Seizure: European Journal of Epilepsy 110 (2023) 153–156

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Editorial

Helping patients with epilepsy during a full-scale war in the country: Some aspects of Ukrainian experience

On February 24, 2022, the troops of the Russian Federation launched a full-scale invasion of the territory of Ukraine. The health care system has suffered the damage and destruction of medical care facilities, medical supply systems, and logistics.

Problems in the medical care system have arisen throughout the territory, but to a greater extent, in territories where hostilities were or are continuing, in areas which were occupied, or occupied and destroyed during the occupation. During a full-scale war, the health care system goes onto a "war footing" with all the consequences this entails.

As of early February 2023, the WHO Surveillance System for Attacks on Health Care has verified over 760 attacks in Ukraine, with close to 700 attacks impacting health facilities directly. The situation is particularly dire in areas close to the front line, or areas recently retaken by the Government of Ukraine. In these areas most health facilities are not functioning, and many of those who stayed behind – the elderly, persons with low mobility, those with physical disabilities – have complex needs that the health system is struggling to meet under the current circumstances [1].

1. Migration of the population of Ukraine as a result of the war

In 2021, the population of Ukraine was 41 million people. Today an estimated 17.6 million people in Ukraine require urgent humanitarian support, including more than 5 million people internally displaced by the war. As of February 2023, over 8 million refugees from Ukraine were recorded across Europe, of which 4.8 million were registered for Temporary Protection or similar national protection schemes [2]. By May 2023 the UNHCR recorded 8,207,977 refugees from Ukraine in different European countries and 5,093,606 as registered for Temporary Protection or similar schemes [3].

In addition to these refugees, over 2 million Ukrainians crossed the border with the Russian Federation and the Republic of Belarus (2,875,215 according to https://data.unhcr.org/en/situations/ukraine as of May 9, 2023 and their subsequent destiny is unknown). Some will have travelled through these countries to Europe, some will have remained in the Russian Federation and Belarus, some returned to Ukraine through European countries, but it is impossible to establish the exact number of people in each of these flows (Tables 1 and 2).

In order to understand the level of the migration of the population of Ukraine as a result of this terrible war, which was unleashed by the Russian Federation, it is necessary to understand that, in addition to the huge number of Ukrainians who escaped and are still escaping from the war to other countries, there is a large number of internally displaced persons who are escaping to safer regions of Ukraine from the horrors the war has inflicted on the areas they lived in before the war started. A significant number of internally displaced persons (IDPs) have significant social, medical and material problems. The health care system, even in regions that are geographically distant from the front line objectively cannot fully cope with such a burden. Data for different regions of Ukraine are shown in Table 3.

Unfortunately, statistical data on the number of people with particular diseases who received temporary shelter in other countries or who are internally displaced are currently not available. Taking into account the average pre-war statistical indicators, as well as the fact that people with disabilities, women with children, and men who were unfit for military service were particularly likely to have left Ukraine (and that these categories include people with epilepsy), the number of people with epilepsy among of displaced persons would be expected to be somewhat higher than indicated by the prevalence of epilepsy in Ukraine's general population before the war. According to our calculations (and based on ULAE data), approximately 51,000 to 83,000 adults and children with epilepsy from Ukraine are currently living in other countries, and at least 50,000 people with epilepsy will have been internally displaced within Ukraine. This does not take into account incomplete statistical data and the increase in morbidity associated with war-related factors.

2. Health care problems resulting from the war

The full-scale war in Ukraine has caused a number of problems in the system of providing medical care, both for patients and doctors.

Our patients faced the greatest difficulties at the beginning of the war. Destruction, closure, termination or suspension of the work of medical institutions. Collapse of the pharmacy network. Danger associated with shelling. Stoppage or reduced operation of urban and suburban public transport. Danger and the associated need to move to safe regions. Loss of medical documentation and test results when temporarily moving to safe places. Loss of contact with the usual medical care provider and the impossibility of being able quickly to access alternative medical care. Patients not understanding the next steps regarding treatment and follow-up. For chronic patients - impossibility of adhering to an acceptable treatment schedule. Additional complexity associated with psychiatric comorbidity and polymorbidity as a result of insufficient treatment and circumstances.

The main problems of our patients who went abroad were the similar but not the same (about 5 million Ukrainians left the country within the first month of the war alone). There were additional difficulties - not understanding their personal and legal status when entering another

https://doi.org/10.1016/j.seizure.2023.06.015
Received 12 June 2023; Accepted 18 June 2023
Available online 18 June 2023

Table 1
Countries featured in the refugee response plan.

Country	Data Date	Refugees from Ukraine for Temporary Protection or similar national protection schemes	Refugees from Ukraine recorded in country	Border crossings from Ukraine*	Border crossings from Ukraine**
Bulgaria	05.09.2023	157 943	49 826	Not applicable	Not applicable
Czech Republic	30.04.2023	515 836	516 100	Not applicable	Not applicable
Estonia	10.04.2023	4 739	69 616	Data not available	Data not available
Hungary	08.05.2023	35 030	35 030	2 636 985	Data not available
Latvia	11.04.2023	47 080	32 380	Data not available	Data not available
Lithuania	11.04.2023	76 540	76 540	Not applicable	Not applicable
Poland	09.05.2023	1 593 860	1 593 860	11 467 172	9 227 726
Republic of Moldova	30.04.2023	Not applicable	107 645	814 622	458 524
Romania	07.05.2023	130 387	97 085	2 344 322	1 937 788
Slovakia	07.05.2023	114 628	114 628	1 364 322	1 084 518
Common		**2 716 043**	**2 692 710**	**18 627 702**	**12 708 556**

Table 2
Other European countries.

Country	Data Date	Refugees from Ukraine for Temporary Protection or similar national protection schemes	Refugees from Ukraine recorded in country
Albania	23.03.2023	28	2 758
Armenia	08.05.2023	Not applicable	575
Austria	09.05.2023	96 766	96 766
Azerbaijan	01.05.2023	Not applicable	4 764
Belgium	02.05.2023	70 686	71 446
Bosnia and Herzegovina	07.05.2023	Not applicable	171
Croatia	07.04.2023	21 640	21 640
Cyprus	12.03.2023	21 642	16 281
Denmark	10.04.2023	39 479	41 560
Finland	10.04.2023	53 318	47 067
France	31.10.2023	118 994	118 994
Georgia	06.04.2023	Not applicable	24 182
Germany	19.04.2023	934 420	1 061 623
Greece	31.03.2023	22 704	22 704
Iceland	28.02.2023	2 674	2 674
Ireland	07.05.2023	81 868	82 834
Italy	21.04.2023	175 107	175 107
Liechtenstein	18.01.2023	536	410
Luxembourg	25.10.2023	6 756	6 756
Malta	19.02.2023	1 744	1 744
Montenegro	08.05.2023	8 298	32 647
Netherlands	10.02.2023	89 730	89 730
North Macedonia	08.05.2023	Not applicable	6 768
Norway	11.04.2023	45 238	45 238
Portugal	26.02.2023	58 242	58 242
Serbia and Kosovo: S/RES/1244(1999)	30.04.2023	1 297	2 880
Slovenia	07.05.2023	9 149	9 149
Spain	08.05.2023	175 962	175 962
Sweden	05.04.2023	53 957	53 957
Switzerland	05.05.2023	83 428	65 601
Turkey	26.01.2023	Not applicable	95 074
United Kingdom	01.05.2023	203 700	203 700
Common		**2 377 563**	**2 640 052**

country; poor knowledge or lack of knowledge of the language of the host country; lack of understanding of the health care system in another country; lack of information about specialized medical care centers.

Medical doctors faced the greatest difficulties at the beginning of the war in and around the war zones. Destruction, closure, termination or suspension of the work of medical facilities. Destruction, closure, termination or suspension of diagnostic centers. Destruction, closure, termination or suspension of laboratory centers. Collapse of the pharmacy network. The dangers associated with shelling, both for doctors and patients. Limited or discontinued operation of urban and suburban public transport. Danger and the associated need to move to safe

Table 3
Information on the number of internally displaced persons registered as internally displaced persons from 24.02.2022 to 15.05.2023 (according to the Ministry of Social Policy of Ukraine in response to the request of the Ukrainian League against Epilepsy).

Region	Number of people
Vinnytsia region	167,282
Volyn region	53,071
Dnipropetrovsk region	460,622
Donetsk region	534,178
Zhytomyr Region	97,561
Transcarpathian region	141,489
Zaporizhzhia region	213,475
Ivano-Frankivsk region.	131,738
Kyiv City	385,038
Kyiv region	331,846
Kirovohrad Region	91,510
Luhansk region	275,792
Lviv region.	236,206
Mykolayiv region	121,770
Odesa region	220,568
Poltava region	210,559
Rivne region	53,307
Sumy region	82,780
Ternopil Region	78,229
Kharkiv region	487,949
Kherson region	35,645
Khmelnytskyi region	139,083
Cherkasy region	152,850
Chernivtsi region	85,669
Chernihiv region	71 104
Crimea	23
Sevastopol	42
Common	**4,859,386**

regions. Impossibility of designing medication regimes acceptable for patients with a chronic disease.

Medical doctors working in areas remote from hostilities ("in the rear") also faced the greatest difficulties at the beginning of the war . A sharp increase in the number of patients. As a result, a significant increase in the burden on the health care system. Reduction of the range and quantity of medicines in the pharmacy network. Lack of medical documentation and test results of forcibly displaced persons. The impossibility of providing acceptable treatments for chronically ill patients and, as a result, a large number of patients with significant deteriorations of their condition. Impossibility of quick follow-up of patients if necessary. The need to adjust treatment regimes in the context of limited and unstable medical supplies. Addition of psychiatric comorbidity and polymorbidity to the clinical picture of the disease, as a result of insufficient treatment and challenging circumstances.

3. War-related problems with the treatment of patients with epilepsy

Due to the above-mentioned problems of providing medical care to all patients, which fully affected the treatment of patients with epilepsy, the Ukrainian League Against Epilepsy (ULAE) had to do what it could to support patients in these difficult times. All events planned by the organization for the spring 2022 were canceled indefinitely. We appealed for humanitarian aid to all possible foreign and domestic authorities. Articles were published in well-known journals - Lancet [4] and Epigraph [5], and we have continued to pursue these activities. Many expressed a desire to help, but neither we nor our partners had the logistic experience of how to do it. We understood that, first of all, we needed antiepileptic drugs and the means of delivering them to our patients. A public organization like the ULEA cannot replace the system of providing medical care either in peacetime or in wartime, because it has much fewer opportunities. However, we also understood that epilepsy is not and cannot be a priority of state health care system in wartime.

As for providing patients with antiepileptic drugs, we contacted all organizations, foundations, individuals who could help with this. Many responded. While the search for possible donors continued, it was necessary to somehow establish possible distribution channels in Ukraine. As early as the beginning of March 2022, a main hub had been created in Lviv, with additional hubs in Kyiv, and near Kharkiv (as it was impossible to set up the hub in Kharkiv itself, it was established in the town Valky in the Kharkiv region). Also, a network of contacts was created of colleagues from other regions who were working in this field, and a telegram channel was created in which colleagues could report the need for medicines. In addition, Google forms were created for patients or their relatives seeking particular drugs for the treatment of epilepsy. These forms could also be completed by doctors who were trying to provide treatment for such patients.

When it was clear that humanitarian aid with drugs for the treatment of epilepsy patients is possible, international organizations and foundations raised questions about which and how many drugs for the treatment of epilepsy were needed for that period (March 2022) in Ukraine as a whole, about how many patients with epilepsy there were in the country at this time, the number of different medications taken by adult patients and children, and the need for emergency medications and the relative frequency of use of each medicine

These needs were discussed at a meeting of the ILAE Emergency Response (Ukraine) Task Force, and we were decided that the Ukrainian League would conduct a rapid survey of members who could be contacted quickly. The telephone survey of pediatric and adult epileptologists was conducted over two days, aiming to achieve maximum possible coverage of different regions of Ukraine. In this survey, epileptologists estimated the percentage of their patients regularly taking a particular ASM or the percentage using a particular drug for emergency care. Although this was only a quick survey, its results were very useful for determining the amount of humanitarian aid and the ratio of different ASMs needed to enable the ULAE to secure assistance for patients with epilepsy in Ukraine during the following months of war. Phenobarbital was not included in the list of requested aid due to the impossibility of importing large quantities of this medication into Ukraine. ASMs that comprised less than 1% of total use were not included either. The results of this survey are summarised in Tables 4–6.

This survey provided only preliminary and approximate data on the spectrum of ASM prescriptions in Ukraine, but comparing this analysis with the population of Ukraine and the average prevalence of epilepsy in Europe made it possible quickly to assess the need for ASM humanitarian help for Ukraine during this war while taking into account the inevitable migration to escape the hostilities and destruction within the country and out of the country.

We are still using the results of this survey now. The findings of this survey were also presented at the 14th European Epilepsy Congress [6].

4. International help with the treatment of epilepsy during the war in Ukraine

It is impossible to list all those who helped Ukrainian patients with epilepsy, but two organizations and one individual deserve to be named: the center “Neurosphere” and the “Emergen” foundation and the general manager of these organizations - Piotrt Zwolinski. Thanks to the work of his team, the logistics of purchasing ASMs and their delivery to Ukraine to the Lviv hub were established very quickly.

At the very beginning of the war, the International League Against Epilepsy and its president, Helen Cross, created an ILAE Emergency Response (Ukraine) Task Force. Thanks to the work of this group, close contact was established between the ILAE and the Ukrainian League Against Epilepsy. In addition to the humanitarian aid with ASM for Ukrainian patients, information about centres providing medical care to patients with epilepsy in countries to which patients from Ukraine were forced to go in order to escape the war was collected. Brief recommendations were developed for patients with epileptic seizures when changing their place of residence and when first contacting a new doctor abroad. This information, together with detailed instructions for patients about information which would be useful to doctors abroad, was very helpful for confused patients and their relatives.

Also, a group of ILAE experts very quickly developed «Treatment strategies for people with epilepsy during times of shortage of antiseizure medications» [7]. This document was quickly translated into Ukrainian. This strategy was very useful in the early months of the war, when drug shortages were most critical.

The documents developed with the support of the ILAE were distributed to doctors engaged in the treatment of epilepsy through widely used social media and communication platforms (Telegram, WhatsApp, Viber), and with the help of e-mail, and the information was promptly posted on the website of the ULAE.

The aspects of this consensus of leading ILAE specialists most relevant for work in the Kharkiv Regional Epilepsy Department are presented below.

The scheme of transition from oxcarbazepine to carbamazepine and from carbamazepine to oxcarbazepine is relevant, but well-known in Ukraine. Eslicarbazepine acetate/oxcarbazepine/carbamazepine, clobazam/clonazepam, brivaracetam/levetiracetam, primidone/phenobarbital exchange ratios were relevant for patients receiving humanitarian aid with drugs not registered in Ukraine. The general

Table 4
Antiseizure medications needed for adults with epilepsy.

ASM	Form	Percent using (%)
Carbamazepine	Tablets	30%
Valproate	Tablets	20%
Lamotrigine	Tablets	15%
Levetiracetam	Tablets	30%
Topiramate	Tablets	5%
Oxcarbazepine	Tablets	5%

Table 5
Antiseizure medications needed for pediatric patients with epilepsy.

ASM	Form	Percent using (%)
Carbamazepine	Tablets	15%
Valproate	Tablets, Syrup, Micropakine	35%
Lamotrigine	Tablets, Soluble forms	13%
Levetiracetam	Tablets, Syrup	20%
Topiramate	Tablets	7%
Oxcarbazepine	Tablets	2%
Vigabatrin	Tablets	3%
Clobazam	Tablets	2%
Clonazepam	Tablets	3%

Table 6
Drugs for emergency care common for adult and pediatric epilepsy patients.

ASM	Form	Percent using (%)
Benzodiazepines	Injectable, nasal, rectal	70%
Valproate	injectable	25%
Phenytoin	injectable	2%
Levetiracetam	injectable	3%

principles of ASM replacement in the absence of one or another drug generally correlate with epilepsy treatment protocols that are relevant in Ukraine [8]. The section "Changing drugs to generics" was the most used. The rectal introduction of ASMs in emergency situations using medication formulations originally intended for other routes of administration was not used. When emergency footing of epilepsy services associated with the continuing war has been resolved, it will be necessary to evaluate the effectiveness of any therapy that was prescribed and to develop an optimal longer-term treatment strategy. This will need to involve a critical appraisal of the effectiveness of the prescribed therapy and the possibility or necessity of its continuation. If the alternative therapy was effective and well tolerated, it may be continued if this is feasible. If the replacement treatment has proven less effective than the therapy that was in place before the national emergency, it would be best to return to the previous therapy, but patients will need to understanding that the previously used therapy may prove ineffective or less effective than it previously was.

Many non-governmental organizations and individuals provided medical assistance to Ukrainian patients with epilepsy. Special mention should be made of the “Brother’s Brother” foundation and the non-governmental organizations “Razom for Ukraine”. These two foundations were the most active in helping patients with epilepsy in Ukraine and doctors who treat such patients.

From the first days of the war, the ULAE did not only start to engage in active communication with foreign foundations and public organizations in their efforts to provide patients with medicines. Since the first days of the war the ULAE also created two groups offering online consultations with epileptologists - specialists in the pediatric and specialists in the adult treatment of epilepsy. The schedule of consultations has been posted on the website of the ULAE and a single call-center for all of Ukraine has been introduced for our patients (Vinnytsia “Neuromed"). It should be noted that this center has continued to operate after the death of some of its employees. In this difficult situation, we are forced to communicate with patients by phone, messenger apps, e-mail, etc. At the beginning of the war, such counseling was forced upon us and absolutely necessary for our patients. Unfortunately, an unexpected problem arose with the online counseling the ULAE intended to provide - counseling by epileptologists was primarily aimed at colleagues who were forced to provide assistance to patients with epilepsy, but it was almost invariably patients themselves who called.

Despite some improvement in the situation, thanks to the good work of the Armed Forces of Ukraine, patients with epilepsy in Ukraine continue to need humanitarian aid with antiepileptic drugs, and aid is continuing to arrive. This is very important to ensure continuity of care for such patients. This help will be relevant throughout the war period and will definitely be required in the post-war period as well.

5. Lessons for the future

Unfortunately, we have experienced situations that one would never wish on anyone, but these are experiences nonetheless and they needs to be analyzed. We emphasize again that a public organization cannot take over the functions of the health care system, but it can do something useful for the cohort of patients with whose care the public organization is involved. It is necessary to clearly understand that helping patients in a crisis situation requires a systematic approach and a "cold mind". It will be necessary to solve problems one did not even have any idea of before.

Thus, the realities of the modern world, the constant threat from aggressor countries even in the continent of Europe, the experience of Ukraine during a full-scale war prove the need to develop guidelines for the treatment and monitoring of epilepsy patients during hostilities and global disasters. We suggest creating working groups to develop guidelines for low-income countries and for countries with high economic development, possibly separately for individual groups of countries by geographic region. The war in Ukraine unfortunately showed that health care systems, even in developed countries, are not ready to overcome global disasters.

Declaration of Competing Interest

No Conflict of Interest for both authors.

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