

PROGNOSTIC VALUE OF PROTON MAGNETIC RESONANCE SPECTROSCOPY FINDINGS IN NEAR DROWNING PATIENTS

Reversibility of the early metabolite abnormalities relates with a good outcome

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Abstract – In two children with near drowning hypoxic encephalopathy and normal-appearing structural MRI, acute proton magnetic resonance spectroscopy (¹H MRS) showed biochemical alterations that correctly indicated prognosis and helped to guide management decisions. Elevation of the lipid-lactate and glutamine-glutamate peaks, on the early (72 hour) ¹H MRS, predicts a poor prognosis. Absence of lipid-lactate and glutamine-glutamate peaks on the early ¹H MRS and reversibility of early mild metabolite abnormalities on follow up examination relates with good outcome.

KEY WORDS: hypoxia, near drowning, magnetic resonance spectroscopy.

Valor prognóstico da espectroscopia de prótons em vítimas de quase-afogamento: reversibilidade das anormalidades metabólicas precoces relacionou-se com bom prognóstico

Resumo – Em duas crianças vítimas de quase-afogamento com encefalopatia hipóxico-isquêmica, que apresentaram ressonância magnética por imagem normal, a espectroscopia de prótons por ressonância magnética (¹H MRS) na fase aguda mostrou alterações bioquímicas que corretamente indicaram o prognóstico e ajudaram a guiar o manejo terapêutico. Elevação dos picos de lipídeo-lactato e glutamina-glutamato na ¹H MRS precoce realizada com 72 horas previu um mau prognóstico. Relacionaram-se com bom prognóstico; a ausência dos picos de lipídeo-lactato e glutamina-glutamato na ¹H MRS precoce, e a reversibilidade no exame de controle (3 meses) das discretas anormalidades metabólicas encontradas no primeiro exame.

PALAVRAS-CHAVE: hipóxia, quase-afogamento, espectroscopia, ressonância magnética.

The term “near drowning” signifies patient survival for more than 24-hours after cardiorespiratory arrest due to submersion. Early prognostic of good outcome *versus* significant neurological deficit or death is important for correctly stratifying patient management^{1,2}.

Magnetic resonance image (MRI) and computed tomographic findings of acute hypoxia ischemic injury are often subtle¹⁻³. We describe the findings of early proton magnetic resonance spectroscopy (¹H MRS) that helped to predict the prognosis.

METHOD

In two children with hypoxic-ischemic insult due to fresh water near drowning and normal-appearing structural MRI are studied.

In each patient single-voxel 1.5 Tesla ¹H MRS was performed in the median biparietal-occipital gray matter using a stimulated echo acquisition mode (STEAM) technique with repetition time: 1,500 ms, echo time: 30 ms, eight excitations, volume of interest: 6 cm³, and acquisition time: 7 minutes. The ¹H MRS data were compared with the standard MRI study obtained at the same session using non contrast sagittal T1-weighted images (WI), coronal and axial T2-WI, axial T2*-WI, axial T2-FLAIR and axial diffusion-WI, followed by gadolinium-enhanced axial T1-WI.

RESULTS

Case 1

This 3-year-old girl suffered near drowning in a swimming pool. She experienced cardiorespiratory arrest, was

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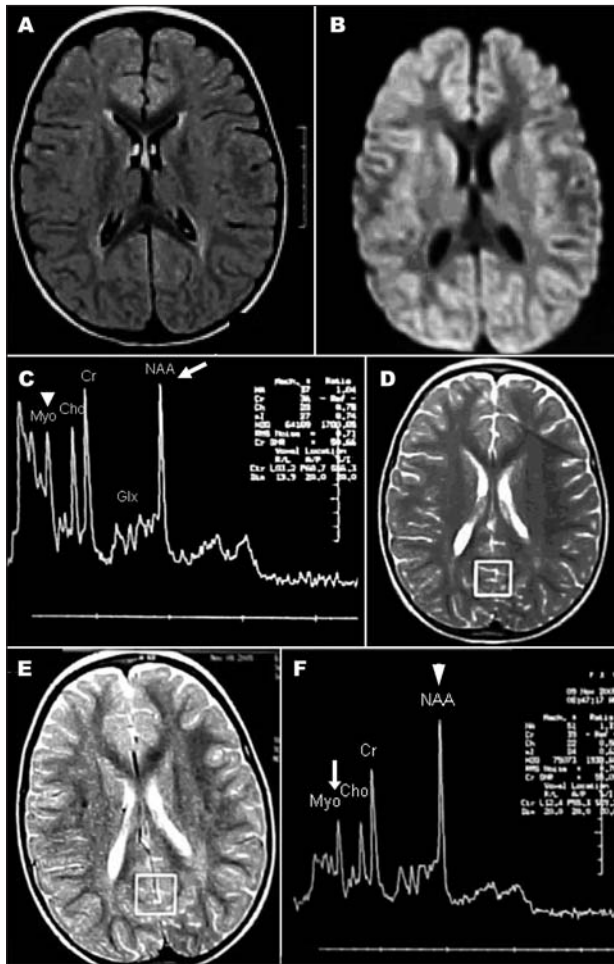


Fig 1. Case 1 – First exam, three days after near drowning. Axial FLAIR (A) and axial DWI (B) are unremarkable. ¹H MRS (C) VOI in the median biparietal gray matter, demonstrate on axial T2 weighted imaging (D), shows a mild decrease of the NAA/Cr ratio (arrow), and mild increase of the Cho/Cr and Myo/Cr ratios (arrowhead). On visual inspection, the Glx levels are normal and no Lip-Lac peak is identified. On follow up exam (3-months later), axial T2 remains unremarkable (E). The follow up ¹H MRS (F) in the median biparietal-occipital gray matter VOI demonstrated on the axial T2 (F), shows a normal spectrum (E) and reversibility and recovery of the metabolite changes (arrow and arrowhead) seen on the initial ¹H MRS (C), in this patient with good prognosis and complete clinical recovery. On visual inspection, the Glx levels are normal in both examinations and no Lip-Lac peak is identified.

resuscitated at poolside immediately after the accident, and arrived at hospital agitated but breathing spontaneously. MRI and ¹H MRS performed 72 hours after the near drowning (Fig 1A-D) showed normal anatomic structure (Fig 1A,B,D) and decrease (Fig 1C) of 20% in the N-acetylaspartate/creatine (NAA/Cr=1.04) ratio, an increase of 26% in the choline/creatine ratio (Cho/Cr=0.76) and 22% in the myoinositol/creatine (Myo/Cr=0.74) ratios, but no lipid-lactate (Lip-Lac) peak. This patient had a good outcome and was discharged after 5 days with a normal neurological examination. Follow-up MRI and ¹H MRS 3 months af-

ter the near drowning (Fig 1E-F) showed normal anatomic structure (Fig 1F) and normal metabolite ratios (Fig 1E). (NAA/Cr=1.21, Cho/Cr=0.56 and Myo/Cr=0.62).

Case 2

This 6-year-old boy also suffered near drowning in a swimming pool. He arrived at the hospital in cardiorespiratory arrest, but was resuscitated and stabilized. MRI and ¹H MRS performed 72 hours after the near drowning (Fig 2A-C) showed apparently normal anatomic structure (Fig 2A-B) but significant metabolic abnormalities (Fig 2C), especially increased Lip-Lac and glutamine-glutamate (Glx) peaks. There was also decrease of 8% of the NAA/Cr (1.2) ratio and increase of 50% of the Cho/Cr (0.9) ratio and 9% of Myo/Cr (0.65) ratio. The metabolic findings were interpreted as evidence of severe hypoxic injury with a poor prognosis. The patient remained comatose for 3 weeks, and progressed to non-progressive spastic/dystonic state, indicating chronic encephalopathy. The follow-up MRI and ¹H MRS was done 3 months after the accident (Fig 2D and E) and demonstrated severe brain atrophy (Fig 2D) and progression of metabolic changes (Fig 2E), with decrease of 54% in the NAA/Cr (0.6) ratio, an increase of 75% in the Myo/Cr (1.05) ratio, persistent of the Lip-Lac. However there was decrease in the Cho/Cr (0.6) ratio and Glx.

DISCUSSION

MRI and ¹H MRS may demonstrate abnormalities the first day after a hypoxic-ischemic near drowning injury, but have greater prognostic value after the third day¹. Edema and T2-hyperintensity in the cerebral cortex or basal ganglia are highly sensitive (100%) and specific (86%) predictors of poor prognosis (vegetative state and death)¹. The two children presented here did not exhibit these features.

The transitory decrease in NAA/Cr ratio seen in our Case 1 with good outcome appears to correspond to reversible *dysfunction* of the neurons and glia after acute brain injury, not cell death, since the metabolites and the patient both recovered with no alteration in brain anatomy MRI on follow-up study. Transitory reduced NAA/Cr ratio has not been reported yet in a patient with good outcome after hypoxic-ischemic insult from near drowning, although had been described in other pathologic conditions^{4,5} and represents cellular dysfunction rather than cell death.

In Case 2 with poor outcome, the Glx levels were elevated on the 72-hour-¹H MRS, then decreased on follow up examination. This most likely reflects early initiation of the excitotoxic cascade in a patient with severe brain injury⁶. The Myo/Cr was increased at 72 hours in both patients. The Myo/Cr returned to normal in Case 1 with

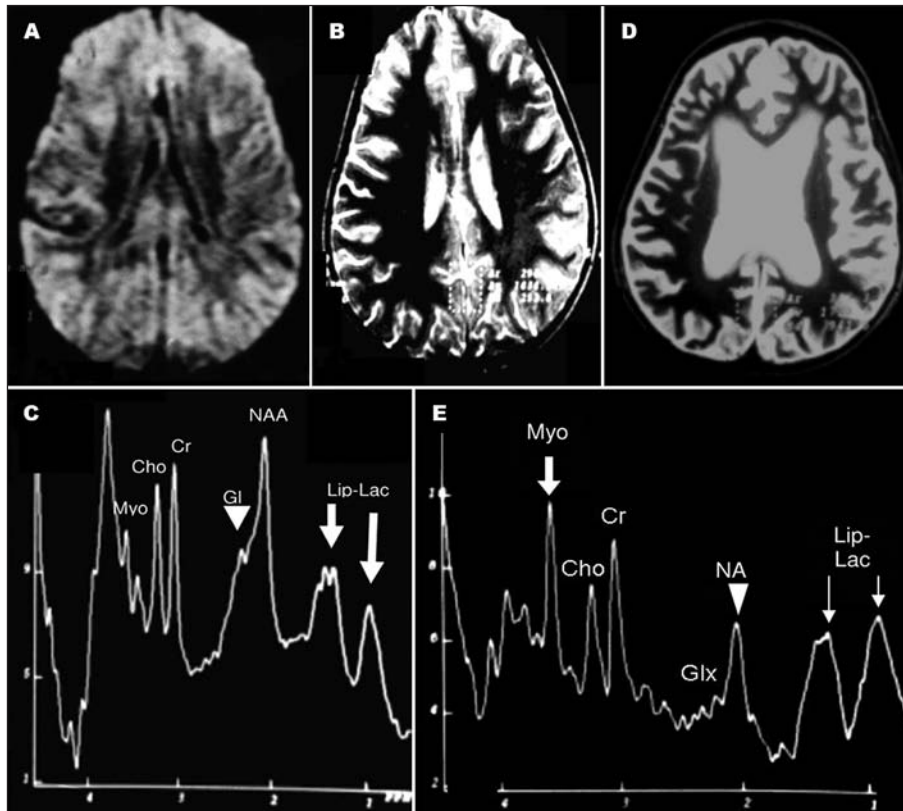


Fig 2. Case 2 – First MRI examination (A and B), three days after near drowning, shows unremarkable axial DWI (A) and axial T2 (B). However the ^1H MRS (C) with median biparietal-occipital gray matter VOI, shows decrease of the NAA/Cr ratio and increase of Cho/Cr ratio and of Myo/Cr ratio. Importantly the ^1H MRS (C) also demonstrates Lip-Lac peaks (arrows) and the visual inspection demonstrates an increase in Glx levels (arrowhead). On follow up exam (D and E), 3-months following the initial near drowning episode, axial T2 (D) demonstrates severe brain volume loss compared with the scan from 3 months earlier (B). ^1H MRS (E) shows progression of the metabolite changes with further decrease of NAA/Cr ratio (arrowhead), an increase of Myo/Cr ratio (arrow), with persistence of the Lip-Lac (arrow). However there is a decrease in the Cho/Cr ratio and Glx.

good outcome, but continued to increase in Case 2 with poor outcome. Myoinositol is found primarily in astrocytes and has a role in brain osmoregulation^{7,8}. The early but transient increase in Myo/Cr in Case 1 most likely reflects its role in osmoregulation⁷. The progressive increase in Myo/Cr in Case 2 most likely reflects astrogliosis within the damaged brain⁶.

Lactate is associated with anaerobic glycolysis, so the presence of Lip-Lac can reflect brain ischemia⁷. Case 1 with no elevation of Lip-Lac on ^1H MRS had a favorable outcome. Case 2 with elevated Lip-Lac levels had a poor outcome. These findings accord well with literature reports that elevated Lip-Lac peaks are strongly associated with poor outcome in brain injury, especially hypoxic-ischemic brain injury^{1,2}.

According to Dubowitz et al.¹ the combination of MRI and ^1H MRS together is superior to either one alone, decreasing the false-negative potential. ^1H MRS complements conventional MRI and clinical findings. ^1H MRS helps to predict the prognosis of near drowning victims with hypoxic encephalopathy and aids in triage, being particularly important in the hyperacute and acute phases, when conventional imaging findings are not prognostic.

In patients with near drowning hypoxic encephalopathy, ^1H MRS can demonstrate biochemical alterations that aid prognosis and guide management decisions. Eleva-

tion of the Lip-Lac and Glx peaks, on the early (72 hour) ^1H MRS, predicts a poor prognosis. Absence of lipid-lactate and glutamine-glutamate peaks on the early ^1H MRS and reversibility of the early metabolite abnormalities on follow up examination correlates with a good outcome.

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REFERENCES

- Dubowitz DJ, Bluml S, Arcinue E, Dietrich RB. MR of hypoxic encephalopathy in children after near drowning: correlation with quantitative proton MR spectroscopy and clinical outcome. *AJNR Am J Neuroradiol* 1998;19:1617-1627.
- Kreis R, Arcinue E, Ernst T, et al. Hypoxic encephalopathy after near-drowning studied by quantitative ^1H -magnetic resonance spectroscopy. *J Clin Invest* 99;97:1142-1154.
- Taylor SB, Quencer RM, Holzman BH, Naidich TP. Central nervous system anoxic-ischemic insult in children due to near-drowning. *Radiology* 1985;156:641-646.
- Tiberio M, Chard DT, Altmann DR, et al. Metabolite changes in early relapsing-remitting multiple sclerosis. A two year follow-up study. *J Neurol* 2006;253:224-230.
- Holshouser BA, Tong KA, Ashwal S, et al. Prospective longitudinal proton magnetic resonance spectroscopic imaging in adult traumatic brain injury. *J Magn Reson Imaging* 2006;24:33-40.
- Shutter L, Tong KA, Holshouser BA. Proton MRS in acute traumatic brain injury: role for glutamate/ glutamine and choline for outcome prediction. *J Neurotrauma* 2004;21:1693-1705.
- Danielsen E, Ross B. Magnetic resonance spectroscopy diagnosis of surgical diseases. Marcel Dekker, Inc USA, 1999.
- Ashwal S, Holshouser B, Tong K, et al. Proton spectroscopy detected myoinositol in children with traumatic brain injury. *Pediatr Res* 2004;56:630-638.