Triggering Risk Factors for Stroke: A Case Crossover Study from a Tertiary Care Hospital in Northwest India

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Abstract

Introduction: The role of traditional risk factors in the pathophysiology of stroke (IS) has been established and is well known. It has recently been shown that 10 risk factors are associated with 90% of the risk of stroke.

Material and methods: A case-crossover study design was used for the purpose of study. 2-hour hazard period immediately before the onset of stroke was compared with the 2-hour control period at the same time on the day before the onset of stroke.

Results: The study assessed the role of seven potential triggers for stroke. Forty four patients (73%) reported exposure to at least one potential triggering factor during the 2 hours hazard period before onset of stroke symptoms. Twenty nine patients (66%) reported exposure to at least one of three (Anger, sudden change in posture, negative emotions) potential triggers during the 2-hour hazard period.

Discussion: The current study examined possible association between exposure to potential triggers during a defined hazard period and triggering of the acute onset of stroke. There have been previously reported observations on the potential effect of emotions as a trigger for MI.

Conclusion: The period of study and the study sample may not be large enough for extrapolation but nevertheless does open up a new area for research in our setup.

Keywords: Triggers; Stroke; Cross-over study

Introduction

Traditional risk factors have a role to play in the pathophysiology of stroke (Ischemic Stroke). This is now well established [1]. Recent studies have shown that 10 risk factors are associated with 90% of the risk of stroke [2]. Inspite of this, it is impossible to predict when a stroke will occur, even in people with a high-risk profile [3]. The patterned occurrence with a morning peak of Ischemic Stroke onset strongly suggest that the disease does not occur randomly [4,5]. Further, it has been hypothesized that vascular events could be precipitated by acute factors, called triggers, which may directly lead to its onset [4,6,7].

Studies conducted on role of triggers, have already demonstrated the role of heavy physical exertion [8], anger, [8] emotional and mental stress [9], sexual activity [10], or acute infection [11,12] on myocardial infarction (MI) occurrence [13]. These factors are speculated to qualitatively alter the stable or quiescent phase of coronary atherosclerosis and initiate a cascade of events that culminates in plaque rupture and thrombosis leading to acute MI [7]. In contrast to this, the role of triggers on the occurrence of Ischemic Stroke is less well established and needs to be researched further [14].

The study was conducted using a case-crossover design. The basic advantage with this study design is that each patient serves as his or her own control, thereby eliminating the problem of confounding by differences in constant subject characteristics of cases and controls [15].

Material and Methods

The study was conducted on patients presenting with stroke to the department of neurology of a tertiary care hospital of Jammu district of Jammu and Kashmir in India. The study was conducted for a period of two months. All patients presented to the department with stroke were considered for inclusion in the study.

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onset of stroke. The interview for this purpose was conducted by a team comprising of neurologist and epidemiologist. Effort was made to elicit information from the patient with regard to potential trigger effects by direct interview. The information was corroborated by conducting an interview with the nearest relative of the patient, who had been with the patient for last two days.

**Questionnaire**

Interviews were conducted 1 to 4 days after stroke onset using a questionnaire especially designed for this purpose. The questionnaire included details on possible exposure to potential triggers and included negative and positive emotions, anger, sudden posture changes as response to a startling event, heavy physical exertion, heavy eating, and sudden temperature changes was assessed for the 2-hour hazard period and for the control periods.

Physical exertion was categorized based on subject’s assessment [18]. Emotional stress was measured using the PANAS scale [19]. The scale had to be culturally and linguistically acceptable to the study population. So we modified PANAS scale by means of a systemic, iterative process. The process was similar to the one used by us in a previous study on a migrant population [20].

Average negative emotion scores were calculated for the nine negative items in the five level PANAS for each patient during the hazard and control periods. The methodology was similar as in study conducted previously on MI [21]. Patients were asked to recall any sudden change in posture during the day preceding stroke onset. For each reported sudden change in posture, the exact time and reason were specified.

Only patients reporting sudden changes in posture in response to a startling event, such as getting up suddenly from bed in response to a triggering event were considered exposed.

**Results**

A total of 61 individuals admitted in the department of neurology for stroke during the three month study period were included in the study. 46% (28) men with mean age 63.8 ± 13.1 and 54% (33) women with mean age 60.9 ± 13.5 were included in the study (Table 1). Out of a total of 61, information on the time of occurrence could be elicited on 54 patients only. In 5 male and 2 female patients, the time of onset stroke was not available. Majority of patients (72%) reported that the time of occurrence of event was before 4 pm (Table 2).

Exposure to seven potential triggers was assessed, as previously described. Forty four patients (73%) reported exposure to at least one potential triggering factor during the 2 hours hazard period before onset of stroke symptoms. Twenty nine patients (66%) reported exposure to at least one of three (Anger, sudden change in posture, physical exertion) potential triggers during the 2-hour hazard period. Ten patients (23%) reported exposure to more than one potential triggers during the 2-hour hazard period. The most common potential trigger during the 2-hour hazard period was reported to be sudden change in posture (11 patients, 25%). This was followed by negative emotion (10 patients, 23%).

**Discussion**

The present study examined a possible association between exposure to potential triggers during a defined hazard period and triggering of the acute onset of stroke. Almost 66% of patients reported exposure to at least one potential trigger. In a previous study, a sharp rise in incidence of AMI and sudden death in Israel was noted during the first days of the Gulf War compared to control periods [22] and increased risk of cardiovascular events was reported during earthquakes [23,24].

Similarly, important sporting events were reported to provide sufficient levels of stress to trigger AMI and stroke [25]. What is known is that brief episodes of mental stress, similar to those encountered in everyday life, may cause transient endothelial dysfunction [26] and induction of coagulation abnormalities by acute stress. A study on triggering of AMI by selected emotions found that feelings of tension, frustration, and sadness could more than double the risk of myocardial ischemia in the subsequent hour. Positive emotions had no significant influence on the risk of myocardial ischemia [27]. It is possible that negative emotions evoke more intense reactions. A significantly elevated relative risk of acute onset of stroke was associated with reported anger. Eighteen percent of the patients reported anger. This percentage is higher than reported in the Stroke Onset Pilot Study, according to which 4% of the patients had an angry outburst during the 24 hours before stroke onset [28].

Reported sudden changes in body posture in response to a startling event immediately before stroke onset are the most important potential triggers according to our findings. Squatting induces rises in blood pressure and was suggested to be a triggering factor for stroke onset [29]. A study on potential precipitating factors of the onset of AMI reported that 21% of the patients were exposed to a sudden body position change in the 30-minute period preceding the cardiac event onset [30]. The most frequent posture changes were from supine to sitting to standing, as in the present study. The proposed triggering mechanism for AMI includes changes in platelet aggregation and fibrinolytic activity [31]. Potential mechanisms for triggering stroke may include in part sympathetic nervous system hyperactivity, hemodynamic effects, and deleterious endothelial effects.

**Limitations**

A potential limitation of such a study design is recall bias. Patients might interpret exposures temporally related to onset of symptoms as potential causes for stroke. In this case, the accuracy of reports for the hazard and control periods may differ. For this reason the whole 24-hour period preceding the stroke onset was treated as a long hazard period.

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**Table 1:** Age and gender wise distribution of cases.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-44</td>
<td>2 (3.3%)</td>
<td>4 (6.6%)</td>
<td>6 (9.8%)</td>
</tr>
<tr>
<td>45-54</td>
<td>8 (6.6%)</td>
<td>9 (14.6%)</td>
<td>17 (21.3%)</td>
</tr>
<tr>
<td>55-64</td>
<td>9 (8.2%)</td>
<td>7 (11.5%)</td>
<td>16 (19.7%)</td>
</tr>
<tr>
<td>65-74</td>
<td>11 (18.0%)</td>
<td>7 (11.5%)</td>
<td>18 (29.3%)</td>
</tr>
<tr>
<td>75-84</td>
<td>8 (6.6%)</td>
<td>8 (13.1%)</td>
<td>16 (26.4%)</td>
</tr>
<tr>
<td>&gt;85</td>
<td>2 (3.3%)</td>
<td>3 (4.9%)</td>
<td>5 (8.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (45.9%)</td>
<td>33 (54.1%)</td>
<td>61 (100.0%)</td>
</tr>
</tbody>
</table>

Minimum age: 36 years, Maximum age: 90 years.

**Table 2:** Distribution of patients according to time of onset of stroke episode.

<table>
<thead>
<tr>
<th>Time of onset of stroke episode</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.00 am–10.00 am</td>
<td>6 (9.8%)</td>
<td>7 (11.5%)</td>
<td>13 (21.3%)</td>
</tr>
<tr>
<td>10.00 am–4.00 pm</td>
<td>13 (21.3%)</td>
<td>11 (18.0%)</td>
<td>24 (39.3%)</td>
</tr>
<tr>
<td>4.00 pm–10.00 pm</td>
<td>3 (4.9%)</td>
<td>9 (14.7%)</td>
<td>12 (19.6%)</td>
</tr>
<tr>
<td>10.00 pm–4.00 am</td>
<td>1 (1.6%)</td>
<td>2 (3.3%)</td>
<td>3 (4.9%)</td>
</tr>
</tbody>
</table>

*In 5 male and 2 female cases the time of onset stroke was not available.*