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PHARMACOLOGYCAL PROPHYLAXIS OF EARLY POSTTRAUMATIC EPILEPSY IN 314 CHILDREN AND ADOLESCENTES

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Abstract

Introduction. Early posttraumatic epilepsies (EPTE) are epileptic attack that appear in first seven days after brain injury, with incidence of 3-5%.

Predictors for development of EPTE are: impressive skull fracture with rupture of dura, intracranial hemorrhage, neurogical deficit (brain contusion), posttraumatic amnesia longer than 24 hours. It is more common in children than in adolescents and adults. It carries four times increased risk for development of late posttraumatic epilepsy. Aspects of pharmacological prophylaxis was often considered, but scientifically neglected, without clear standings regarding controversial data in literature.

Methods. Patients with severe head injury, hospitalised at Neurosurgical Hospital, Clinical Center University of Sarajevo, in period from 6th of April 1992 til 1 th of Julz 1994, were included in studz. Prophzlaxis of EPTE was carried out with Phenobarbital (2 - 3 mg/kg) or Phenytoin (3mg/kg) parenteray. Decision was made upon clinical findings. CT scan was done in 13,5% patients and in 31,2% patients serum concentrations of antiepileptic drugs were monitored.

Results. 314 patients aged 0 – 20 years (106 patients 0-10years, and 209 patients 11-20 years) were investigated. Predictors of EPTE presented were posttraumatic amnesia longer than 24 hours in 90,4%, neurogical deficit in 86,6%, impressive skull fracture with rupture of dura in 81,5% and intracranial hemorrhage in 41, 1%. Only two boys developed EPTE in first 24 hours after injury.

Conclusion. This study has showd that use of antiepileptic drugs can decrease incidence of EPTE. However, problem remains, management of injured patients is still highly individualized, based on different experiences of doctors that treat patient and without clear guidelines.

Key words: eary posttraumatic epilepsy, prophylaxis.

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Introduction

Craniocerebral injuries (CCI) have specific significance in everyday life of a modern man, due to their frequency, severity, neurological and psychological consequences. According to study of Konjhodžić (1995)[1] during the war in Bosnia and Herzegovina, in siege of Sarajevo, from 1992-1995, CCI were extremely severe. In etiology of epilepsies trauma participates in 23% of cases (Oliveros et al. 2002)[2]. Epileptic seizures can appear at different period after the trauma. Early posttraumatic epilepsy (EPTE) consists of epileptic attacks that appear in the first seven days after the head injury. Kuhl et al. (1990)[3] suggest that the incidence of EPTE is 3-6%. Lee et al. (1997)[4] investigated 3340 adults with severe closed head injury and found EPTE in 3,6% of traumatized patients. Predictors for development of EPTE are: impressive skull fracture with rupture of dura, intracranial hemorrhage, neurogical deficit (brain contusion), unconsciousness or posttraumatic amnesia longer than 24 hours[4,5,6,7,8]. EPTE usually presents in the form of partial motor seizures that are closely related to localization of lesion. About 33% of patients can have generalized tonic clonic seizures. Clinicians are still in doubt about pharmacological prophylaxis and use of antiepileptic drugs in patients with EPTE. There are no clear guidelines despite that the first clinical trials have had shown benefit of this therapy 50 years ago (Hoff and Hoff 1947[9]; Birkmayer 1951[10]).

Methods

Patients hospitalized at Neurosurgical department of Clinical Center, University in Sarajevo, between 6th of April 1992 and 1st of July 1994, with severe brain injury and pharmacological prophylaxis of EPTE, were included in study. During the war in Bosnia and Herzegovina we had only Phenobarbital and Phenytoin for parenteral use at disposition. During the studied period we run out of Phenytoin, and had to use only Phenobarbital. Parenteral treatment was started in admission room with Phenobarbital 2-3 mg/kg/day or Phenytoin 3 mg/kg/day. This treatment lasted for 7 days or shorter after the injury, and was followed by per oral administration after steady serum concentrations were achieved. Decision was made upon clinical findings in majority of cases.

Results

We investigated 314 patients aged 0-20 years (105 patients 0-10 years, and 209 patients 11-20 years). There were only 4 patients aged 18-20 years.

Presented predictors of EPTE were: posttraumatic amnesia longer than 24 hours in 284 patients (90,44%), neurogical deficit in 272 patients (86,62%), impressive skull fracture with rupture of dura in 256 patients (81,53%) and intracranial hemorrhage in 129 patients (41,08%).

Only in 42 patients it was possible to perform CT scan (13,38%).

In 98 patients we were able to assess serum concentrations of antiepileptic drugs (31,21%).

Out of 314 patients, 251 (79,94%) were receiving Phenobarbital, and 63 (20,06%) Phenytoin as a prophylaxis for EPTE.

Only two boys developed EPTE in the first 24 hours after injury. One was 6 and other 7 years of age. Both of them developed partial motor seizures, with secondary generalization. One had only one attack, and other had repeated seizure.

Discusion

It is very interesting that the aspect of pharmacological prophylaxis of EPTE was often discussed in clinical trials and basic studies, but scientifically it was neglected. There are still no clear recommendations with precise criteria for treatment, and the data in literature are controversial (Kuhl et al., 1990[3]; Segatore et al., 1993[11]; Kobayashi et al., 1997[12]). Why have we decided for pharmacological prophylaxis of EPTE with Phenobarbital or Phenytoin? There were several reasons. First, craniocerebral injuries were extremely severe, and more than 80% of traumatized patients did have three or more risk factors for development of EPTE. Second reason was that traumatized patients were children and adolescents, and in this age group patients have EPTE more frequently than others. This is in correlation with studies by other authors (Nakamura et al., 1997[13]; Asikainen et al., 1999[7]). Other, newer studies, are confirming that we made appropriate decision (Barlow et al., 2000[14]), and they are pointing that severity of brain lesion is dictating severity of EPTE and later neurological development. Besides that, EPTE carries 4 times greater risk for development of late posttraumatic epilepsy. American Academy of Physical Medicine and Rehabilitation (1998)[15] is also recommending prophylaxis of EPTE. Third, in our study from 1984 done by Konjhodžić et al.[16], with 1830 cases with closed and opened craniocerebral injuries, where the traumas were far less severe, and patients did not get prophylaxis of EPTE, incidence of EPTE was 2,40%.

This problem remains in focus of epileptologists through out the world. Studies from last several months are also recommending prophylaxis of EPTE, and are pointing out the reduction of incidence of

EPTE with appropriate treatment on time (Oliveros et al., 2002[2]; Brophy et al., 2002[17]).

In stead of conclusion we may with certainty say that this study has showed that use of antiepileptic drugs immediately after trauma can prevent EPTE, and probably decrease further invalidity of traumatized persons, as well as later development of late posttraumatic epilepsy.

However, problem remains, management of injured patients is still highly individualized, based on different experiences of doctors that treat patient, and without clear guidelines.

Apstrakt

Uvod. Rana posttraumatska epilepsija (RPTE) su epileptične atake koje se javljaju u prvih 7 dana nakon povrede, a incidenca se kreće od 3-5%. Prediktori za razvoj RPTE su: impresivna fraktura sa ruputurom dure, intrakranijalna krvavljenja, neurološki deficit (kontuzija mozga), posttraumatska amnezija (PTA) duža od 24 sata. Češća je kod djece nego kod adolescenata i odraslih, a značajna je jer nosi četiri puta veći rizik za kasnu posttraumatsku epilepsiju. Aspekt farmakološke prevencije je često razmatran, ali naučno zanemarivan i bez jasnih stavova, sa kontroverznim podacima u literaturi.

Metod. U studiju su uključeni pacijenti hospitalizirani u periodu od 06.04. 1992. do 01.07.1994. na Neurohirurškoj klinici Kliničkog centra Univerziteta u Sarajevu, koji su doživjeli tešku povredu mozga i kod kojih je provođena prevencija RPTE phenobarbitonom (2-3 mg/kg parenteralno) i phenytoinom (3mg/kg parenteralno). Odluka je donesena na osnovu kliničkog nalaza, a kod 13,4% pacijenata je učinjen CT mozga. Kod 31,2% pacijenata su određivani nivoi antiepileptika u serumu.

Rezultati: Ispitano je 314 pacijenata u životnoj dobi od 0-20 godina (105 od 0-10 godina i 209 od 11-20 godina), a prisutni predikatori za razvoj RPTE su bili: PTA duža od 24 h kod 90,4%; neurološki deficit kod 86,6%; impresivna fraktura sa rupturom dure kod 81,5%; intrakranijalno krvavljenje kod 41,1%. Samo dva dječaka su imala RPTE u prva 24h nakon povrede.

Zaključak. Ovo istraživanje je pokazalo da se primjenom antiepileptika može znatno smanjiti incidenca RPTE. Međutim, problem i dalje ostaje otvoren i briga za traumatiziranog je široko individualizirana u skladu sa iskustvima svakog pojedinog liječnika, jer nema jasnih stajališta.

Ključne riječi: *Rana posttraumatska epilepsija, prevencija*

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