Risk of suicide for individuals reporting asthma and atopy in young adulthood: Findings from the Glasgow Alumni study

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A B S T R A C T
There is emerging evidence that asthma and atopy may be associated with a higher risk of suicide. We investigated the association of asthma and atopy with mortality from suicide (n = 32) in the Glasgow Alumni cohort, adjusting for the key confounders of socioeconomic position and smoking. We found no evidence of an association in our a priori atopy phenotypes with suicide, and there were insufficient suicides in the asthma phenotypes to draw any conclusions. In additional analyses, individuals reporting both eczema--urticaria and hay fever and those with family history of atopy were at higher risk of suicide. As these were secondary analyses and based on small numbers of events we cannot rule out chance findings. The lack of evidence in our main hypothesis may be due to the small number of suicides or reported associations between asthma and atopy may be confounded.

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1. Introduction

In 1966 Paffenbarger reported a higher percentage of allergic reaction to irritants and a consistent, “although not statistically significant”, higher percentage of asthma, among students who had died by suicide compared to controls (Paffenbarger and Asnes, 1966). Since then, a systematic review (Iessa et al., 2011) and additional papers (Timonen et al., 2001; Kuo et al., 2010; Qin et al., 2011; Loerbroks et al., 2012) have documented a higher risk of suicide ideation, attempt or death as well as depression among asthmatics and/or people with reported or measured atopy. Despite this increasing evidence, important confounders such as socioeconomic position (SEP), smoking and comorbidities were not available in all studies and so may have confounded these findings. The lack of evidence in our main hypothesis may be due to the small number of suicides or reported associations between asthma and atopy may be confounded.

2. Methods

Students who attended the University of Glasgow between 1948 and 1968 were invited to an annual medical examination at the Student Health Service with approximately 50% of the students attending (n = 15,322, 77% male, mean age 20.9 years (S.D. 4.0)) (McCarron et al., 1999). Sociodemographic and medical data were collected through a physician administered questionnaire and physical examination. Students reported “Past Medical History” of, among other conditions, having ever had i) asthma, ii) eczema--urticaria, and iii) hay fever. Eczema and urticaria were asked jointly in the questionnaire and could not be separated in the analysis. The following asthma and atopy phenotypes were initially investigated: asthma (regardless of atopic status), atopy (eczema--urticaria and/or hay fever, regardless of asthma status), and phenotypes based on the combination of these two conditions: asthma with atopy (asthma and eczema--urticaria or hay fever), asthma without atopy (asthma without eczema--urticaria or hay fever) and atopy alone (eczema--urticaria or hay fever without asthma). Secondary analyses investigated all combinations of the two atopic conditions, eczema--urticaria and hay fever, as well as family history of these conditions. Between 2001 and 2002, members of the cohort who were still alive (n = 8410) were contacted through a postal questionnaire and 5569 (66%) responded to this follow-up. The General Health Questionnaire (GHQ-12) (Goldberg, 1978) and history of depression in adulthood were collected in this subsample; a score of four or more on the GHQ-12 was used to indicate poor mental health. We investigated the association of asthma and atopy reported at baseline with the...
GHQ-12 and history of depression in adulthood in the sub-sample of questionnaire respondents. The National Health Service Central Register (NHSCR) carried out tracing of the students and provided notification of the date and cause of death, area of current residence, and emigration details. Deaths up until the end of 2012 were included. ICD-9 and ICD-10 codes were used to classify suicides into intentional self harm (ICD9: E950–E959; ICD10: X60–X84) and deaths of undetermined intent (ICD9: E980–E989, excluding E988.8; ICD10: Y10–Y34). Deaths of undetermined cause were also included in our analyses as most such deaths were suicides (Linsley et al., 2001).

Cox proportional hazards regression models were used to investigate the association of asthma and atopy with suicide using age as the time axis. The assumption of proportional hazards across exposure groups was formally tested with the Schoenfeld test. All models were adjusted for year of student examination to control for potential confounding from the change over time of disease prevalence or definitions. The final model contained terms for year of student examination, sex, height, number of siblings, birth order, father’s social class measured with occupational class using the Registrar’s Social class classification, body mass index (BMI) and smoking. In addition we investigated the association between poor mental health (GHQ-12 score of 4 or more) and suicide in the subsample.

3. Results

Students who could not be traced or who had missing exposure data were excluded from this analysis, yielding a total sample of 11,463 (8938 male, 78%) individuals among whom there were 32 suicides (29 male) up to the end of 2012. The incidence of suicide in this study was 5.52 per 100,000/year, which was substantially lower than the UK average (11.8 per 100,000/year) (ONS, 2013). The prevalence of asthma was higher in males than females (3.7% vs. 2.3%, p = 0.001), while the prevalence of atopy was higher in females than males (12.3% vs. 9.2%, p < 0.001). The median age of study members at the time of university medical examinations was 19.4 years (range 16–53). We found no evidence of an association of asthma and/or atopy phenotypes in young adulthood with later suicide in our a priori group (Table 1). However, in additional analysis of secondary outcomes, individuals with a combination of eczema–urticaria and hay fever, and a family history of atopy were associated with higher risk of suicide (Table 2).

Students with missing data in the postal questionnaire were excluded, yielding a total subsample of 4746 (3568 male, 75%; 85% of the 5569 students who responded) individuals among whom there were five suicides (5 male) up to the end of 2012. A greater proportion of females reported a diagnosis of depression (19.5% vs. 14.9%, p < 0.001), or reported poor mental health (GHQ-12 > 4) (14.3% vs. 10.0%, p < 0.001) compared to males. There was no evidence of an association between asthma or atopy and suicide in adulthood with later suicide in our a priori group (Table 1). However, in additional analysis of secondary outcomes, individuals with a combination of eczema–urticaria and hay fever, and a family history of atopy were associated with higher risk of suicide (Table 2).

| Exposure | Individuals (%) | Suicides (n) | Model 1 HR (95% CI) | Model 2 HR (95% CI) |
|----------|----------------|--------------|---------------------|---------------------|
| Asthma (with or without atopy) | 387 (3.4) | 1 | 0.92 (0.13–6.76) | 0.92 (0.13–6.73) |
| Atopy (with or without asthma) | 1132 (9.9) | 5 | 1.68 (0.65–4.36) | 1.69 (0.65–4.40) |
| Asthma and atopy phenotypes | | | | |
| No asthma, no atopy (reference group) | 10089 (88.0) | 27 | 1.00 | 1.00 |
| Asthma with atopy | 145 (1.3) | 1 | 2.50 (0.34–18.40) | 2.55 (0.35–18.89) |
| Asthma without atopy | 242 (2.1) | 0 | – | – |
| Atopy without asthma | 987 (8.6) | 4 | 1.51 (0.53–4.32) | 1.51 (0.53–4.34) |

Model 1 adjusted for year of examination. Model 2 also adjusted for sex, height, number of siblings, birth order, fathers social class, body mass index and current smoking.

A potential source of bias could be due to only half of the students who were invited to the medical examination actually attending. If those who did not attend the medical examination had a higher prevalence of asthma/atopy, and there were more suicides in this group of individuals, then the results of this study would be biased towards the null. This limitation is also relevant to
the postal questionnaire where individuals with more severe asthma, atopy or depression may be less likely to respond. This may explain why we failed to find evidence of an association as strong as has been previously reported and thus a lack of evidence supporting our a priori hypotheses.

We report an association between family history of atopy with a higher risk of suicide which supports previous work reporting an association between family history of atopy and depression (Timonen et al., 2003). Twin studies have suggested a shared genetic risk for atopic and depressive symptoms (Wamboldt et al., 2000). However, a shared genetic risk would not fully explain our results as it appears a family history of atopy is a stronger risk factor than having atopy yourself. It may be that atopy conveys risk, but its treatment, in particular with intranasal or inhaled corticosteroids reduces the risk (Woo et al., 2011). In addition, exposure to molecular mediators of atopy, or atopy medication during pregnancy may influence brain development and increase the risk of suicide in the offspring. A limitation of this study is that medication data or data on other physical diseases were not included in the analyses but may be confounding the results. There was only 1 suicide in the asthma group which limited the conclusions that could be drawn.

Our finding that individuals with both eczema–urticaria and hay fever are at a 9 fold higher risk of suicide is consistent with other reports of only severe atopy being associated with suicide in a Danish record-linkage study (Qin et al., 2011) and a dose-response association between air pollen counts and suicide (Qin et al., 2013). This type of dose-response association has also been reported between the severity of asthmatic symptoms and subsequent suicide risk (Kuo et al., 2010). However, in our analysis, the finding was based on only two suicides and there was no association with other measures of mental health, so must be interpreted with extreme caution.

Several mechanisms could explain an association between asthma and/or atopy with suicide: i) confounding due to cigarette smoking, child and/or adulthood deprivation and other demographic characteristics. We could account for some of these in our analysis and through the study design. In addition, depression or other mental health comorbidities may be confounders if they are not on the casual pathway; ii) hopelessness experienced due to suffering a lifelong chronic condition (Goodwin and Buka, 2008); and, iii) a common risk factor, related to inflammatory processes, to which both conditions are related (Miller et al., 2009). Our results point to processes related specifically to atopic conditions. As noted above an association with family history of atopy could suggest shared genetic or biological traits.

This study adds to the growing body of research investigating the association among asthma, atopy and suicide. Our study included deaths from suicide rather than ideation and could account for some relevant confounders. Replication of these findings in other populations with comprehensive information on confounders, particularly life course mental history, and biological markers of potential aetiological mechanisms is necessary.

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Table 2

| Exposure                          | Individuals (%) | Suicides (n) | Model 1 HR (95% CI) | Model 2 HR (95% CI) |
|-----------------------------------|----------------|-------------|---------------------|---------------------|
| Hay fever only                    | 584 (5.1)      | 2           | 1.26 (0.30–5.29)    | 1.22 (0.29–5.15)    |
| Eczema–urticaria only             | 352 (3.1)      | 0           | –                   | –                   |
| Eczema–urticaria and hay fever    | 75 (0.7)       | 2           | 10.02 (2.39–42.07)  | 9.51 (2.24–40.43)   |
| Family history of atopy (with or without atopy themselves) | 693 (6.1) | 6 | 3.56 (1.46–8.65) | 4.25 (1.73–10.44) |
| Family history of asthma (with or without asthma themselves) | 531 (4.8) | 3 | 2.08 (0.63–6.84) | 2.44 (0.74–8.06) |

Model 1 adjusted for year of examination. Model 2 also adjusted for sex, height, number of siblings, birth order, fathers social class, body mass index and current smoking. There were a total of 32 suicides in the cohort of 11,463. All analyses included the 11,463 individuals.
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