Use of Psychotropic Drugs and Risk of Myocardial Infarction: A Case-Control Study in Finnish Farmers

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Background. In 1992 Thorogood et al. reported an increased risk of myocardial infarction in women using psychotropic drugs. The aim of our study is to find out whether there is a link between the use of psychotropic drugs and subsequent myocardial infarction in males.

Method. A cohort of 3172 male farmers was followed from 1 February 1980 to 31 December 1992. Those subjects who had myocardial infarction without any previous symptoms during the follow-up were considered as cases. For every case three matched controls were selected. The matched variables were age, smoking habits, social status and county. The final sample includes 83 cases and 249 controls.

Results. Those who had used psychotropic drugs had increased risk for myocardial infarction, odds ratio (OR) = 2.5, 95% confidence interval (CI) = 1.2-5.2. Most pronounced risk for myocardial infarction was found among users of antidepressants, OR = 5.4 (CI: 1.8-16.1).

Conclusion. The use of psychotropic drugs, especially antidepressants, is associated with increased risk of myocardial infarction. Further attempts are needed to determine whether the relationship between use of psychotropic drugs and risk of myocardial infarction is causal or not.

Keywords: myocardial infarction, psychotropic drugs, depression, case-control study, farmers
TABLE 1 Use of drugs and risk of myocardial infarction during follow-up

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Cases (%) (N = 83)</th>
<th>Controls (%) (N = 249)</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressant</td>
<td>9 (10.8)</td>
<td>5 (2.0)</td>
<td>5.4</td>
<td>1.8–16.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Minor tranquillizer</td>
<td>9 (10.8)</td>
<td>14 (5.6)</td>
<td>2.1</td>
<td>0.9–5.1</td>
<td>0.11</td>
</tr>
<tr>
<td>Neuroleptic</td>
<td>4 (4.8)</td>
<td>6 (2.4)</td>
<td>1.5</td>
<td>0.4–6.0</td>
<td>0.57</td>
</tr>
<tr>
<td>Other psychotropic</td>
<td>2 (2.4)</td>
<td>2 (0.8)</td>
<td>3.0</td>
<td>0.4–21.3</td>
<td>0.28</td>
</tr>
<tr>
<td>Painkiller</td>
<td>41 (49.4)</td>
<td>131 (52.6)</td>
<td>0.9</td>
<td>0.5–1.5</td>
<td>0.70</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>30 (36.1)</td>
<td>67 (26.1)</td>
<td>1.6</td>
<td>0.9–2.7</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Data Collection
The patient records for every selected subject were checked by visiting the local community health care unit. Drug use during the follow-up period was checked from the patient records. The amount of drugs used and the date of starting or stopping drug use were not checked.

Statistical Analysis
The odds ratios (OR) were calculated by a conditional logistic regression analysis for a matched case-control study (EGRET® statistical package). Probability values \( \leq 0.05 \) were considered statistically significant.

RESULTS
Results indicated that 16 (19.3%) cases and 22 (8.8%) controls had used psychotropic drugs during follow-up. The OR for myocardial infarction among users of psychotropic drugs was 2.5 (95% confidence interval [CI] : 1.2–5.2). Antidepressants were most strikingly associated with myocardial infarction (Table 1). Four cases (4.8%) and two (0.8%) controls had used only antidepressants, six (7.2%) cases and 12 (4.8%) controls only minor tranquilizers and one case (1.2%) and three controls (1.2%) only neuroleptics. Four cases had a fatal infarction. Two of them had not used any psychotropic drugs and the other two only minor tranquilizers. When painkillers and cardiovascular drugs were considered, case control differences were not so clear (Table 1). Eleven (13.3%) cases and 17 (6.8%) controls visited a doctor for some psychiatric reason during follow-up. The OR for myocardial infarction among those visiting a doctor for a psychiatric reason was 1.9 (95% CI : 0.9–4.0).

DISCUSSION
There are some possible variables which could have caused bias in our results. Firstly, we used only two categories when matching smoking habits. Smoking has been shown to be a risk factor for both depression and myocardial infarction. Including ex-smokers and current smokers in the same category might have influenced our results. Secondly, we were not able to standardize the serum lipids, especially total cholesterol, of the subjects. However, cholesterol concentration is not necessarily a confounding factor. High cholesterol level is associated with increased risk of myocardial infarction, but is inversely associated with depression.

The subjects in the study of Thorogood et al. were women. Our results indicate that the association between use of psychotropic drugs and risk of myocardial infarction is also true in men. There are at least two different ways to explain the possible association between psychotropic drugs and risk of myocardial infarction. First, there could be an association between depression and myocardial infarction. In men anxiety and stress and in women several psychosocial factors are associated with increased risk of myocardial infarction. Hostility has also been shown to be a strong determinant of myocardial infarction in men. The association may be a causal one, but it is also possible that there is some confounding factor causing both depression and myocardial infarction. According to one hypothesis, cytokines, especially interleukin-2, could be a potential causal factor for both of these disturbances. Second, a direct causal link between psychotropic drugs and myocardial infarction is possible. Tricyclic antidepressants have arrhythmic properties. Antidepressants have also been reported to increase insulin resistance in non-insulin dependent diabetes. Indeed, both of the proposed explanations may be true. Those suffering from depression or a related disorder could have an increased risk of myocardial infarction and hence increased sensitivity to drugs having cardiovascular side-effects.

The association between psychotropic drugs and myocardial infarction need not be specific. The overall
The use of drugs could be more common among cases than among controls. However, the probability of bias of that kind seems not to be very high because no association between, for example, use of painkillers and risk of infarction was found.

Our material was too small for more detailed analysis. Larger samples have to be analysed in future attempts to find out whether the relationship between psychotropic drugs and increased risk of myocardial infarction is due to a causal relationship.

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REFERENCES


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