-Treatment-Seeking Alcoholics and Social Drinkers. Alcoholism: Clinical and Experimental Research. 2004; 28: 1362-1370.

14. NICE. Nalmefene for reducing alcohol consumption in people with alcohol dependence [TA325]. London: National Institute for Health and Care Excellence. 2014.

15. Sobell LC, Sobell MB. Timeline follow-back. Measuring alcohol consumption: Springer; 1992. 41-72.

16. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction. 1993; 88: 791-804.

17. Stockwell T, Hodgson R, Edwards G, Taylor C, Rankin H. The development of a questionnaire to measure severity of alcohol dependence. Br J Addict Alcohol Other Drugs. 1979; 74: 79-87.

18. Owens L, Butcher G, Gilmore I, Kolamunnage-Dona R, Oyee J, Perkins L, et al. A randomised controlled trial of extended brief intervention for alcohol dependent patients in an acute hospital setting (ADPAC). BMC public health. 2011; 11: 528.

19. Summary of Product Characteristics: Selincro, Lundbeck Limited Accessed via

20. D'Onofrio G, Degutis LC. Preventive care in the emergency department: screening and brief intervention for alcohol problems in the emergency department: a systematic review. Acad Emerg Med. 2002; 9: 627-638.

21. McQueen J, Howe TE, Allan L, Mains D, Hardy V. Brief interventions for heavy alcohol users admitted to general hospital wards. Cochrane Database Syst Rev. 2011; 8.

22. Marlatt GA, Witkiewitz K. Update on harm-reduction policy and intervention research. Annu Rev Clin Psychol. 2010; 6: 591-606.

23. van Amsterdam J, van den Brink W. Reduced-risk drinking as a viable treatment goal in problematic alcohol use and alcohol dependence. J Psychopharmacol. 2013; 27: 987-997.

24. Aubin HJ, Daeppen JB. Emerging pharmacotherapies for alcohol dependence: a systematic review focusing on reduction in consumption. Drug Alcohol Depend. 2013; 133: 15-29.

25. Gastfriend DR, Garbutt JC, Pettinati HM, Forman RF. Reduction in heavy drinking as a treatment outcome in alcohol dependence. J Subst Abuse Treat. 2007; 33: 71-80.

26. Cloud RN, McKiernan P, Cooper L. Controlled drinking as an appropriate treatment goal: A critique of current approaches. Alcoholism Treatment Quarterly. 2003; 21: 67-82.

27. Rehm J, Baliunas D, Borges GL, Graham K, Irving H, Kehoe T, et al. The relation between different dimensions of alcohol consumption and burden of disease: an overview. Addiction. 2010; 105: 817-843.

28. Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, et al. Pharmacotherapy for Adults With Alcohol Use Disorders in Outpatient Settings: A Systematic Review and Meta-analysis. JAMA. 2014; 311: 1889-1900.

29. Müller CA, Geisel O, Banas R, Heinz A. Current pharmacological treatment approaches for alcohol dependence. Expert Opin Pharmacother. 2014; 15: 471-481.

30. Rösner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. Cochrane Database Syst Rev. 2010; 9.

31. Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? Addiction. 2013; 108: 275-293.

32. Gual A, He Y, Torup L, van den Brink W, Mann K. A randomised, double-blind, placebo-controlled, efficacy study of nalmefene, as-needed use, in patients with alcohol dependence. European Neuropsychopharmacology. 2013; 23: 1432-1442.

33. van den Brink W, Aubin H-J, Bladström A, Torup L, Gual A, Mann K. Efficacy of as-needed nalmefene in alcohol-dependent patients with at least a high drinking risk level: results from a subgroup analysis of two randomized controlled 6-month studies. Alcohol and alcoholism. 2013; 48: 570-578.

34. Mann K, Bladström A, Torup L, Gual A, van den Brink W. Extending the treatment options in alcohol dependence: a randomized controlled study of as-needed nalmefene. Biol Psychiatry. 2013; 73: 706-713.

35. Mason BJ, Ritvo EC, Morgan RO, Salvato FR, Goldberg G, Welch B, et al. A Double-Blind, Placebo-Controlled Pilot Study to Evaluate the Efficacy and Safety of Oral Nalmefene HCI for Alcohol Dependence. Alcoholism: Clinical and Experimental Research. 1994; 18: 1162-1167.

36. Madras BK, Compton WM, Avula D, Stegbauer T, Stein JB, Clark HW. Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: comparison at intake and 6 months later. Drug and alcohol dependence. 2009; 99: 280-95.

37. Mann K, Hermann D. Individualised treatment in alcohol-dependent patients. Eur Arch Psychiatry Clin Neurosci. 2010; 260 Suppl 2: 116-120.

38. Kaner E, Heather N, Brodie J, Lock CA, McAvoy BR. Patient and practitioner characteristics predict brief alcohol intervention in primary care. British Journal of General Practice. 2001; 51: 822-827.

39. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. The alcohol use disorders identification test. Guidelines for use in primary care. 2001.

Cite this article

Owens L, Thompson A, Pirmohamed M, Gilmore I, Richardson P (2015) Nalmefene in Supporting Alcohol Reduction: Observations from a Clinical Cohort. J Addict Med Ther 3(1): 1012.