



Northern Ireland
Assembly



Queen's University
Belfast



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University

Knowledge Exchange Seminar Series (KESS)

Exploring the relationship between anxiety /sleeping problems and suicidal behaviour

1. Introduction

Anxiety and insomnia are common problems. Lifetime prevalence of anxiety in Northern Ireland (NI) is reported at 22.6% (1) and prevalence of insomnia is reported to be 37% in the UK with an annual incidence of 15% (2).

Clinical guidelines on the management of anxiety recommend a stepped care model of intervention and recommend prescribing of anxiolytic medications for only short courses in specific circumstances (3). Likewise clinical guidelines for insomnia recommend identifying and treating any underlying causes, good sleep hygiene and short term use of hypnotic medication only in specific circumstances. Use of hypnotic medication is generally not recommended for chronic insomnia but Melatonin may be considered (4).

2. Use of anxiolytic and hypnotic medications in Northern Ireland

There are higher rates of prescribing for anxiety and insomnia in NI than in other parts of the UK (5). Considerable work is ongoing across organisations within the health and social care sector to address this issue with significant progress being made in reducing prescribing in all Trust areas, most notably the South Eastern Trust area.

Benzodiazepines are the main group of drugs prescribed for the treatment of both anxiety and insomnia. They are also among the group of drugs most often misused. Benzodiazepines use

(prescribed or non-prescribed) is more than twice as likely in the most deprived quintile of the NI population that the least deprived (6%) (6). Current multiagency action plans include addressing illicit supplies of such drugs.

3. Risks associated with anxiolytic and hypnotic medication

The drugs used to treat anxiety and insomnia are known to be associated with significant adverse effects including risk of dependence, cognitive and psychomotor impairments, falls and unintentional injuries and reports of increased all-cause mortality. A large cohort study of patients attending UK primary care reported that anxiolytic and hypnotic drugs were associated with significantly increased risk of mortality over a seven year period. This remained after adjusting for a range of potential confounders including confounding by indication i.e. trying to exclude the risk associated with underlying conditions. They did not have access to data on specific cause of death and therefore could not comment in relation to risk of suicide (7).

4. Anxiety and sleep disorders– relationship to suicide

While suicide is often discussed in the context of depression and other serious mental illnesses, the relationship between anxiety and suicidal behaviours has been the subject of recent research including a systematic review (8). While the quality of the evidence was reported as low to moderate, it was reported that compared to those without anxiety, patients with anxiety were more likely to have suicidal ideations (OR = 2.89, 95% CI: 2.09, 4.00), attempted suicides (OR = 2.47, 95% CI: 1.96, 3.10), completed suicides (OR = 3.34, 95% CI: 2.13, 5.25), or have any suicidal behaviors (OR = 2.85, 95% CI: 2.35, 3.46). The same research team also examined sleep disorders and found that sleep disorder associated with any psychiatric condition was also found to be associated with an increased risk of suicidal behaviour (9). This highlights the need for GPs and other professionals to be aware of the risk in managing such patients.

5. Relationship between levels of prescribed psychotropic medication and suicide

Prescribing rates are often used as a proxy for levels of mental ill-health in a population. A paper by Mok et al in 2013 (10) entitled '*Why does Scotland have a higher suicide rate than England? An area-level investigation of health and social factors*' examined a broad range of ecological risk factors

for suicide. The paper reported that prescription of psychotropic drugs was the variable most strongly associated with the between-country differences in suicide risk, accounting for 42% of the differential. Drug misuse accounted for 17%

It was reported that this may be explained by a higher prevalence of mental health problems in Scotland compared to England or styles of help seeking behaviour in the population and propensity to demand medication or may reflect prescribing practice and indicate availability of psychological interventions.

6. Rationale for systematic literature reviews regarding use of psychotropic medication and suicide

NI is known to have higher suicide rates than Scotland and the above possible explanations offered by Mok in relation to Scotland may also apply to NI. However it raised the question about whether in fact the drugs themselves may be associated with risk. There have been well publicised concerns about the possibility of increased risk of suicide in young people commencing anti-depressants. Mok was contacted regarding the findings and it was reported that analysis was not carried out by specific category of psychotropic drugs but it was stated that the majority were anti-depressants.

In light of this a series of systematic literature reviews were carried out to explore this issue further. The first of these looked at anti-depressants and suicide and found no positive association between use of anti-depressants and suicide. This was followed up with a review examining anxiolytics and subsequently a review examining benzodiazepines. The literature review looking for evidence for and against an association between use of benzodiazepines and suicide is presented in this seminar.

7. Use of Benzodiazepines in suicidal behaviours

Minor tranquillizers (including benzodiazepines) are the most common drugs involved in intentional self harm in NI (31%) and Republic of Ireland (42%), and this increases with increasing age (11). Involvement of benzodiazepines in self harm has been identified as one of four markers of higher risk of repeat self harm included in the 'Manchester Self Harm Rule', a tool used to help clinicians predict risk. (12)

Benzodiazepines are also commonly used in completed suicides and were detected at post mortem in 24% of suicides in NI where toxicology tests were carried out (13). However only around half of all suicides have toxicology screening carried out, with deaths in younger people more like to have toxicology screening(14). Rates of identification of benzodiazepines in suicides in NI are therefore likely to be underestimated.

The results of a systematic review to examine the epidemiological evidence for and against an association between use of benzodiazepines and suicide is summarised below.

8. A systematic literature review of the epidemiological evidence for and against an association between benzodiazepines and suicide

Methods

Five electronic databases were searched to capture mainstream health, mental health, nursing and allied health, social science, humanity and geography literature in August 2014: MEDLINE, EMBASE, PsychINFO, CINAHL Plus, Web of Science. Key word and exploded subject heading searches for the following search terms were combined: Benzodiazepines, suicide and epidemiological study. The inclusion criteria were

1. The target population was the general population. All ages were included. Studies limited to clinical populations with pre-existing mental health conditions were excluded.
2. The Intervention was use of benzodiazepines.
3. The outcome under investigation was completed suicide.
4. Study designs of interest were population based observational study designs.

1191 records were identified. Titles and abstracts were screened for eligibility for inclusion, and if unclear the full text was read. The full inclusion criteria were met by 18 studies. A data collection form was used to extract information on the following variables: authors, year, country, population, study design and aims, study period, outcome measurements and results. Results were synthesised narratively.

A range of different epidemiological study designs were identified: analysis of toxicology results of completed suicides, case-control, cohort, and population based correlational studies. No prior systematic literature review on this topic was identified.

Thirteen of the studies comprised results of toxicology analysis at post-mortem of people who had completed suicide. These studies were based in England and Wales, USA, Sweden, Scandinavia, Brazil and Australia. Rates of detection of benzodiazepines ranged from 10-51% in the different populations, with the exception of one outlier in the USA where the rate was only 0.5%. This data must be interpreted with caution as each country has different guidelines and protocols for investigation of suicide and toxicology, and rates of these vary widely. However it is noted that in all cases the rate of detection of benzodiazepines was generally higher than prescribing rates for benzodiazepines within the same populations. Benzodiazepines were more commonly found in elderly suicides, and in suicides by fatal self-poisoning.

The Nurses' Health Study was a large prospective cohort study conducted in the USA, published in 2002. The associations between self-perceived stress, diazepam use and death from suicide among adult women were examined. The study included 94,410 women, followed up over 14 years. 73 suicides were identified. Diazepam use was higher among those who completed suicide (14%) compared to those who did not (3%). Diazepam use was significantly predictive of suicide, with a 4.9 fold increased relative risk (CI 2.5-9.7),

In 2014 the English National Confidential Inquiry into Suicide and Homicide by People with Mental Illness was published that examined a sample of primary care patients who died by suicide (n=2,384) and compared these to other patients in primary care (n=46,899) to identify markers of suicide risk over a 10 year period. Psychotropic medication use was analysed. 19% of those who completed suicide were on a benzodiazepine, compared to 3% of controls. The use of benzodiazepine was associated with 7 fold increased risk of suicide (OR 7.0, CI 6.2-7.9). The researchers also found that the combination of benzodiazepine and an antidepressant was associated with an 18 fold increased risk of suicide, and highlighted this combination of drugs as a marker for risk of suicide.

A case-control study of suicide in the elderly in British Columbia was based on 602 completed suicides. 28.4% of those who completed suicide were on benzodiazepines, compared to 5.8% of controls. Use of benzodiazepine was associated with a 4 fold increased risk of suicide (OR 4.5, CI 3.3-6.1).

Two studies examined the relationship between changes in benzodiazepine prescribing over time with trends in completed suicide rate at national level. The first in Sweden examined suicide by self-poisoning in the elderly between 1969 and 1996. They found that benzodiazepines were the main drug used by the elderly for fatal self-poisoning, Over the 27 year study period prescribing of

benzodiazepines for the elderly reduced, however the rates of suicide using benzodiazepines for fatal self-poisoning increased. The second study examined prescription sales of benzodiazepines and suicide rates in Denmark between 1970 and 2000, They found that a 10% increase in benzodiazepine sales was associated with 6% and 10% increase all cause suicide rate in men and women respectively.

9. Summary of findings and cautions regarding interpretation

The bulk of literature identified in this review found that there is an observed association between benzodiazepine utilisation and suicide at a population level. There is some evidence this association is stronger in the elderly. These results must be interpreted with caution for the following reasons. We have not been able to exclude confounding by indication i.e. that the underlying mental health issue has contributed to the observed risk. Drug treatment of anxiety may be reserved for the more severe cases of anxiety and therefore may explain the relatively high odds ratios. There may be other confounders that have not fully been explored accounting for this observed relationship. Further research is warranted on this issue.

Some of the studies were of an ecological nature rather than at individual level and therefore the ecological fallacy may apply, in that an observed association at a population group level may not hold true for an individual within that group.

The quality of these studies is mixed with a wide range of study designs and sample sizes. Some are in settings not directly applicable to Northern Ireland. . The studies are purely observational and prone to a range of biases. However the findings will provide the basis for further research to elucidate the true meaning of this observed association, and its implications within Northern Ireland.

However for a variety of reasons, including the risk of dependence, cognitive and psychomotor impairments, falls and unintentional injuries and reports of increased all cause mortality, there is a need to continue to address the issue of prescribing and misuse of benzodiazepines. A number of recommendations are made below in relation relating to addressing this issue.

10. Recommendations

- Ensuring access to a range of appropriate interventions for people experiencing anxiety and insomnia in line with NICE guidance.
- Ensure suicide prevention initiatives take account of the evidence relating to suicide risk associated with anxiety and sleep disorders.
- Continue surveillance of benzodiazepine prescribing
Continue to work with GPs to promote appropriate prescribing– as per current Action Plans DHSSPS/Public Health Agency, Health and Social Care Board. - ? Increased focus on elderly and long term usage.
- Identify and implement evidence based programmes to reduce benzodiazepine prescribing while offering other appropriate support.
 - Model in SE Trust area highlighted as good practice in the English CMO Report 2013 should be considered for rollout to all areas.
 - PHA initiative on-going in Western Trust area
- Educate prescribers regarding the need for care in prescribing for those at risk of self harm/suicide (and their household) to reduce access to means of self harm/suicide. Use of specific benzodiazepines that are less toxic in overdose.
- Consider introduction of quality initiatives in management of sleep and anxiety disorders in primary care.
- Consider use of information technology systems in primary care to flag patients on benzodiazepines and/or antidepressants who may be at elevated risk of suicide (National Confidential Inquiry recommendation).
- Review guidance relating to toxicology screening in cases of suicide and consider costs and benefits of carrying out toxicology screening in all cases of suicide to better understand the issue at individual level.
- Continue to address the issue of prescription drug misuse as per current multi-agency Action Plans.
- Continue / strengthen efforts to address illicit access – internet/ fraudulent access.
- Further research

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