

*Opšti pregledi/
General reviews*

THE HUNGARIAN EXPERIENCE:
THIRTY-FIVE YEARS OF PROGRESS IN THE
FIELD OF PEDIATRIC ONCOLOGY

MAĐARSKO ISKUSTVO:
TRIDESET I PET GODINA NAPRETKA NA
POLJU PEDIJATRISKE ONKOLOGIJE

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jskih pacijenata sa karcinomom

Abstract

To provide up to date treatments for children diagnosed with malignant diseases is a huge challenge for a small country with limited budget for health care. The incidence of pediatric cancer in Hungary is almost the same as that observed in other countries of European Union, estimated to be 13.9/100,000 in 2003. The approximately 250 children diagnosed with cancer each year were distributed among several hospitals in Hungary. This means that not even the largest Hungarian hospital could cater to enough patients to provide professional medical instruments, special medical doctors and nurses for the cancer children, and moreover to mount randomized clinical trials.

The history of pediatric oncology in Hungary began with the foundation of the Hungarian Pediatric Oncology Network in 1971. The activities of our group consisted of: 1) registration and follow-up of the patients, 2) treatment by the same protocols nationwide, 3) quality control and 4) postgraduate teaching sessions. It proved to be an important step forward, when the Network received a \$2.33 million grant from the U.S. Agency for International Development (USAID) between 1991-1996. In 2004, an Internet-Based Pediatric Cancer Registration and Communication System for the Hungarian Pediatric Oncology Network was established.

In Hungary, health insurance (the compulsory health insurance based on the principle of solidarity) bears the expenses of cytostatic drugs only for children registered and treated according to guidelines of the Hungarian Pediatric Oncology Network. This centralization of the patients' treatments and regular (annual) audits make oncology centers' treatment more economical.

Assurance of high quality and economic treatments has been possible by the centralization of all pediatric cancer patients into pediatric oncology centers, the well organized and reliable pediatric tumor registry and strong international scientific connection of the Hungarian pediatric oncologists.

Background

The incidence of pediatric cancer in Hungary has been estimated to be the same as that evaluated for other countries of European Union, being 13.9/100,000 in 2003. The average annual percentage changes (AAPC) exhibited an increase of 0.3% for leukemias (between 1986-2004) compared with 1.8% for tumors affecting the central nervous

system (CNS).(1) The total population of Hungary was estimated as 10,352,000 in 1971, with the number of children under 15 years of age being 2,126,455. The approximately 250 children diagnosed with cancer each year were distributed among several hospitals in Hungary highlighting the fact that not even the largest Hungarian hospital could cater to enough patients to provide professional medical instruments, special medical doctors and nurses for the cancer

children, and moreover to mount randomized clinical trials. This became evident in 1971, when basic data of the treatment and survival of children with leukemia in Hungary was collected from every hospital in the country.⁽²⁾

History of Pediatric Oncology in Hungary

The history of pediatric oncology in Hungary owes its initiation to the foundation of the Hungarian Pediatric Oncology Network in 1971.⁽³⁾ Voluntary participations were stimulated by the availability of cytostatic drugs free of charge for the hospitals included in to the Network. The center was located in the National Institute of Child Health (Budapest), with nine subcenters in Budapest and all over the country. The low number of MD-s, cancer nurses and especially of technicians, as well as administrators exerted a considerable physical and psychological burden on the Hungarian cancer teams, thereby resulting in the incapability to achieve significant results despite extreme effort.⁽³⁾

The activities of our group were based on: 1) registration and follow-up of the patients, 2) treatment by the same protocols nationwide, 3) quality control and 4) postgraduate teaching sessions.

Registration and Follow-up of the Patients

All pediatric cancer patients in Hungary are now registered and followed in the Hungarian Pediatric Cancer Registry.⁽²⁾ The expenses of the cytostatic drugs are borne by the Health Insurance Fund and refunded to the hospitals only for those patients who are registered, which promotes the compliance with registration procedures. The registry contains patient identification information, date of diagnosis, histological findings (and in solid tumors, stage and primary site of the tumor), treatment and outcome of the oncology treatment (relapses, survival rates).⁽²⁾

Fortunately enough, during 1991-1996 the Network took an important step forward on receiving a \$2.33 million grant from the U.S. Agency for International Development (USAID). The Pediatric Oncology Outreach to Hungary (POOH) project (Winnie the Pooh was the program's mascot) was a "Partnership in Healthcare" sponsored by the USAID, and the support was shared among the University of Kansas Medical Center (KUMC), Kansas City, Kansas; the Second Department of Pediatrics of the Semmelweis University Medical School (SDP), Budapest, Hungary; and the Pediatric Ward of National Institute of Neurosurgery (NINS), Budapest, Hungary.⁽⁴⁾ Funding for the POOH project was awarded by USAID in September 1991. The grant provided an ambulance to transport children for diagnostic tests, besides laboratory equipment and an operating microscope. Further on, USAID organized exchange training programs for pediatric oncologists and nurses, and increased the number of oncologists and nurses with new employments in the Second Department of Pediatric at Semmelweis University. In 1992, programming was completed for an institution-based pediatric tumor registry.⁽⁴⁾

In 2004, an Internet-Based Pediatric Cancer Registration and Communication System for the Hungarian Pediatric Oncology Network was established.⁽⁵⁾ Cancer registration developed in Europe over the last 50 years and in the last decade, intensive joint activities between the European Cancer Registries, in response to the need of pan-European

harmonization of registration practices, have taken place.^(6,7) The goals intending to develop a globally unique open source information system consisted of the following: 1) to raise the quality of the registration system to the European level by developing an Internet-based registration and communication system, modernizing the database, establishing automatic statistical analyses and adding an Internet website; and 2) to support clinical epidemiological studies that can be conducted with international collaborators on detailed analyses of the characteristics of patients and their diseases, evaluation of new diagnostic and therapeutic methods and long-term quality of life and side effects. The benefits of the development of the Internet-based registration and communication system were as follows: a) introduction of an Internet-based case reporting system, b) modernization of the registry database according to international recommendations, c) automatic statistical summaries, encrypted mail systems and document repository, d) application of data security and privacy standards and e) establishment of a public website (<http://www.gyerekdaganat.hu>) and compilation of educational materials. The overall objective of this scientific project was to contribute to the improvement of cancer management and cancer care for the benefit of the public in general and of cancer patients in particular.⁽⁵⁾ In 2003, the Hungarian Pediatric Cancer Registry obtained an international audit from the European Network of Cancer Registries (ENCR).

Diagnosis and Therapy

By 2010, it is estimated that 1 of 250 adults between 18 and 45 years will contribute to be a survivor of pediatric malignancy.⁽⁸⁻¹⁰⁾ In spite of the advanced progress made in the treatment of pediatric cancer in the United States (US) and European Union (EU), it is still the second leading cause of death in those 17 years old or younger. The American Cancer Society (ACS; <http://www.cancer.org>) estimated 1,585 tragic, premature deaths in 2005.

In Hungary, as in most small countries, no institution provides provision for all the complex and expensive diagnostic and therapeutic modalities needed. However, this problem could be solved by a well-organized collaboration with other institutions,⁽²⁾ significantly reducing the time-frame between the first clinical sign and the diagnosis. The Hungarian Pediatric Oncology Network was organized taking into consideration the guidelines for "Pediatric Cancer Centers" published by the American Academy of Pediatrics (AAP) in 1986, 1997 and 2004 with the help of USAID.^(2, 11-14) The following personnel, facilities and capabilities have major benefits of the quality treatments: A.) Personnel: 24 hrs immediate access with primary care physician and/or pediatric oncologist; B.) Facilities: an immediate (within 2 hrs) access to a fully staffed, pediatric oncology and/or intensive care unit; C.) Capabilities: blood bank capable of providing a full range of products (including irradiated, cytomegalovirus-negative, and leucodepleted blood components) and access to stem cell transplantation services.

Therapeutic results are obtained mostly by following international protocols (e.g. EURO-E.W.I.N.G. 99 for patients diagnosed with Ewing sc.), or officially joining them (e.g. International Berlin – Frankfurt – Münster (BFM) Study Group for leukemias). Choosing the appropriate

chemotherapy protocols is based on a democratic and collective discussion and decision between the leaders of the Hungarian Pediatric Oncology Network. The outcomes of the oncological treatments are comparable to the international results. The overall 5-year estimated survival was 78.5% for patients diagnosed with acute lymphoblastic leukemia (ALL) and 52.1% for patients diagnosed with medulloblastoma/PNET in 2004.^(15, 16)

Bone marrow transplantations (both allogenic and autologous) play a major role in the outcome of some pediatric oncology treatments. Hungarian Bone Marrow Transplantation (BMT) Program centralized all of the pediatric allogenic and autologous BMTs into two centers of the Hungarian Pediatric Oncology Network: Budapest: St. László Hospital; Miskolc: Borsod-Abaúj-Zemplén County Teaching Hospital.⁽¹⁷⁾ According to the Hungarian healthcare policy of Health Insurance Fund and the Internet-Based Communication System there is no waiting list for pediatric allogenic and autologous BMTs in Hungary. The two pediatric Hungarian BMT centers are part of the European organization (European Group for Blood and Marrow Transplantation).⁽¹⁸⁾

Quality Assurance

Childhood cancer is a relatively rare disorder, with children's survival rates being 20 to 40 percent better in case their cancer care is coordinated by pediatric oncologists and delivered at comprehensive, multidisciplinary cancer centers that follow established protocols (step-by-step guidelines for treatment).^(19, 20) In addition, these centers participate in specially designed and monitored research studies, which help to develop more effective treatments and address issues of long-term childhood cancer survival.^(21, 23)

Majority of the centers of the Hungarian Pediatric Oncology Networks were accredited the procedure of the International Organization for Standardization (ISO). Based on the ISO9001:2000 requirement, each step of the chemotherapy regimens and the entire oncological treatment had been standardized, monitored and documented.⁽²⁴⁾ Moreover, the protocol compliance is monitored by annual chart reviews of all children with leukemia in Hungary by independent, experienced clinical investigators.

Based on the above-mentioned transparency of the oncological treatment, centers of the Hungarian Pediatric Oncology Network are qualified to take part in international, multi-centers, prospective Phase II clinical trials.⁽²⁵⁾

In-service Training

An adequate number of specially qualified physicians and nurses is an essential component of a modern and effective pediatric oncology network. To achieve this goal, two scientific meetings need to be organized annually, in which the active participation of nurses is necessary (lectures and poster presentations) in these 1-week-long training courses.

Cost Considerations

Health represents the single most important expenditure for European Union governments today, and these countries are spending record amounts on healthcare. (Table 1) But with rising cost pressures, it is becoming more and more dif-

ficult to continue the improvement of quality.⁽²⁶⁾ In Hungary, health insurance (the compulsory health insurance based on the principle of solidarity) bears the expenses of cytostatic drugs only for children registered and treated according to the guidelines of the Hungarian Pediatric Oncology Network. This centralization of the patients' treatments and regular (annual) audits makes oncology centers' treatment more economical. The supportive therapy follows the guidelines of evidence based medicine.⁽²⁷⁾ The indication of expansive recombinant cytokine granulocyte colony-stimulating factor (GCSF) is checked by National Health Insurance Fund. Outcomes of the medical treatment are measured by the overall survival and the event-free survival rates, and by monitoring the quality of life in long-term survivors.

Summary and Conclusion

To provide up to date treatments for children diagnosed with malignant diseases is a huge challenge for a small country with limited budget for health care. Assurance of high quality and economic treatments has been made possible by the centralization of all pediatric cancer patients in to pediatric oncology centers, the well organized and reliable pediatric tumor registry and strong international scientific connection of the Hungarian pediatric oncologists.

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Apstrakt

Pružanje savremenih tretmana deci dijagnostikovanj sa malignim bolestima predstavlja veliki izazov za malu zemlju sa ograničenim sredstvima za zdravstvenu brigu. Incidenca malignih oboljenja među pedijatrijskim pacijentima u Mađarskoj je skoro ista koliko i u drugim zemljama Evropske Unije sa procenom od 13.9/100,000 u 2003 godini. U proseku 250 dece dijagnostikovane sa karcinomom se svake godine raspoređi u nekoliko bolnica u Mađarskoj. To znači da ni najveća bolnica u Mađarskoj ne bi mogla da dovoljno snabde pacijente sa profesionalnim medicinskim instrumentima, doktorima specijalistima i medicinskim osobljem za decu obolelu od karcinoma i šta više da organizuje randomizirana klinička ispitivanja. Istorija pedijatrijske onkologije u Mađarskoj započinje 1971 god. sa osnivanjem Mađarsko Pedijatrisko Onkološke Mreže. Aktivnosti naše grupe se sastoje od: 1) registracija i praćenje pacijenata; 2) primena opšteprihvaćenog protokola u tretmanu lečenja; 3) kontrola kvaliteta i 4) postdiplomske nastavne sesije.

Pokazalo se kao važan korak napred kada je Mreža dobila nagradu od 2.33 miliona U.S. dolara od Američke Agencije za Međunarodni Razvoj (USAID) u periodu od 1991-1996 godine. Godine 2004. je osnovana internet baza registrovanih pedijatrijskih bolesnika sa karcinomom i komunikacioni sistem Mađarsko Pedijatrijske Onkološke Mreže.

U Mađarskoj, zdravstveno osiguranje (obavezno zdravstveno osiguranje je zasnovano na principu solidarnosti) snosi troškove citostatika samo za decu registrovanu i lečenu prema smernicama Mađarsko Pedijatrisko Onkološke Mreže. Ovakav vid centralizacije u tretmanu pacijenata i regularana (godišnja) revizija čini tretman onkološkog centra znatno ekonomičnijim. Garancija visokog kvaliteta i ekonomičnost tretmana je moguća centralizacijom svih pedijatrijskih pacijenata obolelih od karcinoma u pedijatrijski onkološki centar, dobro organizovan i pouzdan registar sa pedijatrijskim pacijentima sa karcinomom i snažna međunarodna naučna saradnja Mađarskih pedijatrijskih onkologa.

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