CLINICAL COURSE AND EPIDEMIOLOGICAL DATA OF TICK-BORNE ENCEPHALITIS IN ELDERLY (OVER 50 YEARS OLD) PATIENTS

ERKINIO ENCEPHALITO EPIDEMIOLOGIJA IR KLINIKINĖ EIGA TARP VYRESNIŲ NEI 50 METŲ AMŽIAUS LIGONIŲ

Angelika Krumina2, Guntis Karelis1, Irina Lucenko3, Ilze Serzante1, Ludmila Viksna2,3, Inara Logina4

1Gailezers Clinical University Hospital
2Riga Stradins University, Infectology and Dermatology Department
3State agency Infectology Center of Latvia
4Riga Stradins University Hospital

ABSTRACT

Key words: tick-borne encephalitis, epidemiology, clinical course, elderly patients.

Objective. To compare frequency clinical symptoms of tick-borne encephalitis and severity of disease outcomes in adult and elderly patients of Latvia.

Material and methods. Retrospective analysis of 234 patients with the serological confirmation of tick-borne encephalitis, who were hospitalized at Gailezers Clinical University Hospital in Riga from 1997 to 2006. Of 234 patients with tick-borne encephalitis, 122 were under 50 years old (adults) and 112 were over 50 years of age (seniors). Frequency of clinical findings as well as demographical characteristics (age, gender, type of employment), and history of tick bite or consumption of unpasteurized milk in two groups were compared. Sequelae of 100 tick-borne encephalitis patients were retrospectively evaluated.

Results and conclusions. The frequency of neurological symptoms of tick-borne encephalitis in acute stage had no significant differences between both age groups. Moderate TBE cases were more frequent among adults (59 %) than in elderly, but severe cases of illness were more often reported in the seniors (31.2 %). Senior patients frequently reported more prolonged health disturbances after tick-borne encephalitis. Tick-borne encephalitis had a serious impact on the quality of life for a longer period of time. More health disturbances requiring assistance of others were revealed in the senior patients group. Incomplete recovery was noted more frequently among the senior patients. No statistically significant difference between general clinical, neurological symptoms and course of disease in both groups of patients was found in our study. Tick-borne encephalitis clinical syndrome course does not correlate with the patient’s age.

SANTRAUKA

Reikšminiai žodžiai: erkinis encefalitas, klinikinė eigą, vyresni nei 50 metų ligoniai.

Darbo tikslas. Palyginti erkinio encefalito klinikinių simptomų dažnio ir pasekmių sunkumo skirstumus suaugusiųjų ir vyresnių amžiaus ligonių grupese Latvijoje.


INTRODUCTION

Tick-borne encephalitis (TBE) is a severe and widespread infection of the central nervous system in Europe [1, 2, 3, 5, 9]. TBE is caused by TBE virus, which is classified as a member within the mammalian group of tick-borne flaviviruses which belong to a family of Flaviviridae. During the past two decades, both new endemic foci and an increase in cases have been reported in many European countries [13, 22]. After the collapse of the former Soviet Union and reduced use of pesticides and vaccine against TBE, the annual incidence increased to more than 10,000 cases worldwide, including more than 3,000 cases in Europe. TBE viruses in Latvia are transmitted by *Ixodes ricinus* and *Ixodes persulcatus* ticks [1, 3, 4, 5, 7, 18].

Until recently TBE was a rather limited problem in some certain endemic regions. However, nowadays one can become infected in any part of Latvia [7, 18, 20]. Latvia has turned into an endemic region with the highest incidence rate in the world [6, 17]. Since 1980 till the beginning of 1990 from 100 to 300 cases were reported annually. More recently, every year the number of cases in Latvia increased until the year of 1998. The highest number of TBE cases (1366 cases) has been reported in 1994. From 1993 to 2006 in total 8395 TBE cases were reported in a country of 2.4 million inhabitants [16, 17]. From 1997 to 2000 TBE morbidity average rate was 26.9 cases per 100,000 inhabitants. The highest morbidity rate was reported in the age group of patients over 40 years old (60.8 cases per 100,000 inhabitants), and the morbidity rate among children was much lower – only 30.6 cases per 100,000 [22]. Between 2002 and 2005, the highest morbidity rate was reported in the age group of 60–69 years old (15.4 cases per 100,000 inhabitants) and the lowest one was for children below 5 years old (1.7 cases per 100,000 inhabitants) [16]. The incidence rate in males was on average 1.3 times higher than among females in all age groups with smaller difference in the age group of 50–59 years. Two thirds of the patients were retired and unemployed, so they visited forests more frequently and spend more time in their private gardens. Most of the TBE cases were reported from June to September, reflecting vocational exposure and berry picking or mushroom gathering period. Percentage of ticks infected with TBE virus was quite high % for cases of human tick bites, and 4.4 % for field collected ticks (6.2 % for nymphs and 3.8 % for adult ticks) [16].

In the population over 40 years of age, the incidence of TBE in Latvia is higher than in younger individuals. With age, especially in the population over 50 years of age, immunity is impaired quantitatively and qualitatively: the protective function of immune system diminishes and thymus function declines [23, 25]. Particularly from the age of 60, there is a significant reduction in antibody and cellular immune response. Age is a factor influencing the responsiveness to vaccines [25]. Serological responsiveness of the elderly to TBE vaccination may be decreased, their immune response is weaker and slower and antibody titres are lower, which leads to administering an additional dose of TBE vaccine in the event of an insufficient response [28].

So, for the age group over 50 years the clinical course of TBE is more severe and more prolonged, they suffer significantly more sequelae, need a longer rehabilitation and have a higher case fatality [2, 6, 8, 25].

Numerous research projects on TBE clinical features in elderly patients over 50 years of age have been carried out in Europe [25]. Eighty percents of patients over 50 years of age develop moderate – severe and severe TBE in comparison with younger patients who experience more frequently mild TBE: meningitis was reported in 70 % of cases among the younger patients. In Germany encephalitis and myelitis were observed more often in patients over 50 years of age as compare with younger patients – 65 % versus 43 % [12].

MATERIALS AND METHODS

We have conducted retrospective analysis of 234 patients with the serological confirmation of TBE, who were hospitalized at Gailezers Clinical University Hospital, Riga, Latvia from 1997 to 2006. Of 234 patients with TBE, 122 were under 50 years old (adults) and 112 were over 50 years of age (seniors). Clinical findings as well as demographical characteristics (age, gender) type of employment, and history of tick bite or consumption of unpasteurized milk in two groups were compared. The average age adult group was 33.96 years and in the senior group – the average age was 61.98 years. The majority of employed patients were under 50 years of age, but the senior group was generally composed of retired and unemployed patients. In both groups about half of patients could recall the history of previous tick bite. Some patients reported consumption of unpasteurized milk or milk products from goat or cows or could recall an initial skin erythema following the previous tick bite. The data were processed by using SPSS 12.0 and EpiInfo Version 6.

RESULTS

The most common general clinical symptoms of the acute TBE stage are presented in Table 2.

Ninety five percent of patients in the adult group and 97.3 % of patients in the senior group reported headaches. Frequency of nausea was a bit different in both age groups – more complaints were reported in the adult group (43.4 %) than in the senior group (42.9 %). Patients in both groups frequently complained of fatigue (25.4 % in the adult group and 32.1 % – in the senior group), of vomiting (13.9 % in the adult group and 25 % – in the senior group).
group), vertigo (20.5 % in the adult group and 23.2 % in the senior group), gastrointestinal tract disturbances (7.4 % in adult group and 11.6 % – in the senior group) as well. Frequency of other general symptoms is shown in Table 2. However, the difference in frequency of general symptoms in both age groups was not significant.

Analyzing the frequency of neurological symptoms of TBE in acute stage, we found some differences between both age groups. In both age groups a similar number of patients with TBE had pareses. Ataxia was slightly more common in the senior patients group (15.2 %), but the difference was not statistically significant. Altered consciousness was more frequent in the elderly patients group (18.8 %) than in younger patient group (16.4 %). In contrast, meningeal symptoms were more often found in the adult people group (88.5 %) than in older patient group (87.5 %). Adults had slightly more frequently peripheral paresis (4.1 % versus 5.4 %) and aphasia (1.6 % versus 1.8 %) than the seniors (Table 3.).

Most of the observed patients in both age groups had a “Meningeal form” of TBE with aseptic meningitis (Table 4.)

Sequelae of 100 TBE patients were retrospectively evaluated. Senior patients frequently reported more prolonged health disturbances after TBE. TBE had a serious impact on the quality of life for a longer period of time. More health disturbances requiring assistance of others were revealed in the senior patients group. Incomplete recovery was noted more frequently among the senior patients.

The most common reported sequelae for both age groups were headache (63.9 % in the adult group and 54.7 % in the senior group) and vertigo (41.7 % in the adult group and 39.1 % in the senior group). These data are shown in the Table 5.

We compared severity of the sequelae after TBE in both patients groups. No statistically significant differences in the frequency of sequelae were reported in both patients groups (Table 6).
The duration of hospital stay was similar in both age groups. Adult patients after acute TBE in 46 % of cases considered themselves completely recovered, whereas only 33 % of elderly patients had no residual disturbances after TBE. Analysis of TBE clinical course showed that moderate TBE cases were more frequently seen among adults (59 %), but severe cases of illness were more often reported in the seniors (31.2 %) as shown in Table 7.

Results of cerebrospinal fluid (CSF) examination revealed higher lymphocytic pleocytosis in adults (343.43 cells) than in seniors (242.44 cells), but total protein and glucose levels were similar in both age groups (Table 8.). It is possible that above mentioned differences are related to the impaired immune system of elderly patients over 50 years of age.

### DISCUSSION
In this study we have evaluated epidemiological data and clinical characteristics of tick-borne encephalitis comparing two age groups. Several investigators from different countries through direct comparison of the clinical course and outcome of TBE revealed several distinctions between adult and elderly patients and indicated clinical TBE course syndrome peculiarities in elderly patients [2, 10, 11, 12, 21, 24, 26, 27].

TBE is a severe infection of central nervous system, which has essential importance in Latvia. Although TBE has been diagnosed and reported for many years, the more detailed evaluation of its clinical peculiarity and sequelae has been started within the last decade. The TBE clinical syndrome peculiarities of different patient age groups were
analyzed in numerous countries by different investigators. Considering this experience we retrospectively evaluated TBE clinical syndrome peculiarities of adult patients (aged 50 or under) and elderly patients over 50 years of age.

Interestingly, our study did not reveal any significant differences in the TBE clinical course while comparing different parameters in adult and senior age groups in Latvia. Epidemiological data were similar, but it should be noted that elderly patients had been consuming raw or goat milk more often. In Lithuania 67.7 % of patients could recall the previous tick bite, and in Slovenia – 83.3 % [2, 24, 26]. Interestingly, 25 % of patients in Slovenia received initial antibacterial therapy, because acute respiratory infection was suspected at the early “flu-like” or “febrile” stage of disease [26].

In respect of clinical picture of TBE elderly patients had slightly more frequent symptoms of nausea, fatigue and gastrointestinal tract disturbances. Frequency of other symptoms was similar. Patients over 50 years of age with neurological syndrome had a slightly frequent ataxia and altered consciousness.

Analysis of sequelae severity after TBE did not show more severe and more prolonged health disturbances in patients over 50 years of age group as compare with the adults. The obtained data did not correspond with the data from the similar studies in other countries [2, 12, 14, 24].

We have to admit that the duration of treatment and hospital stay was quite identical in both patient age groups, which was quite unexpected. In other similar studies elderly patients needed longer duration of hospital treatment.

Neurological syndrome manifested as ataxia in 14.8 % of adult group and in 15.2 % of senior patients group, as central pareses (in 9.8 % and in 9.8 %), as peripheral pareses (in 4.1 % and in 5.4 %), as cranial nerve palsy (in 9 % and in 8.9 %), as altered consciousness (in 16.4 % and in 18.8 %), as meningeal symptoms (in 88.5 % and 87.5 %) and as coma (in 0.8 % and in 0.9 %).

Total of 133 patients with TBE were included in a pros-

<table>
<thead>
<tr>
<th>Table 6. Severity of sequelae after TBE in both patients groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Mild sequelae</td>
</tr>
<tr>
<td>Moderate sequelae</td>
</tr>
<tr>
<td>Severe sequelae</td>
</tr>
<tr>
<td>Age in years (range)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 7. Severity of TBE clinical course and duration of hospital stay in both age groups at acute TBE stage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Complete recovery after TBE acute stage</td>
</tr>
<tr>
<td>Mild TBE course</td>
</tr>
<tr>
<td>Moderate TBE course</td>
</tr>
<tr>
<td>Severe TBE course</td>
</tr>
<tr>
<td>Duration of hospital stay in total (days):</td>
</tr>
<tr>
<td>- meningitis (days)</td>
</tr>
<tr>
<td>-meningoencephalitis, meningoencephalomyelitis (days)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 8. CSF findings in both age groups patients with TBE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Cell count (cells/mm3)</td>
</tr>
<tr>
<td>Total protein level (g/l)</td>
</tr>
<tr>
<td>Glucose concentration (mmol/l)</td>
</tr>
<tr>
<td>Mononuclear cells (%)</td>
</tr>
<tr>
<td>Polymorphonuclear cells (%)</td>
</tr>
</tbody>
</table>
perspective follow-up study in 1998 in the Clinic of Infectious Diseases of Kaunas University of Medicine [2, 24]. Most of the patients (80 %), older than 45 years of age had a moderate or severe TBE in contrast to younger ones, who experienced mild (meningeal) TBE in nearly 70 % of cases. Permanent central nervous system dysfunction as sequelae after 1 year was found in 30.8 % of patients; in 8.5 % of all TBE cases, severe disabilities required adjustment of daily activities. The risk of incomplete recovery was significantly higher among patients with the TBE encephalitis [2,24]. In Kaunas study by Mickiene and colleagues ataxia was reported in 26.3 % of cases, mental disturbances – in 18.8 %, hemipareses – 5.3 %, cranial nerve palsy – in 5.3 %, peripheral pareses - in 3.8 %, and tremor - in 17 % of cases during acute illness period. As compared with our data, Lithuanian study revealed less central pareses and cranial nerve palsy, but more cases of ataxia [2, 24]. Having evaluated sequelae after TBE in Latvia in comparison with the Lithuanian data, we can note that in Latvia sequelae are more long lasting, though quite the same like in Lithuania, patients over 50 years of age experience more severe and distinct sequelae than younger ones under 50 years of age [2, 24]. In a prospective study performed in Slovenia where 60 TBE patients were observed, meningeal symptoms were found in 85 % of cases, tremor – in 50 %, pareses – in 3.3 % of cases [26]. In Latvia, the same percentage of meningeal symptoms in neurological stage of disease was observed, though paresis was observed more often (8.9 %–9.8 %).

In Germany, comparison of individual manifestations of TBE in individual age groups showed a constant increase of more severe course of the disease in later life. The direct comparison of the two most severe (encephalitis and spinal cord inflammation) progressive forms in both age groups showed a significantly higher portion 65 % opposed to 43 % of people over 50 years of age. TBE clinical findings were significantly more frequently observed in patients over 50 years of age. Elderly patients were observed to have such symptoms as: impaired consciousness, delirious status, paralysis of arms/or legs, facial palsy, hearing disorders, dysphasia, speech disorders, disorders of respiratory with the necessity for assisted artificial respiration. Patients over 50 years of age were significantly more frequently attended to at intensive care units, hospitalization was longer, they needed rehabilitation measures more frequently, persisting neurological dysfunctions and discomforts occurred distinctly more often in patients over 50 years of age. The mortality rate due to TBE was 15 times higher in patients over than under 50 years of age [12, 14]. We should note here, that we cannot directly compare data of other studies, because every research study used different methods: in Slovenia children and grown groups were compared, in Germany children (under 14) and adults (over 14), in Lithuania patients under 45 and over 45. In Sweden 10.6 % had peripheral pareses, and that number is higher than in Latvia (in Latvia accordingly - 5 %) [15, 19].

CONCLUSIONS

No statistically significant difference among general clinical, neurological symptoms and course of disease in both groups of patients was found in our study. TBE clinical syndrome course does not correlate with the patient’s age.

LITERATURE

17. www.tick-info.com
19. Gunther G, Haglund M, Lindquist L, Forsgren M, Skoldenberg B. Tick-borne encephalitis in Sweden in relation to aseptic me-