Excess Mortality Related to Alcohol and Smoking Among Hospital-Treated Patients With Psoriasis

Kari Poikolainen, MD, PhD; Jaakko Karvonen, MD, PhD; Eero Pukkala, PhD

Background: Psoriasis is seen as a disease that does not kill. However, it is associated with alcohol intake and smoking. Thus, there could be excess mortality due to causes related to alcohol intake and smoking among patients with psoriasis.

Design: A cohort was identified from the nationwide Hospital Discharge Register from January 1, 1973, through December 31, 1984, and mortality was followed up for 22 years by linkage with the Cause-of-Death Register, from January 1, 1973, through December 31, 1995.

Patients: A cohort of 3132 men and 2555 women admitted to inpatient treatment with psoriasis as the principal diagnosis.

Main Outcome Measures: Date and underlying cause of death.

Results: We observed 1918 deaths in contrast to the 1211 deaths expected on the basis of the national mortality rates. The all-cause standardized mortality ratio (SMR) for men was 1.62 (95% confidence interval [CI], 1.52-1.71); for women, 1.54 (95% CI, 1.43-1.64). Among men, the highest SMRs were found for alcohol psychosis (8.91 [95% CI, 2.89-20.70]) and liver disease, ie, cirrhosis, fatty liver, and hepatitis (6.98 [95% CI, 5.34-8.96]). Among women, the highest SMR was found for liver disease (5.06 [95% CI, 2.70-8.65]). Excess mortality was high for all causes of death directly related to alcohol; the SMR for men was 4.46 (95% CI, 3.60-5.45); for women, 5.60 (95% CI, 2.98-8.65).

Conclusions: Patients with moderate to severe psoriasis are at increased risk for death. Alcohol is a major cause for this excess mortality.

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SORIASIS IS a common and chronic disease that is not thought to kill. Little is known about mortality in this patient group, although alcohol- and smoking-related diseases are associated with psoriasis, and patients with psoriasis have reported higher alcohol and cigarette consumption than control patients in several studies, suggesting that excess mortality due to alcohol- and tobacco-related causes might be found among patients with psoriasis. We therefore studied mortality in patients with psoriasis.

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Results: There were altogether 1918 observed deaths, whereas 1211 were expected. Significantly increased mortality was found for alcohol-related causes, smoking-related causes, causes related jointly to alcohol and smoking, and other causes. Highest excess mortality was found for causes of death directly attributed to alcohol (Table 1). This clearly surpassed the excess mortality in the other cause-of-death groups.

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Among men, there was significant (P<.05) excess mortality due to cancers of the liver, bladder, larynx, and lung, alcohol-related psychosis, alcohol dependence, alcohol poisoning, alcoholic liver cirrhosis, all liver disease (ie, cirrhosis, fatty liver, and hepatitis), hypertension, coronary heart disease, chronic obstructive pulmonary disease, peptic ulcer, and suicide. Among women, significant increases were found in mortality due to cancer of the pancreas, alcoholic liver cirrhosis, liver disease in general, coronary heart disease, and thromboembolic stroke. Excess mortality due to alcohol-related causes was higher than that due to smoking-related causes (Table 2). Mortality was significantly increased during the first 5

From the Jarvenpaa Addiction Hospital, Jarvenpaa, and the Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki (Dr Poikolainen), the Department of Dermatology, Oulu University Hospital, Oulu (Dr Karvonen), and the Finnish Cancer Registry, Helsinki (Dr Pukkala), Finland.
PATIENTS AND METHODS

We first identified all records of patients with the principal diagnosis of psoriasis in the Hospital Discharge Register from January 1, 1973, through December 31, 1984, in Finland. There were altogether 13,406 hospital admissions among 6024 persons. This sample was then linked with the Population Central Register with the help of unique personal identification codes. Of the sample, 4.6% were not found in the Population Central Register because the personal identification codes were erroneous in the Hospital Discharge Register. Of the remaining 5746 patients, 33.4% had died, and 1.0% had emigrated by the end of 1993. Follow-up started from the month following the earliest hospital discharge. The follow-up ended on the date of emigration or death or on December 31, 1995, whichever came first.

The final cohort consisted of 3132 male and 2555 female patients with psoriasis. The respective numbers of person-years of follow-up were 41,684 and 35,892. The mean length of follow-up was almost 14 years, and the length of the study period was 22 years.

The follow-up for causes of death was performed by linking the data for the cohort with those in the Cause-Of-Death Register, with the help of the unique personal identification code. Underlying causes of death were based on official death certificates, coded according to the Finnish modification of the International Classification of Diseases, Eighth Revision and Ninth Revision and obtained from Statistics Finland. The selection of causes of death related to alcohol only, smoking only, and alcohol and smoking was based on epidemiological evidence from a recent meta-analysis and reviews. Alcohol-related causes were further classified into the following 2 groups: directly related if the diagnostic label explicitly mentioned alcohol as a cause (Table 1), and otherwise indirectly related.

The results are presented as standardized mortality ratios (SMRs). These figures express the ratio of observed causes of death to that expected on the basis of the overall mortality rates for the Finnish general population. These ratios have been standardized for age, sex, and calendar period (1973-1978, 1979-1984, 1985-1990, and 1991-1995). Poisson distribution was applied when calculating the 95% confidence intervals (CIs).

years and later during years 6 through 22 of the follow-up (data not shown).

COMMENT

Little is known about mortality among patients with psoriasis. We have found only 2 earlier reports. In a cohort of 428 patients with psoriatic arthritis, excess deaths were found due to diseases of the respiratory system among men and women and due to injuries and poisoning among men. In the Phototherapeutics Follow-Up Study, mortality due to liver cirrhosis was increased (SMR, 4.65 [95% CI, 2.84-7.18]), whereas all-cause mortality was not increased. Among men, the SMR was 0.85 (95% CI, 0.73-1.03); among women, 1.26 (95% CI, 0.94-1.65). This was a follow-up of a special group, 1380 patients with psoriasis who initially took part in a cooperative clinical trial of oral methotrexate photopheresis treatment at 16 university centers in the United States. Clinical trial populations may differ from patients with psoriasis at large. Our study is, to our knowledge, the first nationwide follow-up of all hospital inpatients with psoriasis as the principal diagnosis.

Bias is unlikely to explain the observed relations. The cause-of-death determination is considered to be highly reliable in Finland, and the autopsy rate is high. A skin disease strongly related to tobacco consumption, palmo-plantar pustulosis (known in some countries as palmo plantar pustular psoriasis) is considered a diagnostic entity apart from psoriasis in Finland. Inclusion of patients with the former diagnosis in a cohort of patients with psoriasis would overestimate the role of tobacco. Representative studies on the accuracy of the principal diagnosis in the Hospital Discharge Register are not available. However, when checked against medical records for a case-control study, 240 of the 241 patient records with the principal diagnosis of psoriasis in this register were found to be correct (Anna Hannuksela-Svahn, MD, written communication, May 22, 1999).

If low socioeconomic status would increase the probability of admission to the hospital, high mortality ratios should be observed for stomach cancer, since mortality due to stomach cancer has been found to have a steep socioeconomic status gradient in Finland. This was not the case. In our study, the SMRs for stomach cancer were close to 1 among men and women, supporting the view that the socioeconomic status distribution does not differ materially between these patients and the general population of Finland. Stomach cancer is not related to alcohol consumption, and only weakly related to smoking; compared with nonsmokers, the pooled relative risk was 1.4 for current smokers in a recent meta-analysis.

One possible explanation for increased mortality in our cohort could be that the patients were not admitted to hospital treatment predominantly because of psoriasis but because of coexistent serious and potentially fatal diseases. This seems unlikely, because the principal diagnosis, ie, the main or the only cause for admission to hospital treatment, was psoriasis for all patients in our cohort. If increased mortality were only due to the secondary diagnoses present at the time of admission, one would expect increased mortality during the first years of follow-up that would later taper off. Instead, mortality due to alcohol-related diseases and alcohol poisoning remained high after the first 5 years of follow-up.

Methotrexate treatment is hepatotoxic and may cause liver disease, especially after long-term administration. Part of the observed increased risk for any liver disease could thus be due to this treatment. We do not have any data on this treatment in our cohort. However, we found an increased risk, not only for all liver disease, but also for liver cirrhosis attributed to alcohol in the cause-of-death examination. According to a meta-analysis, the risk for progression of liver disease (fibrosis and cirrhosis) is markedly higher among heavy than light drinkers re-
receiving methotrexate treatment.21 Thus, the possible effect of methotrexate on mortality due to liver disease in this cohort, if any, is likely to have been strengthened by alcohol intake.

Consistent with our hypothesis, we found increased mortality due to alcohol- and smoking-related causes. The most elevated death rates were found for directly alcohol-related causes. Among men, these causes included alcohol-related psychosis, liver disease, and alcohol dependence; among women, liver disease. Some of the smoking-related causes, eg, lung and bladder cancer, were also found to be elevated, but to a lesser degree. These findings strongly support the view that alcohol intake and, less important, smoking increase the

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Observed Deaths</td>
<td>SMR (95% CI)</td>
<td>No. of Observed Deaths</td>
</tr>
<tr>
<td>Alcohol-related</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Directly</td>
<td>202</td>
<td>2.14 (1.84-2.44)</td>
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<tr>
<td>Indirectly</td>
<td>94</td>
<td>4.46 (3.60-5.45)</td>
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<tr>
<td>Smoking-related</td>
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<td>1.47 (1.20-1.75)</td>
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<tr>
<td>Both</td>
<td>13</td>
<td>1.92 (1.02-3.29)</td>
</tr>
<tr>
<td>Other</td>
<td>330</td>
<td>1.72 (1.54-1.91)</td>
</tr>
<tr>
<td>All</td>
<td>1139</td>
<td>1.62 (1.52-1.71)</td>
</tr>
</tbody>
</table>

Table 1. Major Causes of Death Among Patients With Psoriasis*

*SMR indicates standardized mortality ratio; CI, confidence interval.
†Includes underlying causes with direct reference to alcohol in the diagnosis, ie, alcohol-related psychosis, alcoholism, alcoholic polyneuropathy, alcoholic cardiomyopathy, alcoholic gastritis, alcoholic fatty liver, alcoholic hepatitis, alcoholic cirrhosis of the liver, unspecified alcoholic liver damage, alcoholic epilepsy, alcoholic pancreatitis, fetal alcohol syndrome, alcoholic withdrawal syndrome of the newborn, alcohol poisoning, and pregnancy, childbirth, or puerperium complicated by alcoholism.

Table 2. Alcohol- and Tobacco-Related Causes of Death Among Patients With Psoriasis*

*SMR indicates standardized mortality ratio; CI, confidence interval; and ellipses, not calculated.
mortality among patients with psoriasis. These findings indirectly strengthen the evidence of the association of psoriasis with alcohol intake and smoking based on self-reports that have been found earlier in several cross-sectional and case-control studies. Since heavy drinking has been found to be more common among patients with psoriasis than among the controls before the onset of the skin disease, and since among alcoholics alcohol problems have found to precede the onset of psoriasis, alcohol consumption seems to be a risk factor for psoriasis.

Some excess mortality was due to other than alcohol- and smoking-related causes. We do not have a clear explanation. However, psoriasis has been found to be related to increased stress and high intake of fatty foods, which may play a role. The reasons for this excess mortality should be clarified.

We studied patients who had at least once been admitted to the hospital for treatment of psoriasis. Hospitalized inpatients are likely to have more severe cases than outpatients. Thus, our findings pertain to patients with moderate to severe psoriasis, not necessarily to those with mild psoriasis.

Our findings show that patients with moderate to severe psoriasis have excess mortality that is to a great extent explained by alcohol-related causes of death and to a lesser degree by smoking. This excess mortality deserves serious attention. Prevention of excessive alcohol use and smoking among patients with psoriasis could alleviate their disease, improve their quality of life, and increase their life span.

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Reprints: Jaakko Karvonen, MD, PhD, Department of Dermatology, Oulu University Hospital, FIN-90220 Oulu, Finland (e-mail: jaakko.karvonen@oyt.oulu.fi).

REFERENCES