銻-99m HMPAO 腦部單光子電腦斷層掃描於新生兒缺氧窒息與低血糖腦病變之表現及預測價值 (II)

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中文摘要

氧與葡萄糖都是腦部新陳代謝所必須而不可或缺的物質；在新生兒，缺氧窒息或低血糖均是臨床上並不少見的狀況，也有可能因而造成腦部的受損，留下後遺症。為減少神經機能障礙，早期診斷、早期治療和復健是非常重要的。已有研究顯示頭部超音波、X光電腦斷層掃描和磁振造影對臨床處理新生兒缺氧窒息和低血糖有所貢獻；銠-99m HMPAO 腦部單光子電腦斷層掃描由於可在解剖構造改變之前即顯示出功能異常的病變區，故應有相當價值，但目前仍無完整的研究，因此我們進行此研究，並比較缺氧窒息或低血糖在銠-99m HMPAO 腦部單光子電腦斷層掃描上的相異處。

我們總共收集了 19 位低血糖新生兒及 20 位缺氧窒息新生兒，二組病患在年紀與性別上並無統計上的差異。結果顯示銠-99m HMPAO 腦部單光子電腦斷層掃描確實能敏感地偵測出這二組病人的腦病變區，我們再利用統計參數圖的方式分析其病變區的不同處。結果顯示在低血糖新生兒的後腦區有較缺氧窒息新生兒顯著血流降低的現象。

我們認為利用銠-99m HMPAO 腦部單光子電腦斷層掃描可以很敏感地偵測並定位出低血糖與缺氧窒息新生兒的腦病變區，且其易受犯區域在此二種疾病是不相同的。

關鍵字：缺氧窒息腦病變，低血糖腦病變，新生兒，銠-99m HMPAO 腦部單光子電腦斷層掃描。

英文摘要

Glucose and oxygen are both essential for normal brain function, and profound hypoglycemia and hypoxia may result in significant brain damage. Both hypoxia and hypoglycemia are not unusual in neonates and can lead to sequelae. Early diagnosis, treatment and rehabilitation are very import to reduce the severity of neurologic disabilities. Some studies have showed the usefulness of cranial ultrasound, X-ray CT scan and magnetic resonance imaging in the management of neonatal hypoxic-ischemic and hypoglycemic encephalopathy. Tc-99m HMPAO brain SPECT is a sensitive examination that can demonstrate functional alterations in the pathological areas before anatomical changes. Therefore, it may be valuable for neonates suffering from hypoxia or hypoglycemia. Nevertheless, there is no systematic investigation. We therefore underwent this study to explore the usefulness of Tc-99m HMPAO brain SPECT in neonatal hypoxic-ischemic and hypoglycemic encephalopathy. In addition, we compared the different scintigraphic manifestations in the two disorders.

A total of 19 hypoglycemic and 20 hypoxic-ischemic neonates were enrolled in this study. There was no significant difference in age and sex between the two groups. We
found that Tc-99m HMPAO brain SPECT was a sensitive tool to detect the brain lesions. By using statistical parametric mapping, neonates with hypoglycemic encephalopathy were noted to have significantly lower cerebral perfusion in the posterior cerebrum than those with hypoxic-ischemic encephalopathy.

In conclusion, we found hypoglycemic and hypoxic-ischemic encephalopathy can be easily detected by Tc-99m HMPAO brain SPECT. There were different vulnerable regions in neonatal hypoglycemia and hypoxia.

**Key words:** Hypoxic-ischemic encephalopathy, Hypoglycemic encephalopathy, Neonate, Tc-99m HMPAO brain SPECT

## 計畫緣由

Glucose as well as oxygen is of essential and fundamental importance for brain metabolism. Hypoglycemia and hypoxia are common disorders in neonates. According to different definite, the incidence of neonatal hypoxia in per 1,000 live birth is between 2.9 to 6.9 (1), it is about 0.7% to 11.4% for neonatal hypoglycemia (2). Both diseases may lead to permanent neurological sequelae, including seizure (3). Because the topography and severity of cerebral injuries determine subsequent neurological sequelae, imaging studies may provide useful information. Though there were studies about the usage of cranial ultrasound, X-ray CT scan and magnetic resonance imaging in neonatal hypoglycemia and hypoxia, only one case report presenting radionuclide cerebral perfusion study of three neonates with hypoglycemic encephalopathy has been reported and no systematic investigation has been undergone (4).

## 計畫目的

Because radionuclide cerebral perfusion study, such as Tc-99m HMPAO brain SPECT, can demonstrate functional alterations in the pathological areas before anatomical changes, it may be valuable for neonates with hypoglycemia or hypoxia. The purpose of this study was to explore the usefulness of Tc-99m HMPAO brain SPECT in neonatal hypoglycemic and neonatal hypoxic-ischemic encephalopathy. In addition, we assessed if there was different vulnerable regions in these two disorders.

## 結果

We enrolled neonates with hypoxia or hypoglycemia. For neonates with hypoxia, they should fulfill at least three of the following items: 1) intrapartum distress; 2) meconium-stained amniotic fluid; 3) Apgar scores ≤ 3 and ≤ 5 at the first and fifth
minutes; 4) requirement of bag and mask ventilation for at least one minute immediately after birth; 5) arterial blood pH < 7.2 or base deficit > 14 mmol/l within one hour following birth. Neonates with hypoglycemia were those met the criteria of blood sugar less than 2.6 mmol/l accompanied by clinical symptoms of tremor, apathy, tachypnea, irritability, hypotonia, feeding difficulty and disappearance of the symptoms following recovery of blood sugar. None of the babies had evidence of congenital malformation or inherited metabolic disorder.

All neonates underwent Tc-99m HMPAO brain SPECT. For brain SPECT perfusion imaging, each subject was injected intravenously with 111 MBq (3 mCi) of Tc-99m HMPAO (Ceretec, Amersham, UK) in a quiet environment about 10 minutes after placement of an intravenous line. Radiochemical purity exceeded 85% at time of injection. Imaging was initiated approximately 20 minutes later. We used a triple-headed rotating gamma camera (Multispect3; Siemens, Hoffman Estates, USA) with ultra high-resolution fan-beam collimators, which yields an image resolution of approximately 8.5 mm FWHM. The SPET data were acquired over a circular 360° rotation, 120 steps, 30 seconds per step, in a 128 x 128 x 16 matrix. Reconstruction was performed by filtered backprojection using a Butterworth filter (cut-off frequency: 0.4 Nyquist; power factor: 7) with attenuation correction by the Chang method.

For visual interpretation of Tc-99m HMPAO brain SPECT, the images were viewed on a color monitor using a spectrum scale of 255 colors. Transverse, coronal, and sagittal images were displayed. They were first normalized to the maximum of the entire data set. The observers then were allowed to alter the intensity and background scale interactively. A nuclear medicine physicians who were unaware of the patient's diagnosis visually assessed the SPET images.

To objectively determine the difference between neonatal hypoglycemia and hypoxic-ischemia, a statistical parametric map (SPM) 99 image analysis software (Institute of Neurology, University College London, London, UK) was used. Firstly, all the transverse images of the two groups of patients were realigned to a randomly selected image to create a single mean image of all realigned images. Then all the images were normalized to this mean image by a 12-parmeter affine (linear) transformation. Smoothing of the images was then performed with a 12 mm FWHM Gaussian filter. Proportional scaling was used for the global cerebral blood flow and the gray matter threshold was set at 0.8. Statistical comparisons between the two groups were performed on a voxel-by-voxel basis using t statistics to constitute an SPM of the t-statistic SPM{t}. The data were subsequently transformed to the unit of normal distribution SPM{Z} map. The significance of the regions was obtained in terms of peak height and spatial extent applying the Gaussian random field theory.
A total of 39 neonates were enrolled in this study. There were 19 with neonatal hypoglycemia and 20 with neonatal hypoxic-ischemia. The age and sex were not significantly different between the two groups.

By visual interpretation, areas of abnormally decreased cerebral perfusion were detected sensitively by Tc-99m HMPAO brain SPECT in the two groups. In addition, decreased cerebral perfusion in the posterior cerebrum was more prominent in neonatal with hypoglycemia than those with hypoxic-ischemia (Fig. 1). Compared by the statistical parametric mapping technique also demonstrated significantly lower cerebral perfusion of the posterior cerebrum in the neonatal hypoglycemia group (Fig. 2).

Fig. 1. Tc-99m HMPAO brain SPECT, sagittal images. Decreased cerebral perfusion in the posterior cerebrum (arrowheads) is more prominent in the neonate with hypoglycemic encephalopathy (A) than the hypoxic-ischemic neonate (B).

Fig. 2. Three orthogonal projects of the statistical parametric map from SPM analysis for comparisons between neonates with hypoglycemia and those with hypoxia. Clusters with significantly relative decreases of regional cerebral blood flow (rCBF) in neonates with hypoglycemia can be seen in the posterior cerebrum.

討論
At birth, there is a brutal interruption of a major glucose and oxygen infusion from the mother to the fetus and the neonate is at risk from hypoglycemia and hypoxia. Actually, neonatal hypoglycemia and hypoxia are common disorders. Severe hypoglycemia can cause cerebral dysfunction or even neuronal death (5). Although the initial physiologic response to hypoglycemia is the increase of cerebral blood flow (CBF) to compensate for insufficient glucose (6), delayed hypoperfusion has been observed following moderate and severe hypoglycemia (7). The occurrence of hypoperfusion is important because it is related to brain injury (8, 9). Therefore, delineating the degree and extent of hypoperfusion may be crucial. As to neonatal hypoxia, it causes multiple alterations due to failures in the gas exchange system. These include hypercapnia and low blood pH, as well as redistribution of the blood flow with preservation of perfusion in vital organs such as the brain, heart and adrenal glands (10).

The topography of brain injury is very important because it closely related to the neurological sequelae. Imaging studies may provide valuable information. In neonates with hypoxic-ischemic encephalopathy, structural imaging studies provide important diagnostic information in identification of diffuse cortical injury in severe selective neuronal necrosis, injury to basal ganglia and thalamus (which may precede status marmoratus), periventricular leukomalacia, and focal and multifocal ischemic brain necrosis (3). In addition to demonstrate insulted areas, radionuclide functional study revealed that changes in cerebral glucose metabolism is an early postnatal indicator of fetal asphyxia (11). As to neonatal hypoglycemia, the vulnerability of the posterior cerebrum to hypoglycemia in neonates has been noted in prior studies by use of MRI and pathology (12, 13). Though normal infants have higher regional CBF in the occipital regions (14), other factors, including efficiency of cerebral glucose utilization, metabolic requirements and influx of glucose, also contribute to vulnerability to hypoglycemia (15).

This study clearly demonstrated that Tc-99m HMPAO brain SPECT is sensitive in detecting the extent and severity of hypoglycemic and hypoxic injury during the neonatal period. Besides, the posterior cerebrum is more vulnerable to damage in neonates with hypoglycemia than in those with hypoxia.

計畫成果自評

Our study demonstrated that Tc-99m HMPAO brain SPECT is a sensitive tool for depicting and localizing neonatal hypoglycemic and hypoxic-ischemic encephalopathy. The vulnerability of the two disorders is different in different brain areas. Our findings are useful for predicting the subsequent neurological sequelae in these neonates.
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