Previous studies have shown an association between low serum cholesterol concentration and suicide; however, conflicting results have also been reported. To examine this potential association, cholesterol levels in 99 patients admitted to an emergency ward following an attempted suicide were compared with those in 74 nonsuicidal psychiatric inpatients, and those in 39 psychiatrically normal individuals with accidental injuries. Cholesterol concentrations in suicide attempters were found to be significantly lower compared with both psychiatric and normal controls, when sex, age, psychiatric diagnosis, and physical conditions (serum total protein and red blood cell count) were adjusted for. This significant relationship was observed in mood disorders and personality or neurotic disorders, but not in schizophrenia spectrum disorders. These results support the previous claim that lower cholesterol level is associated with an increased risk of suicidal behavior.

Key Words: Attempted suicide, cholesterol, depressive disorder, psychiatric diagnosis

BIOL PSYCHIATRY 1997;41:196-200

Introduction

Muldoon et al (1990) examined the effects of cholesterol-lowering dietary and/or pharmacologic interventions on total and cause-specific mortality by using meta-analysis on six randomized primary prevention trials (in total of 24,847 male participants), and reported that although mortality from coronary heart disease was reduced, total mortality was not affected by treatment interventions, partly because of a significant increase in deaths from accidents, suicide, or violence in groups receiving treatment to lower cholesterol concentrations. Spontaneous low cholesterol levels, which are not caused by treatment interventions, have also been found to be associated with an increase in deaths from external causes including suicide by recent cohort studies (Lindberg et al 1992; Schuit et al 1993), although conflicting results have been reported (Farchi et al 1987; Pekkanen et al 1989; Davey Smith et al 1990).

On the basis of these observations, research interest has extended to the relationship between lower cholesterol concentration and potential changes in brain functions leading to psychiatric problems (McLoughlin and Clarke 1989; Engelberg 1992). Horrobin (1990) postulated that given the higher violent death rate in the low-cholesterol population, lowering cholesterol possibly produces a general shift to a more violent pattern of behavior and increases a milder form of violence. This view accords with an earlier series of studies by Virkkunen; low cholesterol concentration was found among patients with violent or aggressive conduct disorder (Virkkunen 1979; Virkkunen and Penttinen 1984), homicidal offenders with
histories of violence, and suicide attempters related to alcohol (Virkkunen 1983).

Since individuals with severe depressive symptoms are at risk for suicidal or violent behavior, it is also intriguing to examine whether low cholesterol is associated with depressive symptoms. In studies of the elderly population, some research groups (Dealberto et al 1993; Morgan et al 1993) found the association between low cholesterol and increased depressive symptoms, but others reported no significant association (Strandberg et al 1993) or the inverse relationship [i.e., high cholesterol and depressive symptoms (Simons et al 1993)]. A more recent study by Brown et al (1994) showed that low cholesterol was significantly associated with severe depressive symptoms, but that after self-reported health and physical functioning were controlled for, the significant association disappeared. Thus, the previous studies that examined the elderly general population have provided inconsistent results.

On the other hand, some investigators looked into the potential risk effect of low cholesterol concentration on suicidal behavior by examining samples of psychiatric patients. Sullivan et al (1994) investigated depressive patients and found that those with high suicidality had significantly lower cholesterol concentrations, compared with those with low suicidality. Modai et al (1994) examined 584 psychiatric inpatients and showed that patients with a history of attempted suicide had significantly lower serum cholesterol than nonsuicidal patients. They reported that when the diagnostic groups were analyzed separately, this significant difference was present in patients with depressive disorder, but not in schizophrenic or bipolar patients. This raises the possibility that the postulated association between low serum cholesterol and suicidal behavior may have relevance to biological mechanisms operating in depression. Golier et al (1995), who examined 650 psychiatric inpatients, found male patients with low cholesterol levels (less than or equal to 25th percentile) more likely to have ever made a serious attempted suicide than those with higher cholesterol levels.

The aim of this study is to examine in a Japanese sample whether low serum cholesterol is a risk factor for suicidal behavior. We hypothesized that cholesterol levels in suicide attempters would be lower than in nonsuicidal individuals.

Methods

We have carried out a case-control study consisting of two separate control groups for comparison. First, cholesterol concentrations in psychiatric patients admitted to an emergency ward immediately after an attempted suicide (cases) were compared with those in psychiatric inpatients who had no history of attempted suicide. Even if the postulated association of low cholesterol with suicidal behavior was found in this comparison, this could be accounted for by physical damage in the case subjects, which was concomitant with attempted suicide. To ensure any conclusion that can be drawn from the first case-control examination, further comparison was made between the cases and the other control group consisting of those who were admitted to the same emergency ward with similar physical condition to the cases but had no history of attempted suicide or psychiatric problems.

Cases

SUICIDE ATTEMPTERS. We identified all individuals (N = 196) who were admitted to the emergency ward at the Teikyo University Hospital, Tokyo, during the period from January 1988 to December 1991 following an attempted suicide and were subsequently discharged alive. Every patient was referred to a liaison psychiatrist, and his or her psychiatric diagnosis was made routinely according to DSM-III-R criteria (American Psychiatric Association 1987). Individuals who met the following criteria were included in the study: 1) serum total cholesterol concentration (TC) was measured immediately after admission (i.e., within 24 hours); serum sampling was carried out in the morning of the day following admission; 2) serum total protein level (TP) and red blood cell count (RBC) were simultaneously measured; and 3) patients without a diagnosis of substance abuse, including alcoholism, or organic brain syndrome. Data on TP were used to control for nutritional status, which may influence TC. Although changes in TC immediately after physical injuries are unknown, we assumed that the physical damage might affect TC and, in fact, we found RBC (parameter for the amount of bleeding) had a positive correlation with TC (see results), and thus we obtained data on RBC. Ninety-nine patients with a psychiatric illness met the inclusion criteria and constituted the cases (suicide attempters; SAs). Psychiatric diagnoses were categorized into three: 1) schizophrenia spectrum disorders (schizophrenia or delusional disorder); 2) mood disorders; or 3) personality or "neurotic" disorders.

Two Controls

PSYCHIATRIC CONTROLS. We identified 197 individuals who were consecutively admitted to the psychiatric ward at the same university hospital during the period from January 1989 to December 1991. DSM-III-R diagnosis was made during their admission. For patients who were admitted twice or more in the period, we referred to the diagnosis and laboratory data given during the last
Table 1. Characteristics and Mean Serum Total Cholesterol (TC) of 99 Suicide Attempters and 74 Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>Suicide attempters (N = 99)</th>
<th>Psychiatric controls (N = 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (%)</td>
<td>39 (39)</td>
<td>30 (41)</td>
</tr>
<tr>
<td>Age (years) (SD)</td>
<td>40.0 (16.7)</td>
<td>39.6 (15.5)</td>
</tr>
<tr>
<td>Psychiatric diagnosis* (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia spectrum</td>
<td>37 (37)</td>
<td>29 (39)</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>37 (37)</td>
<td>32 (43)</td>
</tr>
<tr>
<td>Personality or neurotic disorders</td>
<td>25 (25)</td>
<td>13 (18)</td>
</tr>
<tr>
<td>Physical conditionb (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury</td>
<td>53 (53)</td>
<td>--</td>
</tr>
<tr>
<td>Burn</td>
<td>3 (3)</td>
<td>--</td>
</tr>
<tr>
<td>Intoxication</td>
<td>38 (38)</td>
<td>--</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>5 (5)</td>
<td>--</td>
</tr>
<tr>
<td>Mean TC (mg/dL) (SD)</td>
<td>155 (37)</td>
<td>184 (39)</td>
</tr>
</tbody>
</table>

*The main diagnosis was determined for patients with two or more DSM-III-R diagnoses.

bOne main physical condition was determined for each suicide attempter. Injuries were caused, for example, by cutting, stabbing, or jumping from high buildings; intoxication was by overdose medication or intake of toxic agents; hypoxia was by hanging.

admission. We scrutinized their case records and referral documents, and excluded 71 patients who were found to have a history of attempted suicide. Of the remaining 126 patients, 74 patients met the criteria applied to the cases and were designated as psychiatric controls (PCs).

NORMAL CONTROLS. Another comparison group comprised randomly selected patients who were admitted to the same emergency ward during the same period as for the SAs after accidental injuries not due to suicidal acts or self-mutilations. As with the SAs, those who were discharged alive and whose TC, TP, and RBC were simultaneously measured on the day following admission, were included. We examined their case notes and excluded those with a current or past history of psychiatric treatments. Since accidental intoxication or hypoxia was rare in normal adults, those normals who had a diagnosis of trauma or burn caused by an accident, for example, traffic accident or accidental fire, were used as the other control group (normal controls; NCs, N = 39). Among the 99 SAs for the first comparison, 56 patients were treated under similar physical conditions (i.e., trauma or burn secondary to suicidal acts; see Table 1). The second comparison was thus made between these 56 SAs and 39 NCs.

Results

In all the subjects (SAs, PCs, and NCs; N = 212), TC showed highly significant linear correlations with age (Pearson’s r = .28, p < .001), TP (r = .43, p < .001), and RBC (r = .27, p < .001). Mean TC in men (155 mg/dL) was significantly lower than in women (176 mg/dL) (t = 3.74, df = 210, p < .001).

Comparison between the SAs and the PCs

The distributions of sex, diagnostic categories, and physical condition, and mean age and TC, between the SAs and the PCs are shown in Table 1. The SAs had significantly lower TC than the PCs (t = 5.0, df = 171, p < .001). ANCOVA analysis, in which potential confounders were adjusted for, also showed that TC in the SAs was significantly lower than the PCs (F = 6.9, df = 1, 158, p = .010). When diagnostic categories were examined separately, no significant difference in TC between the two groups was found in schizophrenia spectrum disorders (F = 0.0, df = 1, 59, p = .99), whereas a significant difference was present in mood disorders (F = 5.4, df = 1, 62, p = .023) and in personality or neurotic disorders (F = 4.3, df = 1, 31, p = .046).

Comparison between the SAs and the NCs

The distributions of sex, age, psychiatric diagnosis, and physical condition, and mean TC are shown in Table 2. Mean TC in the SAs was significantly lower than that in the NCs (t = 2.6, df = 93, p = .012). Even after adjusting for sex, age, RBC, and TP by ANCOVA, the SAs had significantly reduced TC compared with the NCs (F = 5.4, df = 1, 88, p = .023).
Table 2. Characteristics and Mean Serum Total Cholesterol (TC) of 56 Suicide Attempters and 39 Normal Controls Who Had Injury or Burn

<table>
<thead>
<tr>
<th></th>
<th>Suicide attempters (N = 56)</th>
<th>Normal controls (N = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (%)</td>
<td>26 (46)</td>
<td>21 (54)</td>
</tr>
<tr>
<td>Age (years) (SD)</td>
<td>38.8 (16.3)</td>
<td>33.5 (13.4)</td>
</tr>
<tr>
<td>Psychiatric diagnosis (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia spectrum</td>
<td>26 (46)</td>
<td>-</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>19 (34)</td>
<td>-</td>
</tr>
<tr>
<td>Personality or neurotic disorders</td>
<td>11 (20)</td>
<td>-</td>
</tr>
<tr>
<td>Physical condition (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury</td>
<td>53 (95)</td>
<td>36 (93)</td>
</tr>
<tr>
<td>Burn</td>
<td>3 (5)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Mean TC (mg/dL) (SD)</td>
<td>145 (34)</td>
<td>166 (45)</td>
</tr>
</tbody>
</table>

Discussion

We found significantly lower total cholesterol concentrations in suicide attempters compared with nonsuicidal psychiatric inpatients and normal controls. The observed lower TC in the SAs than in the PCs was not due simply to physical damage subsequent to suicidal acts, since TC in the SAs was also significantly lower than the NCs who had accidental physical damages.

It has been pointed out that a possible explanation for the relationship between low serum cholesterol and suicidal behavior is that depressive patients with decreased appetite, which lowers cholesterol concentration, are liable to commit suicide because of mood attributable to the illness but not to the low cholesterol (Goble and Worcester 1992; Davey Smith and Shipley 1993). In our study, however, a significant difference in TC was observed after adjusting for TP, which is a commonly used clinical parameter for nutritional status and, in fact, had a highly significant correlation with TC. Therefore, the low TC observed in the SAs cannot be accounted for by loss of appetite.

In the present study, TC was measured after attempted suicide but not before. Although we restricted the subjects to those whose TC was measured within 24 hours after their admission, this measure may not be optimum if physical condition consequent upon suicidal behavior exerts some lowering effect on TC in a prompt manner. To allow for this limitation, we compared TC for the SAs with that for the NCs measured within 24 hours after admission following similar physical condition to the SAs. The fact that the results were retained in this comparison indicates that low TC found in the SAs cannot be ascribed to any bias related to their physical changes after suicidal acts. Furthermore, we found RBC to correlate with TC and thus RBC was adjusted for in the analysis. If RBC had not been controlled for, the effect of TC on suicidal behavior would have been overestimated provided that the SAs were likely to have had blood loss due to injuries resulting in lowering TC. The previous studies in psychiatric samples (Modai et al 1994; Sullivan et al 1994; Golier et al 1995) have not taken into consideration the effect of physical damage subsequent to suicidal acts on TC.

The second comparison group, the NCs, comprised individuals who suffered from accidental injuries or burns. The previous studies suggest that low cholesterol may be a risk factor for accidental death as well as suicide (Muldoon et al 1990; Lindberg et al 1992; Schuit et al 1993); however, the SAs showed significantly lower TC compared with those with accidental injuries or burns, suggesting that low TC has more relevance to suicidal behavior than behaviors predisposed to accidental injuries.

When diagnostic groups were examined separately, the association between lower cholesterol and attempted suicide was observed in patients with mood disorders and personality or neurotic disorders, but not in those with schizophrenia spectrum disorders. To our knowledge, the study of Modai et al (1994) is the only one that examined the relationship between lower TC and risk of suicidal behavior in different psychiatric diagnostic groups. They reported the significant association between lower TC and suicidality in depressives but not in schizophrenics, as is consistent with our results.

Although we detected a significant association between TC and suicidal behavior, the relatively small sample size weakens this study. The diagnostic distribution of the SAs was different from those reported in Western countries (e.g., Rudd et al 1993); the proportion of schizophrenic subjects (37%), in particular, was increased, suggesting that the SAs in our sample may not have been accurately representative for suicide attempters in the general population; however, we controlled for psychiatric diagnosis in the comparison between the SAs and the PCs. Furthermore, the increased proportion of individuals with schizophrenia spectrum disorders in the SAs may have reduced rather than exaggerated the difference in TC between the SAs and the NCs, because no significant difference in TC
was found between the suicidal and nonsuicidal schizophrenic subjects.

The present study gives support for the previous claim that low cholesterol level is associated with suicidal behavior; however, the biological mechanisms for the relationship are still unclear and hence it may be premature to conclude that low TC is causal to suicidal behavior.

Nevertheless, we believe that low TC is a risk indicator for suicidal behavior and that further investigations in this issue are warranted.

Dr. Takei was supported by the Stanley Foundation.

References


