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The relationship between the prescription of psychotropic drugs and suicide rates in older people in England and Wales

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Abstract

Background: Several studies have reported an inverse correlation between general population and elderly suicide rates and antidepressant prescribing rates. Correlations between general population and elderly suicide rates and prescribing rates of other psychotropic drugs have also been reported. All studies of elderly suicide rates have used data over a decade old.

Methods: The relationship between elderly suicide rates and prescription rates of psychotropic drugs by the broad British National Formulary (BNF) categories, for individual psychotropic drug groups within the BNF categories (e.g. SSRIs), and for individual psychotropic drugs was examined over a 12-year period (1995–2006) using Spearman's rank correlation. All data were ascertained from the archives of the National Statistics Office.

Results: There was an absence of significant correlations between elderly suicides rates and rates of prescriptions of psychotropic drugs in the broad BNF categories, individual psychotropic drug groups and individual psychotropic drugs. Discussion: The findings may be due to methodological flaws. However, if they are genuine, then the following approaches require consideration to further reduce suicide rates: (1) development of strategies to ensure continued prescription of psychotropic drugs at the current level; (2) development of strategies to improve non-pharmacological measures, including improved mental health services provision for older people, improved assessment of suicide risk, increased availability of psychosocial interventions and restricting the availability of methods of suicide; and (3) development of strategies to implement improvement in distal risk (e.g. societal socio-economic status) and protective (e.g. societal educational attainment) factors for suicide at a societal level.

Keywords

Elderly suicides, psychotropic drugs, antidepressants

Introduction

Suicide rates generally increase with ageing (Shah, 2007a; Shah & De, 1998). However, suicide rates in older people of both genders declined over the 24-year period between 1979 and 2002 (Shah, 2007b) and the 10-year period between 1993 and 2002 (Shah, Bhat, MacKenzie & Koen, 2008) in the whole of the UK. Similarly, in England and Wales suicide rates in older people of both genders declined between 1960 and 1997 (McClure, 2000), 1979 and 1981, 1997 and 1999 (Pritchard & Hansen, 2005) and between 1985 and 1996 (Hoxey & Shah, 2000; Shah, Elanchenny & Collinge, 2001), and over the 24-year period between 1979 and 2002 (Shah & Coupe, 2009). This decline in suicide rates in older people over time has also been observed in several other countries (Shah et al., 2008; Shah & Coupe, 2009).

The decline in suicide rates in older people in England and Wales may have been due to several national

initiatives including: legislation encouraging general practitioners to offer annual physical and mental examination to those over the age of 75 years; the Defeat Depression Campaign organized by the Royal Colleges of Psychiatrists and General Practitioners; the governmental Health of the Nation and Our Healthier Nation suicide-reduction targets; the National Confidential Inquiry into Suicides and Homicides for England and Wales; the National Service Frameworks for Mental Health and for Older People; the

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National Suicide Prevention Strategy for England (Hoxey & Shah, 2000; NIMHE, 2007; Pritchard & Hansen, 2005; Shah, 2007b; Shah & Coupe, 2009; Shah et al., 2001). One of the several possible mechanisms explaining the effect of these initiatives in reducing suicide rates may be that they have led to an improvement in the recognition and treatment of depressive illness in older people (Lodhi & Shah, 2004; Shah, 2010; Shah & Bhat, in press). The vast majority of older suicide victims have depressive illness (Cattell, 1988; Shah & De, 1998) and depressive illness is generally under-treated in people who commit suicide (Anderson, Anderson, Rosholm & Gram, 2001; Henriksson, Boethius & Isacsson, 2001; Isacsson, Holmgren, Wasserman & Bergman, 1994; Isacsson, Holmgren, Druid & Bergman, 1997; Isacsson, Holmgren, Druid & Bergman, 1999).

Several studies have demonstrated an association between changes in prescribing patterns for psychotropic drugs and suicide rates. A Swedish study of suicides in all age groups combined reported a decrease in suicides due to barbiturate poisoning subsequent to a decrease in their sales, whereas an increase in the sale of antidepressants was associated with an increase in suicides due to these drugs (Carlsten, Allebeck & Brant, 1996). Another Swedish study of suicide in older people reported that an increase in sales of antidepressants in the category selective serotonin reuptake inhibitors (SSRIs) was associated with a decrease in suicide rates in older people (Carlsten, Waern & Allebeck, 1999). The same study reported an increase in suicides due to benzodiazepines despite a decline in their sales (Carlsten et al., 1999). A naturalistic study in Sweden of suicides in all age groups combined suggested that an increase in the use of antidepressants, probably due to the introduction of the SSRIs, might be one contributory factor for a decline in suicide rates (Isacsson, 2000). A further Swedish study reported an increase in the rate of decline of suicide rates in all age groups combined after the introduction of SSRIs (Carlsten, Waern, Ekedahl & Ranstram, 2001). An Australian study also reported a decrease in suicide rates with increased exposure to antidepressants, particularly SSRIs (Hall et al., 2003); this effect was more pronounced in older age groups. An English study reported that a decline in suicide rates in older people was associated with an increase in the prescriptions of tricyclic antidepressants, SSRIs, antimanic drugs and antipsychotic drugs (Lodhi & Shah, 2004). The same study reported that an increase in suicide rates in older people was associated with an increase in prescriptions of antidepressants in the category monoamine reuptake inhibitors (MAOIs), hypnotics, anxiolytics and barbiturates (Lodhi & Shah, 2004). A review of 16 ecological studies concluded that there was an inverse relationship between suicide rates and use of antidepressants across all age groups (Isacsson, 2008). Another study across 26 countries concluded that an increase in SSRI sales of one pill per capita reduced suicide by 5% (Ludwig, Marcotte & Norberg, 2009).

However, only a few studies have examined the relationship between elderly suicide rates and they have all used data at least a decade old. Moreover, there has been recent debate about the impact of the prescribing of antidepressants on the reduction of suicide rates (Isacsson, Rich, Jureidini & Raven, 2010). With this in view, the association between elderly suicide rates and the prescribing rates of psychotropic drugs in England and Wales, for the latest 12-year period for which data were available, was examined with the unidirectional hypothesis that a decline in elderly suicide rates would be associated with an increase in the rates of prescriptions of psychotropic medication (antipsychotics, antidepressants and antimanic drugs). It was also hypothesized that a decline in elderly suicide rates would be associated with a decline in the prescription rates of hypnotics and anxiolytics (including barbiturates).

Methods

Suicide rates

Data on suicide rates for both genders in the age bands 65–74 years and 75+ years in England and Wales were ascertained for each of the 12 years (1995–2006) from the World Health Organization (WHO) website. This time period was specifically chosen because a previous similar study had examined the study hypotheses using data until 1996 (Lodhi & Shah, 2004), and the current data set is the latest available with a two-year overlap with the previous study.

National prescribing patterns for psychotropic drugs

Data on the total annual number of prescriptions issued for the broad British National Formulary (BNF) categories for psychotropic drugs and individual drugs within these broad BNF categories for each of the 12 years between 1995 and 2006 for England were ascertained. Data for each year between 1998 and 2006 were ascertained from the Department of Health (DH) website (http://www.dh.gov.uk/ en/Publicationsandstatistics/Statistics/StatisticalWorkAreas/ Statisticalhealthcare/DH 4086488# 4). Data for each year between 1995 and 1997 were not available in an electronic format and were ascertained from a DH publication. The data consisted of the number of National Health Service (NHS) prescriptions dispensed. The broad categories of psychotropic drugs examined were antipsychotics, antidepressants, mood stabilizers, hypnotics and anxiolytics. Within each broad psychotropic drug category, individual drug groups (e.g. SSRI and MAOI in the antidepressant category) and individual drugs were also examined.

Data on the total population size for England and Wales for each of the 12 years 1994–2006 were acertained from

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the WHO website. The rates of prescribing of psychotropic drugs by the broad BNF categories, for individual psychotropic drug groups within the broad BNF categories (e.g. SSRIs), and for the individual psychotropic drugs in the general population were calculated by dividing the number of annual prescriptions issued by the the general population size for each of the 12 study years.

Data analysis

Spearman's correlation coefficient (ρ) was used to examine the relationship between suicide rates in both age bands for both genders and the annual prescription rates of psychotropics drugs by the broad BNF categories, for individual psychotropic drug groups and for the individual psychotropic drugs within these BNF categories. This approach has been successfully used in previous studies in this area (Lodhi & Shah, 2004; Isacsson, 2000).

Spearman's correlation coefficient (ρ) was also used to examine the relationship between the study years and (1) the suicide rates in both age bands for both genders; (2) the annual prescription rates for the broad BNF categories of psychotropic drugs (antipsychotics, antidepressants, mood stabilizers, hypnotics and anxiolytics); (3) individual drug groups in the broad BNF categories (e.g. SSRIs and MAOIs); and (4) individual psychotropic drugs. This allowed examination of the overall trends in suicide rates and psychotropic prescribing over time. This method has been successfully used before (Hoxey & Shah, 2000; Lodhi & Shah, 2004; Shah, 2007a, 2007b; Shah et al., 2001; Shah et al., 2008; Shah & Coupe, 2009).

Results

The median (range) of suicide rates (per 100,000 of relevant age group) for the 12-year study period for males 65–74 years, males 75+ years, females 65–74 years and females 75+ years was 9.1 (3.6–11.1), 12.35 (3.7–15.7), 3.6 (2.7–4.2) and 4.0 (3.0–5.3), respectively.

There was no significant correlation between suicide rates in males and females in either age band and annual prescription rates for any of the broad BNF categories of psychotropics (antipsychotics, antidepressants, mood stabilizers, hypnotics and anxiolytics). Similarly, there was no significant correlation with any individual psychotropic drug group and any individual psychotropic drug.

There was no significant correlation between study years and suicide rates in males 65–74 years, males 75+ years, females 65–74 years and females 75+ years. This suggests that suicide rates in males and females in both age bands did not significantly change over the 12-year study period. There was a significant increase over the 12-year study period in the prescribing of oral antipsychotics ($\rho = 0.99$, p < .00001), tricyclic antidepressants ($\rho = 0.99$, p < .00001), SSRIs ($\rho = 1$), all antidepressants ($\rho = 1$) and antimanic

Table 1. Changes in rates of the prescribing of psychotropic drugs over the study years.

| Drug | ho | Þ |
|---|-------|----------|
| Oral antipsychotics | 0.99 | < .00001 |
| Depot antipsychotics | -0.53 | .075 |
| Tricyclic antidepressants | 0.99 | < .00001 |
| Selective serotonin reuptake inhibitors (SSRIs) | I | 0 |
| Monoamine reuptake inhibitors (MAOIs) | -0.96 | < .0000. |
| All antidepressants | 1 | 0 |
| All mood stabilizers | 1 | 0 |

drugs ($\rho = 1$) (Table 1). There was a significant decrease in the prescribing of depot antipsychotics ($\rho = -0.53$, p = .075) and MAOIs ($\rho = -0.96$, p < .00001).

Discussion

The main findings were an absence of significant correlations between suicides rates in both genders in both age bands and prescription rates of psychotropics drugs in the broad BNF categories, individual psychotropic drug groups and individual psychotoropic drugs.

Methodological issues require consideration before discussing the results. First, the 12-year study period may be comparatively short, and this may have biased the findings due to type II statistical error. The initial study year was carefully chosen to overlap the earlier study (Lodhi & Shah, 2004) by two years, but the last year of the current study was limited by the availability of the latest data. There are clear difficulties in interpreting observational studies that are not powered to detect predetermined differences. Consideration was given to conducting reverse power calculation to estimate the effect size that could be excluded. However, upon statistical advice this was not pursued because this area is controversial, purists argue that posthoc statistical analyses are inappropriate, and it is difficult to conduct such analysis with non-parametric time series data using rank correlations. Second, data on the prescribing of psychotropic drugs were for England only, whereas data on suicide rates were for England and Wales. This is unlikely to have influenced the findings as the absolute number of elderly suicides in Wales is comparatively small (Lodhi & Shah, 2004). Third, data on the prescribing of psychotropic medication were for all age groups rather than specifically for the elderly as age-specific data on prescriptions were not available and this may have biased the findings. Fourth, there were no data on compliance, on the accuracy of treatment and the actual number of patients treated and this has implications for aetiological interpretation of the findings. Fifth, this study examined rates of pure suicides and this may be an underestimate of the true suicide rates as accidental deaths and those due to undetermined causes contain concealed suicides (O'Donnell & Farmer, 1995). Sixth, the correlational analysis undertaken did not control for confounding variables (Isacsson et al., 2010). Finally, the design of the study involved analysis over time, and correlational analysis over time has limitations because the effect of time itself cannot be examined. The study was confined to England and Wales and the findings cannot be generalized to the rest of the UK or other developed countries.

The absence of significant correlations between elderly suicide rates and prescription rates of broad groups of psychotropics drugs, individual psychotropic drug groups and individual psychotropic drugs is in contrast to earlier studies. Studies from Sweden, Australia and England and Wales have reported an inverse relationship between elderly suicide rates and prescription rates of SSRIs (Carlsten et al., 1999; Hall et al., 2003; Lodhi & Shah, 2004). The Swedish study also reported an increase in suicides due to benzodiazepines despite a decline in their sales (Carlsten et al., 1999). The study from England and Wales also reported a decline in elderly suicide rates with an increase in the prescriptions of tricyclic antidepressants, antimanic drugs and antipsychotic drugs, and an increase in elderly suicide rates with an increase in prescriptions MAOIs, hypnotics, anxiolytics and barbiturates (Lodhi & Shah, 2004). The negative findings of the present study may be due to the methdological difficulties described earlier.

However, the possibility that the findings are genuine requires careful consideration. First, an earlier study from our group covering the 12-year period between 1985 and 1996, using identical methodology, demonstrated significant negative and positive correlations between elderly suicide rates and a number of groups of psychotropic drugs. Thus, methodological issues alone cannot explain the current negative findings. Second, a few other studies have also reported an absence of an inverse correlation between general population suicide rates and the prescribing of antidepressants (Barbui, Campomori, D'Avanzo, Negri and Garattini, 1999; Guaiana et al., 2005; Safer & Zito, 2007). Third, it is possible that the psychotropic drugs had an impact on suicide rates, but some other factor, hitherto unknown, and which changes over time, has had an opposite effect on suicide rates, and hence there was no apparent correlation within this ecological design. However, there is no evidence to support this hypothesis. Fourth, there is the possibility that elderly suicide rates have declined to a comparative low level and further changes in psychotropic prescribing rates may have little impact on suicide rates. In other words, the optimum impact of changes in psychotropic prescrbing may have already been acheived. An inverse correlation between general population suicide rates and use of SSRIs in the USA was present between 1990 and 1999, but was absent between 2000 and 2004 (Safer & Zito, 2007). Fifth, the possibility that elderly suicide rates were declining well before there was an increase in the prescription of antidepressants requires consideration. A decline in general population suicide rates preceding the onset of the use of SSRIs has been reported in several countries (Safer & Zito, 2007), although this does not preclude any additional impact of SSRIs on suicide rates. It is therefore possible that previous studies have shown a spurious inverse correlation, which was absent in the current study because there was no further decline in elderly suicide rates during the study period. Finally, the role of non-pharmacological factors – including important changes in the provision of mental health services for older people, improved assessment of suicide risk, increased availability of psychosocial interventions, strategies to reduce social isolation and restricting the availability of methods for suicide - may also be important in reducing suicide rates (Hall et al., 2003; Isacsson et al., 2010; Lodhi & Shah, 2005; Shah, 2009, 2010).

The above arguments, taken together, could be synthesized into a composite explanatory model for the findings. First, elderly suicide rates were declining prior to changes in psychotropic prescribing rates. Second, changes in psychotropic prescribing rates, particularly antidepressants, initially had an additional impact on elderly suicide rates. Third, as the elderly suicide rate reached a threshold of comparative low level, further changes in psychotropic prescribing rates no longer had an impact on elderly suicide rates. At the same time, suicide rates were no longer declining further. Finally, the role of non-pharmacological factors, including important changes in mental health service provision for older people, improved assessment of suicide risk, increased availability of psychosocial interventions and restricting the availability of methods for suicide, may become important in reducing suicide rates at this stage (Hall et al., 2003; Isacsson et al., 2010; Lodhi & Shah, 2005; Shah, 2009, 2010).

Conclusion

Suicide is a rare and often unpredictable event. The findings of an absence of correlation between elderly suicide rates and psychotropic drug prescription rates in this ecological study do not necessarily imply an absence of causation. However, if the findings are genuine, the following approaches need to be considered to ensure further reduction in elderly suicide rates: (1) development of strategies to ensure continued prescription of psychotropic drugs at the current level; (2) development of strategies to improve non-pharmacological measures, including improved mental health service provision for older people, improved assessment of suicide risk, increased availability of psychosocial interventions and restricting the availability of methods of suicide (Isacsson et al., 2010; Lodhi & Shah, 2005; Shah, 2009, 2010); and (3) development of

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strategies to implement improvement in distal risk (e.g. societal socio-economic status) and protective (e.g. societal educational attainment) factors at a societal level to reduce elderly suicide rates (Shah, 2010; Shah & Chaterjee, 2008).

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Role of authors

AS conceived the idea for the study and developed the protocol. SZ, GZ and MS collected the data. AS analysed the data and wrote the first draft. All authors then improved the draft paper.

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