D. Surkov

USING OF DEXMЕDЕТОМІDІNЕ IN TERM NEONATES WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

MI «Dnipropetrovsk Regional Children’s Clinical Hospital» DRC neonatal intensive care unit Kosmichna, 13, Dniprop, 49100, Ukraine e-mail: densusurkov@hotmail.com КЗ «Дніпропетровська обласна дитяча клінічна лікарня» ДОР відділення анестезіології та інтенсивної терапії для новонароджених (головн. лікар – Н.А. Дементьєва) Космічна 13, Дніпро, 49100, Україна

Key words: hypoxia, ischemia, encephalopathy, dexmedetomidine, neonates, mechanical ventilation

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Abstract. Using of dexmedetomidine in term neonates with hypoxic-ischemic encephalopathy. Surkov D. The negative impacts of standard pharmacologic sedative agents suggest that alternative agents should be investigated. Dexmedetomidine could be the new option for sedation in newborns with hypoxic-ischemic encephalopathy requiring mechanical ventilation. The aim – to determine the impact of dexmedetomidine and other sedatives on the cerebral blood flow and outcomes of hypoxic-ischemic encephalopathy in term neonates. Data of 205 term infants with hypoxic-ischemic encephalopathy by Sarnat scale stage II-III were collected during ≤72 hours of life. The infants were divided using a simple open randomization by pharmacological sedative agents during mechanical ventilation into dexmedetomidine group (n=46) and the control group (n=159), which included morphine, sodium oxybutyrate, and diazepam in standard recommended doses. A comparative analysis of the effect of dexmedetomidine and other drugs on cerebral perfusion and outcomes of hypoxic-ischemic encephalopathy was performed. A significant difference between groups in days of trachea extubation (p=0.022) was found; the chance for babies to be extubated before the 7th day of treatment was significantly higher in the dexmedetomidine group 68% versus 33% in the control group (p=0.018) with HR 0.48 (95% CI 0.27-0.86, p=0.011). Also, the NIRS index rSO2 differed significantly between the studied and control groups on the 1st day of treatment (65% versus 79%, p=0.012) and on the 2nd day of treatment (74% versus 81%, p=0.035). Mean arterial pressure was higher in the dexmedetomidine group compared to the control group – (58 [51-65] mm Hg versus 53 [46-60] mm Hg, p<0.001), with a lower dose of dobutamine (EV -1.87, 95% CI from -3.25 to -0.48, p=0.009). In the dexmedetomidine group, the rate of seizures was significantly lower on the 1st day of observation (4.3% versus 48.3%, p <0.001); the incidence of unfavorable outcome such as cerebral leukomalacia was also 7 times lower in the dexmedetomidine group compared to the control group (2.2% versus 15.1%, p=0.018). Dexmedetomidine is a safe sedative agent with a stable hemodynamic profile, without adverse influence on cerebral perfusion and possible neuroprotective effects in term infants with HIE, as addition to standard therapeutic hypothermia.

Résumé. L'utilisation de la dexmedétomidine chez les nouveau-nés à terme avec une encéphalopathie hypoxique-ischémique. Surkov D. Les impacts négatifs des agents démotifs standards suggèrent l’investigation d’agents alternatifs. La dexmedétomidine pourrait être une option nouvelle pour le sédatif dans les nouveau-nés avec une encéphalopathie hypoxique-ischémique nécessitant un ventilation mécanique. L’objectif – déterminer l’impact de la dexmedétomidine et d’autres démotifs sur le flux sanguin cérébral et les résultats de l’encéphalopathie hypoxique-ischémique chez les nouveau-nés à terme. Des données concernant 205 nouveau-nés à terme avec une encéphalopathie hypoxique-ischémique de Sarnat scale stage II-III ont été collectées durant ≤72 heures de vie. Les nouveau-nés ont été répartis par simple randomisation ouverte par agents démotifs pharmacologiques durant la ventilation mécanique en deux groupes – groupe dexmedétomidine (n=46) et groupe contrôle (n=159), qui incluaient la morfine, le sodium oxybutyrate et le diazépam à des doses recommandées standard. Une analyse comparative de l’effet de la dexmedétomidine et d’autres drogues sur le flux sanguin cérébral et les résultats de l’encéphalopathie hypoxique-ischémique a été réalisée. Un différences significatives entre les groupes en jours de décontamination trachéale (p=0.022) ont été trouvées; la chance pour les bébés de se décontaminer avant le 7ème jour de traitement était significativement plus élevée dans le groupe dexmedétomidine 68% versus 33% dans le groupe contrôle (p=0.018) avec HR 0.48 (95% CI 0.27-0.86, p=0.011). De plus, l’indice NIRS rSO2 a différencié significativement entre les groupes étudiés et le groupe contrôle le 1er jour de traitement (65% versus 79%, p=0.012) et le 2ème jour de traitement (74% versus 81%, p=0.035). La pression artérielle moyenne était plus élevée dans le groupe dexmedétomidine par rapport au groupe contrôle – (58 [51-65] mm Hg versus 53 [46-60] mm Hg, p<0.001), avec une moindre dose de dobutamine (EV -1.87, 95% CI from -3.25 to -0.48, p=0.009). Dans le groupe dexmedétomidine, le taux de crises a été significativement plus bas le 1er jour d’observation (4.3% versus 48.3%, p <0.001); l’incidence d’un outcome défavorable, telle que la leukomalacie cérébrale, a été 7 fois moins élevée dans le groupe dexmedétomidine comparé au groupe contrôle (2.2% versus 15.1%, p=0.018). La dexmedétomidine est un démotif sûr avec un profil hémodynamique stable, sans influence adverse sur le flux sanguin cérébral et des effets neuroprotecteurs possibles dans les nouveau-nés à terme avec HIE, en plus de la thérapie standard hypothermique.
Hypoxic-ischemic encephalopathy (HIE), despite significant advances in diagnostics and understanding of the fetal and neonatal pathologies, remains one of the most frequent reasons for cerebral palsy and other types of severe neurodevelopmental impairment in children [6, 41]. In the United States and most technologically developed countries of the world the frequency of HIE according to different authors varies from 1.5-4 to 1.8 cases per 1,000 childbirths [8, 18, 19]. HIE morbidity is much higher in resource-limited settings and can reach as many as 26 cases per 1,000 newborns [1, 29]. In total it is associated with at least a quarter of all newborn deaths, however in the low-resources countries it could share amounts to 96% of all 1.15 million cases of HIE revealed in the world [15, 24, 31].

Sedation of neonates with HIE requiring mechanical ventilation is one of the debatable issues in neonatal intensive care. Conventionally, opiates or benzodiazepines are the pharmacologic agents most often used for treatment [23]. Questions regarding the efficacy, safety, and neurodevelopmental impact of these therapies remain. They possess certain advantages and disadvantages over each other, consequently, no ideal sedative agent for neonates has been established so far [13, 22]. Such pharmacological agent should provide mild to moderate depth of sedation with retaining a spontaneous breathing pattern, without serious negative effect on the systemic hemodynamics as well as on blood, coagulation, metabolism, liver function, kidneys, etc. It may cause neither long-term addiction in case of withdrawal nor neurodevelopmental retardation. The negative impacts of standard pharmacologic agents suggest that alternative agents should be investigated. So, recently great attention has been paid to such sedative drugs as clonidine [37] and its derivate dexmedetomidine [21, 32].

Dexmedetomidine is an \( \alpha_2 \)-adrenoceptor agonist, clonidine derivate, with sedative, anxiolytic, sympatheticetic, and analgesic-sparing effects, and minimal depression of respiratory function. Compared with clonidine, an \( \alpha_2 \)-agonist that has been used for several decades, dexmedetomidine has a greater selectivity for \( \alpha_2 \)-receptors. As activation of central \( \alpha_2 \)-adrenoceptors reduces sedative effects of \( \alpha_2 \)-receptors, dexmedetomidine is a more potent sedative than clonidine. Dexmedetomidine exerts its hypnotic action through activation of central pre- and postsynaptic \( \alpha_2 \)-receptors in the locus coeruleus, thereby inducting a state of unconsciousness similar to natural sleep, with the unique aspect that patients remain at mild sedation level. This aspect, combined with the minimal influence on respiration, makes dexmedetomidine an interesting alternative sedative in long-term ventilated patients. The impact on the cardiovascular system depends on the dose; in case of lower rates of infusion, the central action prevails, which leads to the decrease in heart rate and arterial pressure. At higher doses, peripheral vessel-constricting effects prevail, it leads to the increase in the systemic vessel resistance and arterial pressure whilst the bradycardic effect becomes manifested [7].

The evidences of the efficacy and safety of dexmedetomidine in adults have been obtained in some multi-center controlled studies [2]. The data on newborns (28-44 weeks of gestation) have been limited so far and administration of dexmedetomidine is considered mainly in low doses (≤0.5 mcg/kg/h) [10, 40]. No significant pharmacokinetic difference depending on the gender and age of patients was revealed. Newborn babies can be more sensitive to bradycardic effects of dexmedetomidine at therapeutic hypothermia and in clinical conditions when the heart rate depends on the cardiac output [17, 44]. However according to the data of the clinical observations, the episodes of bradycardia were registered in neonates more seldom compared to the pediatric population, but the children required higher doses of dexmedetomidine, therefore bradycardic side effect is dose-dependent [12].

To date there are no age-based contraindications to the administration of dexmedetomidine, and the experience of its using shows dexmedetomidine to be a safe and effective sedation agent for both term...
and preterm neonates, it is well tolerated and possesses no severe side effects [3].

Moreover in recent years, additional experimen-
tial information on relatively neuro-protective fea-
tures of dexmedetomidine has been accumulated in
researches on animals, at the expense of apoptosis slo-
wing down, including neurons [25, 26, 27, 30, 43].

Purpose – to determine the impact of dexme-
detomidine and other sedatives on the cerebral blood
flow and outcomes of hypoxic-ischemic encephalo-
pathy in term neonates.

MATERIALS AND METHODS OF RESEARCH

Single-center, prospective, randomized control-
led study was performed in 205 full-term infants
with HIE treated in neonatal intensive care unit
(NICU) level III of Dnipro Regional Children's
Hospital (Ukraine) in the period of 2012-2017.

Inclusion criteria: gestational age – 37 to 42 weeks,
term infants with the present signs and symptoms of
moderate to severe HIE by Sarnat score (in Hill A.,
Volpe J.J. modification, 1994) at admission during
the first 72 hours of life.

Exclusion criteria: gestational age less than 37
weeks, infants aged over 72 hours of life, birth
trauma, congenital malformations, early onset of
neonatal sepsis.

All the babies were treated by mild therapeutic
hypothermia 33-35 ºC for 72 hours, assisted posi-
tive-pressure ventilation under routine control of
acid-base balance, monitoring of SpO₂ and etCO₂,
control of systemic hemodynamics (heart rate, mean
blood pressure (MBP), cardiac output). Cerebral
hemodynamics was evaluated by non-invasive
method based on conventional ultrasound Doppler
transfontanel measurement of blood flow in the front
cerebral artery with estimation of systolic (Vs),
diastolic (Vd), mean velocity (Vm) and calculation
of Pourcelot Resistive Index (RI) and Gosling
Pulsatility Index (PI) using ultrasound SonoSite
Titan (USA) with microconvex probe 5-8 MHz [39].

RI – resistance index of brain arteries by Pour-
celot (Pourcelot Resistive Index) [20, 36] according
to the equation:

\[ RI = \frac{(Vs - Vd)}{Vs} \]

\[ PI = \frac{(Vs - Vd)}{Vm} \]

\[ Vm = \frac{(Vs + 2 \cdot Vd)}{3} \]

Cerebral regional tissue oxygenation index
(rScO₂) by INVOS™ 5100C Cerebral Oximeter
(Somanetics, Medtronic, USA) was monitored
during the whole 72 hours’ period of therapeutic
hypothermia [33]. The targeted reference range of
rScO₂ was considered within 60-80% [35].

Continuous monitoring of amplitude integrated
electroencephalography (aEEG) had been carried out
in 72 hours with the application of the diagnostics
complex Neuron-Spectrum, “Neurosoft” (Russia).

In addition to the routine lab studies and moni-
toring the serum concentrations of neuron-specific
enolase biomarkers (NSE) and protein S-100 were
taken on day 1 and day 3 of intensive care. Serum
levels of the neuron-specific enolase (NSE) and
protein S-100 were determined by the immuno-
chemical method with electrochemical luminescent
detection (ECLIA, Synevo Laboratory, GCLP 2011,
ISO 9001:2000). The referent range according to
the standards of the laboratory for NSE up to 16.3 ng/ml
was considered, for protein S-100 – up to
0.105 mcg/l. According to Simon-Pimmel J. et al.
(2017), in neonates and infants up to 1 month old
the upper limit of protein S-100 is <0.51 mcg/l, although
according to Abbasoglu A. et al. (2015) the normal
value of NSE concentration in term healthy neonates
is 18.06±12.83 ng/ml (95% CI 13.94-22.19 ng/ml)
[11, 34].

Using simple open randomization, all the babies
were divided into group of dexmedetomidine (DEX
group, n=46) and the control group of standard
sedation (n=159). Infants of DEX group received
dexmedetomidine in dose of 0.5 mcg/kg/hour via
continuous infusion. Neonates of control group
(n=71) received morphine infusion in loading dose
of 50 mcg/kg not earlier than 30 min followed by
maintaining dose of 10-40 mcg/kg/hour, in mono-
therapy or in combination with sodium oxybutiras
(n=78) in dose of 50-100 mg/kg or/and diazepam
(n=29) in dose of 0.05-0.1 mg/kg every 4-6 hours if
needed.

The end-points included: total days of the respira-
ry support including invasive and non-invasive
ventilation; total days in NICU, and the rate of
unfavorable outcome as cerebral leukomalacia.

The diagnosis of cerebral leukomalacia was based
on the routine daily neurosonography screening; in
case of ultrasound signs of leukomalacia the diagnosis
was confirmed by CT/MRI scanning.

The study was approved by Biomedical Ethical
Commission of the Dnipropetrovsk Medical Aca-

The statistics analysis of the study data was done
using software JASP 0.9.0.1 (Amsterdam, The
Netherlands, 2018) in accordance with the generally
accepted standards of the mathematical statistics.
Before the statistical analysis all the data had been
examined for normal distribution using Shapiro-
Wilk W-test. For nonparametric data the initial
statistical analysis included the calculation of the
median M, 25% and 75% percentiles. For the
**RESULTS AND DISCUSSION**

The results of treatment of 205 term neonates were analyzed, the average gestation age in weeks was 39.6±1.4 (37-42); birth weight in grams was 3583±554 (2440-5300). By gender: 128 neonates (62.4%) were boys, and 77 (37.6%) were girls. All the infants were transferred to the NICU from tertiary hospitals level II. 56 babies (27.4%) were admitted to the NICU in 0-6 hours after delivery, during 6-24 hours – 144 (70.2%), in the first 24-72 hours – 5 (2.4%) babies. 28 days’ mortality was 3 of 205 babies (1.46%).

First delivery occurred in 82 cases (40%), and 123 (60%) were subsequent. The rate of caesarean sections was 42 of 205 infants (20.5%). From 42 neonates born with Caesarean section, 17 (40.5%) were first born and 25 (59.5%) with subsequent deliveries (p=0.994). The Apgar score at 1st minute was 4.0±2.27 points; at 5th minute – 5.88±1.82 points; at 20th minute (estimated only in 56 babies) – 6.29±1.19 points. Serum lactate level at admission was 7.93±5.44 [0.9-25.1] mmol/l (normal range 0.9-2.7 mmol/l).

Demographic data of the dexmedetomidine group and the control group at the baseline is presented in Table 1.

**Table 1**

<table>
<thead>
<tr>
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<th>Control group, n=159</th>
<th>DEX group, n=46</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation, weeks (M±SD [min-max])</td>
<td>39.6±1.5 [36-42]</td>
<td>39.6±1.2 [36-42]</td>
<td>0.852</td>
</tr>
<tr>
<td>Birth weight, kg (M±SD [min-max])</td>
<td>3.5±0.5 [2.4-5.3]</td>
<td>3.7±0.6 [2.8-4.8]</td>
<td>0.097</td>
</tr>
<tr>
<td>Boys, n (%)</td>
<td>95 (59.8%)</td>
<td>34 (73.9%)</td>
<td>0.080</td>
</tr>
<tr>
<td>Girls, n (%)</td>
<td>64 (40.2%)</td>
<td>12 (26.1%)</td>
<td>0.080</td>
</tr>
<tr>
<td>Admission 0-6 hours, n (%)</td>
<td>41 (25.8%)</td>
<td>15 (32.6%)</td>
<td>0.360</td>
</tr>
<tr>
<td>Admission 6-24 hours, n (%)</td>
<td>113 (71.1%)</td>
<td>31 (67.4%)</td>
<td>0.631</td>
</tr>
<tr>
<td>Admission 24-72 hours, n (%)</td>
<td>5 (3.1%)</td>
<td>0 N/A</td>
<td></td>
</tr>
<tr>
<td>1st delivery, n (%)</td>
<td>67 (42.1%)</td>
<td>24 (52.2%)</td>
<td>0.228</td>
</tr>
<tr>
<td>&gt;1 delivery, n (%)</td>
<td>92 (57.9%)</td>
<td>22 (47.8%)</td>
<td>0.228</td>
</tr>
<tr>
<td>C-section, n (%)</td>
<td>32 (20.1%)</td>
<td>9 (19.6%)</td>
<td>0.933</td>
</tr>
<tr>
<td>C-section, 1st delivery, n (%)</td>
<td>12 (17.9)</td>
<td>6 (25)</td>
<td>0.454</td>
</tr>
<tr>
<td>C-section, &gt;1st delivery, n (%)</td>
<td>20 (21.7)</td>
<td>3 (13.6)</td>
<td>0.395</td>
</tr>
<tr>
<td>Apgar, 1st min. (M±SD [min-max])</td>
<td>3.9±2.3 [0-9]</td>
<td>4.5±2.1 [1-8]</td>
<td>0.125</td>
</tr>
<tr>
<td>Apgar, 5th min. (M±SD [min-max])</td>
<td>5.8±1.9 [1-9]</td>
<td>6.3±1.7 [2-8]</td>
<td>0.107</td>
</tr>
<tr>
<td>Apgar, 20th min (M±SD [min-max])</td>
<td>6.2±1.1 [5-8]</td>
<td>6.5±1.1 [5-8]</td>
<td>0.614</td>
</tr>
<tr>
<td>Lactate, mmol/l (M±SD [min-max])</td>
<td>8.5±5.6 [0.9-25.1]</td>
<td>5.2±3.7 [1.0-15.6]</td>
<td>0.019</td>
</tr>
<tr>
<td>pH (M±SD [min-max])</td>
<td>7.38±0.1 [7.14-7.69]</td>
<td>7.42±0.1 [7.23-7.73]</td>
<td>0.035</td>
</tr>
</tbody>
</table>

Basing on data of Table 1, there were no statistically significant differences between groups in birth weight, sex, and time of admission, proportion of 1st delivery, caesarian section rate and Apgar score at birth. pH was significantly but slightly different between the groups (7.38±0.1 vs. 7.42±0.1, p=0.035). The serum lactate level was significantly lower in the DEX group (8.5±5.6 vs. 5.2±3.7, p=0.019), but it was noticeably higher than normal range in both groups.

The comparative statistics of the dexmedetomidine group and the control group is presented in Table 2.
Table 2

<table>
<thead>
<tr>
<th></th>
<th>Control group n=159</th>
<th>DEX group n=46</th>
<th>P</th>
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<tbody>
<tr>
<td>rScO2 on Day 1, %</td>
<td>79 [68-85]</td>
<td>65 [50-73]</td>
<td>0.012</td>
</tr>
<tr>
<td>rScO2 on Day 2, %</td>
<td>81 [73-93]</td>
<td>74 [67-86]</td>
<td>0.035</td>
</tr>
<tr>
<td>MBP, mmHg</td>
<td>53 [46-60]</td>
<td>58 [51-65]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Seizures on Day 1, n (%)</td>
<td>77 (48.3%)</td>
<td>2 (4.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extubation (days)</td>
<td>5 [4-8]</td>
<td>5 [4-6]</td>
<td>0.022</td>
</tr>
<tr>
<td>Cerebral leukomalacia, n (%)</td>
<td>24 (15.1%)</td>
<td>1 (2.2%)</td>
<td>0.018</td>
</tr>
</tbody>
</table>

Note: n – number of neonates in each group; in [ ] – interquartile range; p – statistical significance of a result; rScO2 – regional mixed cerebral oxygen saturation; MBP – mean blood pressure.

There was no significant difference between the studied groups in indices RI and PI on day 1 (p=0.944 and p=0.671 respectively) and on day 3 of treatment (p=0.923 and p=0.385 respectively). Similarly, as to NSE and S-100 level there was no difference on day 1 (p=0.524 and p=0.572 respectively) and day 3 (p=0.384 and p=0.353 respectively). It confirms that the severity of the brain damage and the preservation of autoregulation for cerebral blood flow were comparable in both groups, and newborns from two groups were comparable by the degree of hypoxic-ischemic encephalopathy.

No reliable difference was revealed between the DEX group and the control group in total days of the respiratory support (p=0.071) and total days in NICU (p=0.362). But the terms of extubation were significantly different (p=0.022). Prospective data show that DEX patients were significantly more often extubated during 7 days comparing to control group (68% vs. 33% with log-rank p-value of 0.018). Retrospective dataset shows no difference. Pooled analysis demonstrated slightly less difference but the difference of 68% vs. 42% was statistically significant (p=0.011), with hazard ratio of 0.48 which is interpreted that after DEX treatment 52% neonates were still intubated by day 7 (95% CI 0.27-0.86, Cox’s regression 0.013). NIRS data of rScO2 were reliably different between the groups on day 1 (65% vs. 79%, p=0.012) and on day 2 of treatment (74% vs. 81%, p=0.035), but the same was not observed on day 3 of the study (p=0.600).

The data analysis revealed significantly different level of mean blood pressure between both groups. MBP was higher in the DEX group (p=0.001), at the same time infants from DEX group demanded lower doses of dobutamine (EV -1.87; 95% CI -3.25 to -0.48, p=0.009). A significantly lower rate of seizures was revealed in DEX group on day 1 comparing to control group (p<0.001). And the most essential finding is that the rate of unfavorable outcome such as cerebral leukomalacia was also lower in the DEX group in comparison with the control group (2.2% vs. 15.1%, p=0.018).

Dexmedetomidine appeared to be well-tolerated in neonates with HIE requiring therapeutic hypothermia. No adverse effects of dexmedetomidine such as hypotension or bradycardia were experienced during the study, its infusion rate was not changed during this time. The most probable explanation is the administration of dexmedetomidine in dose not exceeding 0.5 mcg/kg/hour, which matches the results of Estkowski L.M., et al. (2015) [12]. Because dexmedetomidine does not have significant effects on respiratory drive, it may present a good sedation option in babies requiring therapeutic hypothermia to preserve their spontaneous breathing pattern. Considering earlier extubation of trachea, the advantage of dexmedetomidine over other sedative agents has been confirmed by the data of O’Mara K., Weiss M.D. (2018) [28].

Data of the NIRS monitoring for cerebral oximetry look quite remarkable and demonstrate the reliably lower rScO2 indices in the dexmedetomidine group compared to the control group. However the interpretation of the data makes it possible to state that in the DEX group rScO2 index remained within the normal reference range of 60-80% [38], while in the control group this index insignificantly exceeded the upper limit of the conditionally normal values. It is important to notice that mixed blood saturation rScO2 supposes the estimation of the balance between oxygen supply and consumption by the
brain. If the decrease in rScO2 <40% testifies to the condition of severe hypoxia-ischemia, then rather high value of rScO2 >80% according to Sood B., et al. (2015), Hyttel-Sorensen S., et al. (2017), Garvey A., et al. (2018) and Herold F., et al. (2018) means the decrease in the consumption of oxygen and metabolic slowdown, and the value of rScO2 >90% is the evidence of the deep metabolism inhibition, stop in oxygen consumption by the brain tissue. Although this interpretation cannot be absolutely fair for the period of therapeutic hypothermia, when the metabolism of the brain is slowed down on purpose and under control [5, 14, 16]. Therefore nowadays the cerebral oximetry in the near-infrared spectrum according to Van Meurs K. and Bonifaci S. (2017) becomes essential as a component of the required neuroresuscitation monitoring [42].

The reliability of the influence of dexmedetomidine on the rate of unfavorable outcome of HIE such as cerebral leukomalacia, and the reliably of a smaller percent of neonates with seizures during the acute period of HIE in comparison with the control group requires further investigations, but the results match with the data of the experimental works by Endesfelder S., et al. (2017) and Kurosawa A. et al. (2017) on neuroprotective features of dexmedetomidine [9, 25].

CONCLUSIONS

5. Dexmedetomidine is a safe sedative agent with a stable hemodynamic profile, without adverse cerebral influence and possible neuroprotective effects in term infants with HIE, additional to standard therapeutic hypothermia.

6. The determined peculiarities make it possible to use dexmedetomidine in the daily practice of the neonatal intensive care, but additional data needs to be collected before any further conclusions can be drawn.

Conflicts of interest. Author has no conflict of interest to declare.

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