The aim of this study was to determine the prognostic value of proton magnetic resonance spectroscopy in neonatal encephalopathy. Studies were carried out in 11 consecutive term newborns with encephalopathy probably caused by hypoxic-ischemic injury. The clinical evaluation included pregnancy data, labor conditions, encephalopathy grade, presence of seizures, and necessity of antiepileptic drug therapy. Polygraphic recordings were obtained in all cases. Interest areas evaluated by spectroscopy were the basal ganglia and thalami. Among the cases, N-acetylaspartate/creatine, choline/creatine, and lactate/creatine ratios were calculated and related to the clinical variables, polygraphic recordings, and 6-month neurodevelopmental outcome. Abnormal follow-up occurred in 5 of 11 patients (45.4%) and was clearly related to an Apgar score <5 at 5 minutes (P = 0.003), encephalopathy grade (P = 0.02), early neonatal seizures (P = 0.02), and antiepileptic therapy (P = 0.01). No relationship was observed between spectroscopy results and polygraphic recordings profile. The lowest mean N-acetylaspartate/creatine ratio was observed in four of five patients with an adverse outcome and, although not statistically significant, demonstrated a clear trend to unfavorable follow-up (t test = 0.06). The choline/creatine ratios could not be related to follow-up in our sample. The most consistently observed abnormality on the spectra was the presence of the lactate peak in four of five patients with unfavorable outcome, with a high relative risk to determine evolution in the sample, relative risk 7.0 ($\chi^2 = 0.01$, 95% confidence interval = 1.1-42.9).


Introduction

Neonatal encephalopathy is a clinically defined syndrome of disturbed neurologic function in the earliest days of life in term newborns, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal level of consciousness, and often by seizures [1]. Although perinatal asphyxia persists as the major cause, other antenatal and intrapartum risk factors make this diagnosis heterogeneous. Early identification of newborns with encephalopathy secondary to perinatal asphyxia is crucial, so as to avoid the cascade of biochemical events that eventually may lead to irreversible brain injury [2]. A number of biochemical markers in the blood serum and cerebrospinal fluid have been proposed as predictors of early and long-term neurodevelopmental outcome. However, the results are often delayed or inconsistent [3,4]. Proton magnetic resonance spectroscopy ($^1$H-MRS) is a noninvasive method that can be used to detect these alterations and measure the intracerebral metabolites in vivo [5]. It has a definite use in accurate prediction of adverse outcome in newborns with encephalopathy secondary to perinatal asphyxia, mainly when performed near the “hypoxic-ischemic” event [6]. The optimal timing appears to be towards the end of the first week after birth [7]. However, at this time most of the newborns with perinatal asphyxia are still clinically unstable because of cardiovascular or multisystemic dysfunction and frequently mechanical ventilation that does not permit magnetic resonance imaging evaluation. The objective of this study was to identify, through encephalic proton magnetic resonance spectroscopy performed after “optimal timing”, early predictors of adverse neurologic outcome at 6 months of age.
Design and Methods

Patient Population and Study Design

Eleven term neonates born between March 2003 and March 2004 and admitted to the Neonatal Intensive Care Unit of São Lucas Hospital, the University Hospital from Pontifícia Universidade Católica do Rio Grande do Sul, School of Medicine in Porto Alegre, Brazil, were consecutively enrolled in the study and submitted to cerebral proton magnetic resonance spectroscopy. This unit is a referral center for the entire state of Rio Grande do Sul and receives social security patients who are generally from low socioeconomic classes. All newborns presented encephalopathy probably as a result of hypoxic-ischemic injury. The clinical data were obtained from hospital charts and include information about pregnancy, labor condition, Apgar scores at 5 minutes, and gestation. The presence of seizures (diagnosis based on clinical observation and classified according to Volpe’s scheme [8]), time of occurrence related to birth date (classified as early if seizures began in the first 24 hours of life and late between 48 hours and the 28th day of life), frequency, and necessity of antiepileptic drug therapy were also evaluated. Neonatal encephalopathy was categorized into three profiles by the pediatric neurologist (L.F.G.S.), with the most severe grade within the first 72 hours of life assigned to each patient. Profile 1 was defined as an altered level of consciousness that included somnolence or irritability, periods of spontaneous eye opening, jitters, abnormal muscle tone, and abnormal reflexes. Profile 2 was defined as stupor with absence of spontaneous but presence of stimulated eye opening, abnormal muscle tone, neonatal seizures, and brainstem dysfunction. Profile 3 was defined as coma, with no spontaneous or elicited eye opening, seizures, and brainstem dysfunction with abnormal cranial nerve or respiratory abnormalities [9]. The probable hypoxic-ischemic etiology was diagnosed by one of the authors (L.F.G.S.) if profiles 1, 2, or 3 were present, associated with Apgar score at 5 minutes <5, need of immediate resuscitation in the delivery room, and, when information was available, cord blood acidosis [9]. Exclusion criteria considered were progressive metabolic diseases, brain malformations, and congenital or acquired central nervous system infections.

Polysomnography Recordings

Polysomnographic recordings were obtained in all cases at the Clinical Neurophysiology Laboratory. The registration process lasted at least 1 hour or a complete sleep cycle. Scalp electrodes were placed according to the International 10-20 System modified for newborns [10]. The first 10-12 channels monitored electroencephalography, and five channels monitored extracerebral parameters which were chin electromyogram, electro-oculogram, electrocardiogram, nasal air flow, and thoracic-abdominal respiratory movements. The recording speed was 15 mm/s. The recordings were all videotaped with a split screen to help recognition of abdominal respiratory movements. The recording speed was 15 mm/s. The recordings were blind interpreted and classified into four profiles [10] by a specialist in neonatal polysomnography (M.L.N.). Profile 1 was defined as normal. Profile 2 was considered mildly abnormal, with background less than or equal to 0.05 μV and presence of discharges with or without ictal correlation. Profile 3 was defined as moderately abnormal, with low amplitude of background (5-15 μV) and presence of discharges with or without ictal correlation. Profile 4 was defined with low amplitude of background (<5 μV), burst-suppression pattern, or electrographic evidence of status epilepticus.

1H-MRS Procedures

After obtaining informed consent from the parents and when medically stable, patients were submitted to the magnetic resonance examination. The patients were monitored by an anesthesiologist during the magnetic resonance imaging and spectroscopy studies. Sedation with nitric oxide plus oxygen was provided as needed.

All studies were performed using a circularly polarized head coil in a conventional 1.5 Tesla whole-body imaging system (Magnetron Vision Plus; Siemens AG, Erlangen, Germany). The magnetic resonance imaging protocol included axial and coronal T1 sequences (repetition time [TR] = 1700 milliseconds, echo time [TE] = 110 milliseconds, flip angle = 160°), fast fluid-attenuated inversion-recovery (TR = 9000 milliseconds, TE = 110 milliseconds, flip angle = 180°), and diffusion (TR = 5700 milliseconds, TE = 139 milliseconds), followed by axial and coronal T1 pulse sequences (TR = 9.7 milliseconds, TE = 4 milliseconds, flip angle = 12°). The spectroscopy was performed using the point-resolved spectroscopy, bidimensional, multivoxel, and chemical selective saturation, to suppressed signal from water (TR = 1500 milliseconds, TE = 135 milliseconds, field of view 240 × 240 mm, flip angle 90°, and 16 × 16 phase encoding steps) [11]. The field of view with a nominal voxel size of 7.5 × 7.5 × 15 mm was located in the basal ganglia and thalamus bilaterally, without bone or cerebrospinal fluid contact, because these areas are most sensitive to the effects of perinatal asphyxia and are known to reflect the global disturbances in hypoxic-ischemic encephalopathy [12]. Spectral postprocessing was analyzed using the software Luise (Siemens AG, Erlangen, Germany), and included k-space zero filling interpolation to 32 × 32 phase encoding steps, and multiplication of corrected time domain signal by a Gaussian function, Fourier transform to the frequency domain, and manual zero order phase correction. The peak areas were integrated for the choline, creatine, N-acetylaspartate, and lactate resonances, and peak area ratios were calculated. The metabolite ratios of the right and left sides were averaged for statistical analysis. Total creatine was selected as the spectroscopy reference metabolite because of its relative stability after hypoxia-ischemia and better reflection of deranged energy metabolism [13]. All spectra were analyzed by a basic scientist (M.A.) with extensive experience in spectroscopy, who was unaware of the patient’s clinical picture. One experienced neuroradiologist (J.R.H.F.) blinded to the newborn’s clinical condition scored the magnetic resonance imaging examinations. One previously validated magnetic resonance imaging scoring protocol included axial and coronal T2 sequences (repetition time [TR] = 135 milliseconds, TE = 300 milliseconds, field of view 240 × 240 mm, flip angle 90°, and 16 × 16 phase encoding steps) [14]. Newborns were classified as abnormal if the magnetic resonance imaging score was greater than 0. Total time taken for imaging and spectroscopy ranged between 50 and 60 minutes.

After discharge, all infants were reexamined clinically for their neurodevelopmental progress. Clinical outcome was classified as normal, abnormal (based on Denver II Neurodevelopmental scale [15] and neurologic examination), or fatal. The first evaluation was performed at 30 days after discharge, and the next at 3 and 6 months, respectively.

The project was approved by the Ethics Committee of Pontifícia Universidade Católica do Rio Grande do Sul, and parents gave informed consent to participate in the study.

Statistical Analysis

The statistical methods compared patients with neonatal encephalopathy, abnormalities identified at proton magnetic resonance spectroscopy, and the follow-up after the neonatal period. Because of insufficient patient number, the neurodevelopmental outcome was divided into normal and abnormal for the purpose of statistical analysis. Analysis between clinical and neurophysiologic variables with spectroscopy results was performed by means of the chi-square test or Fisher’s Exact Test. Metabolite ratios, N-acetylaspartate/total creatine, choline/total creatine, and lactate/total creatine of the groups with normal and abnormal follow-up were compared by independent two-tailed t test. Differences in the frequency of lactate detection in each group were examined by chi-square test, and to identify prognostic indicators relative risks with 95% reliability interval were estimated. The adopted significance level was 0.05. All the tests were performed using the Statistical Package for Social Sciences, version 10.0 and Excel 97.
Results

Clinical Characteristics—Gestational, Perinatal, and Neonatal Period

Between March 2003 and March 2004, 575 newborns were admitted to the neonatal intensive care unit of São Lucas Hospital. From this database, six males and five females were diagnosed with neonatal encephalopathy and included in this study. All of them were term neonates with an average 39.1 ± 1.2 (S.D.) weeks of gestation, 81.8% (n = 9) appropriate for gestation, and 18.2% (n = 2) large for gestation. Vaginal delivery occurred in 72.7% (n = 8) of cases; the remaining 27.3% (n = 3) had cesarean section. Immediately after birth, resuscitation was necessary in 72.7% (n = 8) of patients.

Adverse prenatal events took place in 27.3% (n = 3) of pregnancies; urinary tract infection in two, and premature membrane rupture in one. Adverse events took place in 36.4% (n = 4) of labors; difficult extraction in two and tight nuchal cord in two. One patient included did not manifest any prenatal or birth complication, but developed a cardiac arrest 6 hours after birth and developed neonatal encephalopathy.

With respect to encephalopathy grade, 27.3% (n = 3) were diagnosed as grade 1, 45.4% (n = 5) as grade 2, and 27.3% (n = 3) as grade 3.

Neonatal seizures occurred in 63.6% (n = 7) of the total sample; early seizures in relation to birth were observed in four cases, all of them with neonatal encephalopathy grade 3. Seizures were classified in the sample as exclusively subtle in 14.3% (n = 1), exclusively clonic in 14.3% (n = 1), subtle plus clonic in 42.8% (n = 3), subtle plus clonic plus tonic in 14.3% (n = 1), and clonic plus tonic in 14.3% (n = 1) of cases. Maintenance of antiepileptic drug therapy to control seizures was necessary in 45.5% (n = 5) of patients.

Polysomnography Results

All the patients were submitted to a polysomnographic recording at an average 7.9 ± 4.6 (S.D.) days of life. With regard to polysomnography classification, we observed 9.1% (n = 1) normal examination and 90.9% (n = 10) abnormal examinations. Profile 2 corresponded to 72.7% (n = 8), profile 3 to 9.1% (n = 1), and profile 4 to 9.1% (n = 1) of cases. Burst-suppression pattern or neurophysiologic evidence of status epilepticus were not observed. The only profile 4 case was diagnosed as having diffuse low voltage. No relationship was observed between spectroscopy results and electroencephalographic recording patterns. The fact of having presented clinical seizures also did not relate to any specific electroencephalographic recording profile. However, the polysomnography profile 2 cases (n = 8) were statistically related to clinical neonatal encephalopathy profiles 1 and 2 (P = 0.05).

Spectroscopy Results and Outcome

The entire cohort was submitted to a brain magnetic resonance imaging and spectroscopy examination at an average 13.6 ± 4.0 (S.D.) days after birth. A summary of the clinical findings, magnetic resonance imaging scores, spectroscopy results, and outcome at 6 months of age is presented in detail in Table 1. Overall, thalamic abnormalities were observed in only 1 of 11 newborns with neonatal encephalopathy (Fig 1).

No fatal outcome was detected, so all the patients included were reexamined after discharge at the outpatient

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>NE (grade)</th>
<th>MRI Score</th>
<th>NAA/Cr*</th>
<th>Col/Cr†</th>
<th>Lac/Cr†</th>
<th>Outcome at 6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0.97</td>
<td>1.20</td>
<td>0.21</td>
<td>Abnormal</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0.88</td>
<td>1.66</td>
<td>0.46</td>
<td>Abnormal</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>3</td>
<td>0.74</td>
<td>2.97</td>
<td>0.81</td>
<td>Abnormal</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0.81</td>
<td>3.25</td>
<td>0.68</td>
<td>Abnormal</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0.85</td>
<td>1.37</td>
<td>ND</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>0</td>
<td>1.26</td>
<td>1.61</td>
<td>ND</td>
<td>Normal</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>0</td>
<td>1.11</td>
<td>1.44</td>
<td>ND</td>
<td>Normal</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>0</td>
<td>1.58</td>
<td>1.92</td>
<td>ND</td>
<td>Normal</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>0</td>
<td>1.00</td>
<td>1.30</td>
<td>ND</td>
<td>Abnormal</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>0</td>
<td>0.85</td>
<td>1.58</td>
<td>ND</td>
<td>Normal</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>0</td>
<td>1.24</td>
<td>1.67</td>
<td>ND</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Abbreviations:
Cr = Creatine
Col = Choline
Lac = Lactate
MRI = Magnetic resonance imaging
NAA = N-acetylaspartate
ND = Not detectable
NE = Neonatal encephalopathy
* Minimum peak-area ratios.
The average follow-up time was 9.1 ± 3.9 (S.D.) months of life. Abnormal neurodevelopmental outcome was confirmed by one pediatric neurologist (M.L.N.) in 5 of 11 patients (45.4%) and was clearly related to some neonatal clinical aspects and spectroscopy results, as summarized in Table 2.

The N-acetylaspartate/creatine, choline/creatine, and lactate/creatine ratios were also calculated among the groups with favorable and unfavorable outcomes. The lowest mean N-acetylaspartate/creatine ratios were observed in four of five patients with an adverse outcome and though not statistically significant, demonstrated a clear trend to unfavorable follow-up. The choline/creatine ratios could not be related to follow-up. The most consistently observed abnormality on the spectra was the presence of lactate peak in four of five patients with unfavorable outcome. In this group, the relative risk determined to an unfavorable evolution was 7.0 ($\chi^2 = 0.01$, 95% confidence interval = 1.1-42.9). The presence of this metabolite was undetectable in those who later had a normal evolution. Table 3 describes in detail these results and the t test for independent samples.

**Discussion**

**Clinical Characteristics: Gestational, Perinatal, and Neonatal Period**

The aim of this study was to identify, through magnetic resonance spectroscopy obtained after the first week of life, the relationship between neonatal clinical variables and identification of lactate peak on spectroscopy with outcome. Table 2 describes the relationship between neonatal clinical variables and identification of lactate peak on spectroscopy with outcome.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Lac +</th>
<th>AB Follow-up</th>
<th>Significance*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apgar &lt; 5 at 5 minutes</td>
<td>4/4</td>
<td>4</td>
<td>$P = 0.003$</td>
</tr>
<tr>
<td>Seizures</td>
<td>4/7</td>
<td>5</td>
<td>$P = 0.19$</td>
</tr>
<tr>
<td>Early seizures</td>
<td>4/4</td>
<td>4</td>
<td>$P = 0.02^\dagger$</td>
</tr>
<tr>
<td>Antiepileptic drugs</td>
<td>4/5</td>
<td>5</td>
<td>$P = 0.01^\dagger$</td>
</tr>
<tr>
<td>NE grade 3</td>
<td>3/3</td>
<td>3</td>
<td>$P = 0.02^\dagger$</td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test.

† $P < 0.05$.

**Table 2. The relationship between neonatal clinical variables and identification of lactate peak on spectroscopy with outcome.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unfavorable Outcome (n = 5)</th>
<th>Favorable Outcome (n = 6)</th>
<th>$t$ Test*</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAA/Cr‡</td>
<td>0.90 (0.74–1.00)</td>
<td>1.17 (0.85–1.58)</td>
<td>$P = 0.06$</td>
</tr>
<tr>
<td>Col/Cr‡</td>
<td>1.70 (1.20–3.25)</td>
<td>1.60 (1.37–1.92)</td>
<td>$P = 0.17$</td>
</tr>
<tr>
<td>Lac/Cr‡</td>
<td>0.57 (0.21–0.81)</td>
<td>0.00</td>
<td>$^*P = 0.01^\dagger$</td>
</tr>
</tbody>
</table>

Abbreviations:

- CI = Confidence interval
- Col = Choline
- Cr = Creatine
- $^1$H-MRS = Proton magnetic resonance spectroscopy
- Lac = Lactate
- NAA = $N$-acetylaspartate
- † Independent samples test.
- $^\dagger P < 0.05$ (95% CI).
- $^\dagger$ Values are given as medians and ranges.
life, prognostic indicators for neonatal encephalopathy. The study group may be considered small to obtain any significant results; however, as an etiologic factor, hypoxic-ischemic encephalopathy persists as a major cause, with a prevalence of 1-2/1000 live births [8]. During the study period, 575 newborns were admitted to the neonatal intensive care unit of our institution, thus we consider our sample appropriate.

It is difficult to determine the exact etiologic factor of neonatal encephalopathy, and a clear history of asphyxia, even during pregnancy or labor, could not be obtained in many cases [1,16,17]. In the sample, adverse prenatal events were present in three gestations and abnormal neurodevelopmental outcome was identified in one of them. However, the unfavorable outcome was attributed to perinatal events and abnormalities identified in magnetic resonance spectroscopy.

Vaginal delivery, at least in animal studies, could be related to signs of brain hypoxia-ischemia. In humans this relationship has not been confirmed, and conclusions are based much more on biochemistry results than clinical parameters [8]. In this group the adverse labor events took place in four vaginal deliveries, with no correlation to spectroscopic results or outcome. These findings are in agreement with previous studies [18,19].

Although an Apgar score of less than 5 at 5 minutes of life was not able to predict outcome, it was nevertheless useful to determine the necessity of resuscitation maneuvers in the delivery room. In premature infants, its reliability is even less [20]. In the sample described herein, recently delivered infants were included and—when analyzed in conjunction with other clinical parameters, particularly neonatal encephalopathy grade, metabolic disorders, electroencephalographic examinations, and neuroimaging studies—asphyxia was the most probable etiologic factor.

Seizures are still the most important clinical manifestation of neurologic disorders in the neonatal period [21,22]. A close association between neonatal seizures and permanent deficits has been described in previous papers [23,24]. In the present sample, seven patients were diagnosed as having seizures and four of them with early presentation. With these patients, the identification of lactate peak on spectroscopic examinations probably meant a more severe neonatal encephalopathy, with an additional tendency to an unfavorable outcome.

Despite the low efficacy reported, newborns with seizures are eventually administered antiepileptic drugs [25]. Antiepileptic drugs were prescribed for five neonates, four of them with lactate peaks identified on spectroscopic examination. The duration and need for a great amount of these drugs are indicators of clinical severity and unfavorable prognosis [26,27] as occurred with this sample.

The neonatal encephalopathy grade appears associated with severity of the neonate’s brain insult [8,22,24,27]. These observations are in agreement with the results of the present study, where those neonates classified as grade 3 were also diagnosed as having lactate peaks on spectroscopic examination and 6-month abnormal neurodevelopmental outcomes.

**Polysomnography Recordings**

Because of its noninvasive, easy-to-use nature, neonatal polysomnography has become an important assessment method for neurologically damaged infants. Polygraphic evidence of status epilepticus, hypovoltage, and burst-suppression pattern has played an important role in predicting neurologic disabilities [28,29]. In the present cohort, all the patients were submitted to an electroencephalographic recording during the first weeks of life and no patient was diagnosed as having a polygraphic status epilepticus or burst-suppression pattern. The low voltage observed in only one patient is in agreement with literature of unfavorable outcome [30]. Polygraphic abnormalities when related to spectroscopy results were not significant. Besides the small number of cases, both diagnostic tests are sensitive and the majority of patients included had alterations in both electroencephalographic and spectroscopic procedures.

**1H-MRS**

The clinical utility of proton magnetic resonance spectroscopy rests upon two important properties. First, the concentrations of brain chemicals identified are remarkably constant; and second, these neurochemicals are of clinical relevance in healthy and diseased brains [5,6,9,31]. Predicting outcome in neonatal encephalopathy remains difficult, because not all abnormal magnetic resonance imaging results are predictive of an unfavorable outcome. The basal ganglia abnormalities appear extremely predictive of neurodevelopment follow-up and are in close relationship to the severity of neonatal encephalopathy [4,6,14]. In the present cohort, only neonates with clinical or laboratory results compatible with asphyxia were included [32,33], and the necessity of clinical stabilization was crucial to our results. In only one case basal ganglia alterations were demonstrated by magnetic resonance imaging. Lactate peaks were detected in four spectroscopy examinations. Usually the increased lactate/creatinine ratio in the hours after hypoxic-ischemic insult is an indirect evidence of impaired cerebral energy metabolism [34]. The detection of lactate/creatine ratios in the sample could not be explained by this reason, because the spectroscopy examinations were obtained during the second or third weeks of life. However, there are several mechanisms that could be implicated in abnormal cerebral energy metabolism in chronic phases after hypoxic-ischemic brain insult. Among them, impaired oxidative metabolism due to mitochondrial damage, reduction in the activity of pyruvate dehydrogenase complex, and increased activity of microglia with infiltrating phagocytes [35]. In the present sample, lactate could be detected even later due to several mechanisms associated with hypoxia.
and ischemia described earlier and possibly also due to seizures [36]. Technical aspects of spectroscopy acquisitions also influenced the results. The long TE method has been used preferably in neonates to produce better detection of lactate/creatinine ratios even at a later date [37].

Patients studied 1-2 weeks after hypoxic-ischemic insult and who developed neurologic deficits were more likely to have reduced N-acetylaspartate/creatinine metabolite ratios compared with those who had good outcomes [12,15]. The magnitude of change in the metabolite ratios correlates with the severity of subsequent neurologic disability [38]. The findings reported here are in agreement with previous descriptions once the lowest mean N-acetylaspartate/creatinine ratios were observed in four of five patients with unfavorable outcome.

In term infants with encephalopathy, the clinical characteristics are not sufficient to determine etiology and prognosis, particularly when a clear history of asphyxia could not be obtained [39]. The proton magnetic resonance spectroscopy in these cases is a useful tool for determining etiology and prognosis. Accurately predicting an adverse outcome at 1 year with a specificity of 93% and positive etiology and prognosis. The findings reported here are in agreement with previous studies in term infants with encephalopathy [37] and ischemia described earlier and possibly also due to seizures [36]. The number of patients in the present study was relatively small, the data support that proton magnetic resonance spectroscopy, performed after the first week of life, can be used to identify neonates with encephalopathy at risk of unfavorable outcomes, particularly when secondary to hypoxic-ischemic brain injury and with normal magnetic resonance imaging.

References


Garcia da Silva et al: 1H-MRS in Neonatal Encephalopathy 365