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Quantitative Analysis Acetazolamide Effect on Cerebral Blood Flow and Cerebrovascular Response by Radionuclide Angiography of ^{99m}Tc-hexamethylpropylene Amine Oxime

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ABSTRACT

The effects of acetazolamide (Diamox®) on cerebral blood flow and cerebral vascular response were investigated using radionuclide angiography of ^{99m}Tc-hexamethylpropylene amine oxime. Absolute values of cerebral blood flow (CBF) and cerebral blood volume indices (BVI) were calculated in 10 patients with cerebrovascular diseases by the graphical analysis. After administration of Diamox, significant increases of both parameters were observed. Change rates of BVI were larger than those of CBF. This method was considered to be useful to assess the drug effect on cerebral blood flow and blood volume.

KEY WORDS

Technetium-99m hexamethylpropylene amine oxime, Brain perfusion, Brain blood volume, Cerebrovacular disorder, drug effect

INTRODUCTION

^{99m}Tc-hexamethylpropylene amine oxime(^{99m}Tc-HMPAO) is widely used for the evaluation of cerebral blood flow (CBF), but most of previous reports are only qualiative. We have reported quantitative use of this radiopharmaceutical by the angiographic method[1]. This technique is also able to estimate a vascular component, that is cerebral blood volume, of the brain. In this report, drug effects on both parameters were evaluated.

SUBJECTS

Ten patients with cerebrovascular diseases were examined, 8 men and 2 women, aged 41~73 (mean 54 years). Diagnoses were based upon the clinical histories, neuroligical signs, angiography, X-ray computed tomography (CT) and magnetic resonance imaging (MRI) findings. Eight patients had brain infarction, 1 subarachnoid hemorrhage, 1 moyamoya disease.

METHODS

Radionuclide angiography was performed by intravenous bolus injection of 740 MBq of ^{99m}Tc-HMPAO into the right brachial vein, followed by SPECT. Data acquisition and analysis were performed using the same method described in the previous study[1]. Eight patients received CBF

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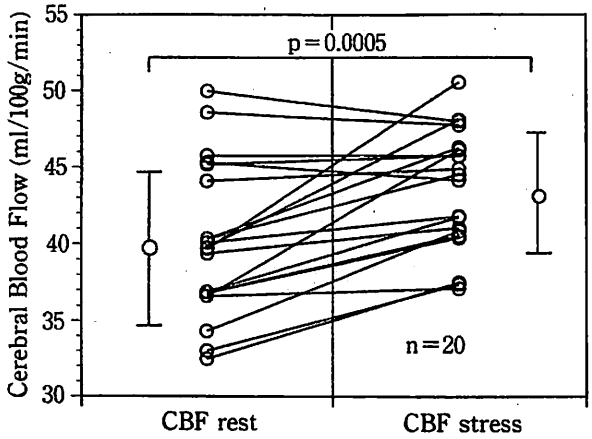

Fig. 1 Comparison of absolute values of mean cerebral blood flow (mCBF) of before and after administration of Diamox. Mean value of mCBF of 20 hemispheres on the baseline study was 40.1±5.0ml/100g/min (mean±s.d.), and increased to 43.5±3.9ml/100g/min on stress study significantly (p=0.0005).

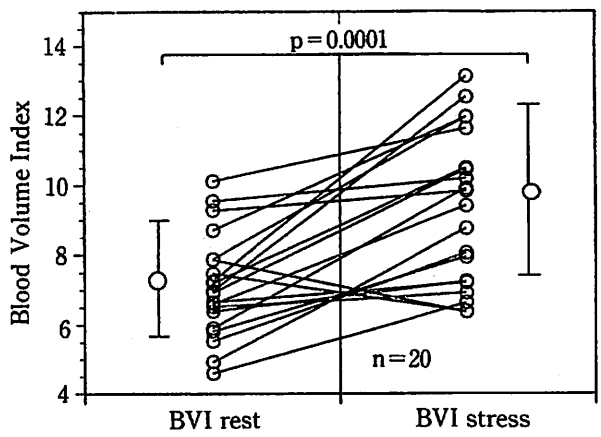

Fig. 2 Comparison of absolute values of blood volume indices (BVI) of before and after administration of Diamox. Mean value of BVI of 20 hemispheres on rest study was 7.1±1.5, and increased to 9.3±2.2 on stress study significantly (p=0.0001). Mean value of % change of BVI was 34.1±30.2%.

studies on separate days, firstly without administration of acetazolamide (Diamox® ; baseline study) and secondly with it (post-Diamox study) at 4-11 days interval, and consective CBF studies before (baseline study) and after (post-Diamox study) administration of acetazolamide were performede in 2 patients.

The theoretical model of blood-brain exchange previously reported was employed in this study[2)-4)]. In the unidirectional transfer process, brain radioactivity as a function of time, B (t), was expressed as follows :

$$B(t) = k_u \bullet \int_0^t A(\tau)d\tau + V_n \bullet A(t) \qquad (1)$$

where A(t) is the arterial activity as a function of measurement time (t), τ is time, ku is the unidirectional influx rate, Vn is the initial distribution volume for the tracer. Dividing Equation (1) by A(t) yields

$$\frac{B(t)}{A(t)} = k_u \bullet \frac{\int_0^t A(\tau)d\tau}{A(t)} + V_n \qquad (2)$$

The graphical approach by plotting B(t)/A(t) versus from each group of data gives an unidirectional influx rate of ku as a slope of a straight line and Vn as the ordinate intercept of this line[1)]. Absolute values of mean CBF (mCBF) and cerebral blood volume index (BVI) were calculated from ku and Vn[1)]. We evaluated absolute values of both parameters on condition with and without administration of the drugs, and % changes were calculated.

RESULTS

The mean value of mCBF of 20 hemispheres on the baseline study was 40.1±5.0ml/100g/min (mean± s.d., ranging from 32.5 to 49.9ml/100g/min), and increased to 43.5±3.9ml/100g/min (37.1 to 50.5ml/100g/min) on the post-Diamox study significantly (p=0.0005). The mean value of % change of mCBF was 9.2 ±9.4%(−4 to 27.3% ; Fig. 1).

Mean value of BVI of 20 hemisperes on rest study was 7.1±1.5 (4.6 to 10.1), and increased to 9.3±2.2 (6.4 to 12.5) on stress study significantly (p=0.0001). Mean value of % change of BVI was 34.1 ±30.2% (−19.1 to 81.0% ; Fig. 2).

Percentage changes of BVI were larger than those of mCBF in most patients. Relationship between both parameters of each patient was shown in Figure 3.

DISCUSSION

Graphical analysis for quantitation of CBF gives two parameters, the first one is unidirectional influx rate constant (ku), which is given as a slope of a straight line of the plot, and the other is the initial distribution volume for the tracter (Vn), given as the ordinate intercept of the plotted line. The units of ku and Vn are ROI_{brain} size/ROI_{arota} size/s and ROI_{brain} size/ROI_{arota} size, respectively[1)] (ROI, region

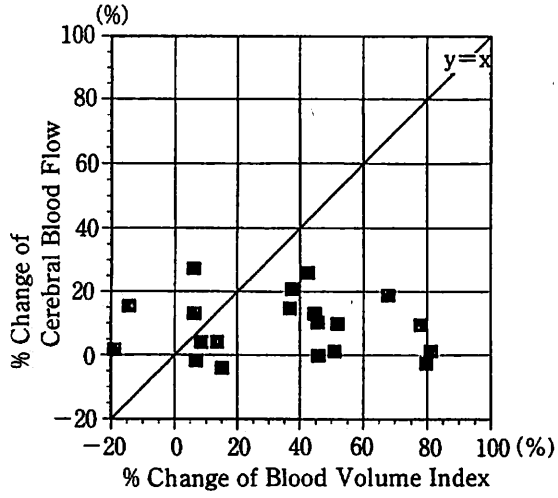

Fig. 3 Correlation of % change between blood volume index (BVI) and cerebral blood flow (CBF) before and after administration of Diamox.

of interest). It is necessary for clinical usefulness to correct ku and Vn by the ratio of ROI_{brain} size to ROI_{arota} size. After correction by the ratio of ROI size, we call the corrected ku as brain perfusion index (BPI), and the corrected Vn as blood volume index (BVI). Hemispheric BPI values showed highly significant correlation with hemispherical mean CBF obtained from ^{133}Xe CBF SPECT study[1]. So we calculate CBF value from BPI using regression line equation.

The vasodiatory effect Diamox is mediated by inhibition of carbonic anhydrase[5)-7)]. This inhibition has been suggested to produce an increase of CBF by pH reduction, similar to the effects of breathing carbon dioxide[8)]. In normal tissue, this reaction is smoothly occurred, but at the region perfused by aterosclerosed vessels, this reaction is poor. So perfusion of this area might be decreased on administration of Diamox due to steal phenomenon.

We previously reported quantitative determination of CBF using an SPECT image substraction technique[9)]. But by this method, underrestimation of CBF after administration of Diamox was occured, possibly because of the nonproportionality of HMPAO. Our new approach, significant increase of CBF and BVI were observed after administration of Diamox. This method was considered to be useful to assess the drug effect on cerebral blood flow and blood volume.

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^{99m}Tc-HMPAO RI アンジオグラフィを用いたアセタゾラミドによる脳血流変化および脳血管反応性の定量評価

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要　旨

脳血流および脳血管におよぼすアセタゾラミド(ダイアモックス®)の効果を^{99m}Tc-HMPAOによるRIアンジオグラフィを用いて定量評価した。10例の脳血管障害患者についてPatlak plot法を用いて脳血流の絶対値と脳血液量指数を求め，アセタゾラミド投与前後で比較した。脳血流，脳血液量指数とも，アセタゾラミド投与により有意の増加を認めた。また両者の変化率の比較では，脳血液量指数の方が大であった。本法は脳血流，脳血液量におよぼす薬剤の効果を評価するのに有用と考えられた。