NEUROCOGNITIVE IMPAIRMENTS AT VARIOUS STAGES OF CLINICAL OPIATE ADDICTION

In opiate addicts with various duration of drug use neurocognitive impairments as well as a number of typical physical changes occurring in the brain were registered. The opiate addicts' cerebral hemodynamics and higher brain functions were examined by drug use duration and patient's age.

Keywords: Central nervous system, computed tomography, drug use duration, neurocognitive impairment, opiate addiction

UDC: 616.89+ 613.83

Opiate addiction (OA) facilitates toxic affection of various organs and systems, primarily, of central nervous system (CNS) and higher brain functions. Neurocognitive impairments are the most typical manifestations of CNS organic disorders, the degree of their intensity varying from mild to severe (Baulina, 2002; Mendelevich, 2003; Seledtsev, 1994). Complexity and many-sidedness of opiate addiction problem requires work-up in various directions with synthesis of findings accumulated in the course of studying not only psychic sphere, but CNS as a whole, higher brain functions included. Opiate addiction is associated with affection of neurochemical and neurophysiological processes, morphological changes in the brain, as well as with psychic and behavioral disorders. Both addiction duration and age of drug use onset determine the intensity of OA-associated neurocognitive impairments and other organic psychic disorders. The earlier the drug use starts and the longer it continues, the more severe organic changes take place in the addict’s brain and the more pronounced neurocognitive impairments are.

Torpid thinking (apathetic mindset), poor imagination, lack of capability to generalize and single out the key point can be specified as the OA-associated cognitive deficits. Memory defects, problems with attention concentration, incapability to follow subject-matter of a conversation, high distractibility and attention switching ability are frequently registered. Defective operative and short-term memory as well as low motivational activity can be specified as typical manifestations. Heroin affects formation of complex inductive inferences, visual-spatial coordination, understanding of logical-grammatical relations, spatial analysis and synthesis; disorders of visual memory, tactile perception and praxis being registered as well (Bushev and Karpova, 1990; Rokhlina et al., 2005; Rokhlina and Kozlov, 2001; Rokhlina and Kozlov 2000; Seledtsev,1994). According to Rokhlina (2000) and Kozlov (2001) intellectual mnestic disorders occurred in 100% of opiate addicts, their degree assessed as mild, moderate and severe in 34%, 56% and 10%, respectively.

Occurrence of OA-associated neurocognitive impairments, organic psychic disorders as well as their clinical picture and dynamics are determined by a number of factors, such as, overdose usually associated with onset of encephalopathy of various severity, frequent use of homemade psychoactive substances with high concentrations of toxic foreign bodies directly affecting and poisoning CNS to result in rapid formation of toxic encephalopathy with intellectual mnestic disorders (Hickman et al., 2003; Krupitsky et al., 2006).

It is a popular misconception that opiate addiction causes no reduction in neurocognitive capabilities. Sometimes reduction of intellectual activity is explained by a compromise of emotional-volitional ego qualities. Intellectual mnestic difficulties, as well as asthenia and anergy are thought transient to be leveled down after termination of drug use and prolonged remission (Orudjev, 2002; Fishbein et al., 2007; Wang et al., 1999). Though diagnosis of mild organic psychic disorders seems not to be a problem, verification of
mild organic disorders could be challenging (Bushev and Karpova, 1990; Seledtsev, 1994; Vanbockstaele et al., 2000). The study was initiated to elucidate OA-associated hemodynamic and neurovisualization markers, facilitating diagnosis of neurocognitive impairments focusing on the assessment of cerebral hemodynamics and higher brain functions in opiate users by addiction duration and the patients’ age.

Materials and methods

We examined 35 opiate addicts, 19 women (54.3%) and 16 men (45.78%) among them, hospitalized at the Tertiary Detox Center, Public Health Ministry, Republic of Uzbekistan (Tashkent). Informed consent of all patients was obtained. To be included into the study the patients were to be diagnosed with “Mental and behavioral disorders due to use of opioids, drug dependence syndrome” (International Statistical Classification of Diseases and Related Health Problems, ICD 10 code F 11.2) or with “Withdrawal state” (ICD 10 code F 11.30). The study enrolled 18 and 17 opioid users with various drug use duration: from 4 months to 5 years and 5 years and more, respectively. The inclusion into the study was performed after detoxification. The study was performed after detoxification. Table 1 shows distribution of the patients by age of drug use onset. Given the clinical signs of acute abstinence syndrome, standard therapy was performed starting from the day of hospitalization.

<table>
<thead>
<tr>
<th>Age of drug use onset</th>
<th>Group 1 (n=18)</th>
<th>Group 2 (n=17)</th>
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<tbody>
<tr>
<td>Abs.</td>
<td>%</td>
<td>Abs.</td>
</tr>
<tr>
<td>Under 15</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>15-18</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>18-29</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Over 20</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>17</td>
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Brain computed tomography CT was prescribed to all participants, the procedure being performed in 15 examinees (7 and 8 patients from the 1st and 2nd groups, respectively) on a CT Philips, type “AURA”, 2000. Conventional methods were used to perform qualitative evaluation. All participants underwent neuropsychological assessment by means of Mini-Mental State Exam (MMSE) scale. Brain CT demonstrated expansion of lateral ventricles of cerebrum (LV) and subarachnoid space as well as presence of the reduced density centers in white (substantia alba) and gray (substantia grisea) substances. The changes were less pronounced in examinees with the drug use duration under 5 years than in those being drug addicts for more than 5 years (Table 2).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group 1 (n=7)</th>
<th>Group 2 (n=8)</th>
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<tbody>
<tr>
<td>LV breadth, mm</td>
<td>2.38 ± 0.01</td>
<td>2.62 ± 0.03</td>
</tr>
<tr>
<td>LV index, %</td>
<td>13.1 ± 1.2</td>
<td>20.3 ± 1.6</td>
</tr>
<tr>
<td>Extension of subarachnoid space</td>
<td>0.26 ± 0.05</td>
<td>0.35 ± 0.02</td>
</tr>
<tr>
<td>Additional reduced density centers, %</td>
<td>-</td>
<td>61.8</td>
</tr>
</tbody>
</table>

Thus, not only heroin intoxication, per se, but also drug use duration can be seen to make impact on brain CT picture. Prolonged hypoxia affects morphological structures of the cerebral tissue, presenting as cerebral cortex atrophy with extension of subarachnoid space and lateral ventricles; changes in density of white and gray substances being registered.
Brain rheoencephalography (REG) demonstrated OA typical peculiarities. Thus, rheographic index (RI) was found reduced (0.125±0.002 Ohm, versus normal 0.10-0.15 Ohm); conversely, the increase in dicrotic index (DI) could be seen (83.5±0.44% versus normal 40-70%) to be the evidence for enhancement of vascular tone but reduction in blood supply of cerebral vessels. As to changes in REG parameters by drug use duration, in patients with opioid dependence under 5 years they were less pronounced than in those with drug use duration over 5 years (RI 0.129±0.002 Ohm and DI 65.5±0.64% versus RI 0.122±0.003 Ohm and DI 89.6±0.59%, respectively).

The disorders in blood supply and elastic-tonic properties of cerebral vessels are probably associated with autoregulation injury of blood flow taking place in opioid users. Tone characteristics of cerebral vessels and parameters of blood supply were found to have similar relationship; the longer drug use duration is the less blood supply of cerebral vessels as well as lower dicrotic index characterizing vascular tone can be observed.

As it can be seen, opiate addiction affects cerebral hemodynamics characteristics with reduction of elastic-tonic properties and blood supply of cerebral vessels. Clinical severity is determined by close relationship between worsening of cerebral hemodynamics and drug use duration. Characterizing condition of higher brain functions cognitive impairments can serve as early clinical manifestations of cerebral disorders. Clinical-neuropsychological method is a highly sensitive one in assessment of changes in psychic function not only in local lesions of the brain structure, but also in lack of support for brain activity on other levels (Baulina, 2002).

Results and discussion

Study demonstrated intactness of intellectual mnestic sphere in 78.2% of patients with lower drug use duration (under 5 years), scoring not less than 27 according to MMSE scale. Results of tests of attention, concentration and attentional depletion were found most variable. According to Burdon’s test attentional capacity coefficient and fatigue rate were 19.4±0.5% and 0.5±0.08, respectively, word learning rate being 77±0.5%.

Thus, as compared with the standard parameters for healthy subjects, patients with less drug use duration demonstrated short-term memory and short attention span reduction by 22.6% and 8.8%, respectively; fatigue rate being found increased. In these patients flexibility of higher psychic functions was found more easily depleted, no gross neuropsychological syndromes observed.

Conversely, significant changes in neuropsychological characteristics in patients with longer drug use duration (over 5 years) were registered. In this group, we observed cognitive impairments, such as, attention concentration reduction and rapid attentional depletion, memory defects as well as emotional and behavioral disorders coinciding with those seen at pre dementia and dementia stages (24.3±0.4 according to MMSE scale). Other characteristics were found compromised, as well. Thus, a 10-word learning test scored 47.4±0.4%; that is, being reduced by 52.6% as compared with the normal result. Attentional capacity coefficient was found 17.4±0.4% to be lower by 39.2% as compared with normal, fatigue rate being 0.42±0.04.

Reduction of attention concentration, rapid attentional depletion, memory defects, as well as emotional and behavioral disorders have been registered; the findings being the evidence for confident (p<0.05) cognitive differences between patients with drug use duration under 5 years and those with opiate addiction for more than 5 years. Comparison of characteristics in opiate addicts with longer drug use duration demonstrated reduction in number of intellectual tasks performed per definite period of time.

Thus, opiate addiction has been found to result in cerebral tissue hypoxia leading to multifocal affection of the brain. Probably, in persons with prolonged heroin intoxication injury of blood flow autoregulation occurs with cerebral hemodynamics impairments presenting as vascular tone enhancement and reduction in blood supply of cerebral
vessels. Hematoencephalic barrier can be damaged too, to result in cerebral cortex atrophy, extension of subarachnoid space and lateral ventricles as well as appearance of additional centers with the reduced density in white and gray substances.

**Conclusion**

CT findings demonstrated that the intensity of the OA-associated morphologic structural changes in the brain varied from insignificant cerebral atrophy to extension of subarachnoid space and lateral ventricles, appearance of low density centers in the white and gray substances depending on drug use duration, age of drug use onset and premorbid background. OA-associated damage of cerebral hemodynamics presenting as vascular tone enhancement and blood supply reduction has been found to contribute to formation of cognitive impairments, such as, attention concentration reduction and rapid attentional depletion, memory defects as well as emotional and behavioral disorders coinciding with those observed at pre-dementia and dementia stages as per MMSE scale.

Early diagnosis of cerebral disorders is relevant from both theoretical and practical point of view since at this stage both preventive and curative interventions can be more efficient.

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