

## 백서의 가역성 및 비가역성 뇌허혈 모형의 실험적 고찰\*

송광철 · 최병연 · 김성호 · 배장호 · 김오룡 · 조수호

= Abstract =

### Experimental Analysis in the Reversible and Irreversible Cerebral Ischemic Models in the Rat

Kwang Chul Song, M.D., Byung Yon Choi, M.D., Seong Ho Kim, M.D.,  
Jang Ho Bae, M.D., Oh Lyong Kim, M.D., Soo Ho Cho, M.D.

Department of Neurosurgery, Yeungnam University, College of Medicine, Taegu, Korea

**Objective :** The purpose of our experimental study was to analysis the advantages and disadvantages in the reversible and irreversible cerebral ischemic models with rats by staining with Neutral Red(NR) solution, 2% 2,3,5-triphenyltetrazolium chloride(TTC) and Hematoxylin & Eosin(H & E).

**Methods :** We have measured the range of cerebral infarction in the rat to get a suitable ischemic model along the object of study with and without craniectomy. With craniectomy, 9 rats were sacrificed for irreversible cerebral ischemic model by means of ligation at proximal(group ) and distal(group ), and coagulation at proximal(group ) middle cerebral artery. Also, 6 rats were sacrificed for irreversible(group ) and reversible(group ) cerebral ischemic model using nylon thread without craniectomy. The sizes of infarction were measured by staining the coronal sections of the brain with NR solution, TTC and H & E.

**Results :** There are no difference of physiological parameters comparing the each group. Cerebral infarction was not observed in group , but it's volume was largest in group .

Disadvantages of craniectomy group( , , ) are the long duration of operation and cortical damage by procedure. It's advantage is confirmation of the middle cerebral artery occlusion and cessation of blood flow through the operative microscope. In case of ischemic models using nylon thread (group , ), it is hard to identify the interruption or recirculation of blood flow through the middle cerebral artery, but the advantage is the simplicity of operative technique which reduces the operation time and minimizes the cerebral damage due to craniectomy. Therefore, it seems important to set up the reversible and irreversible ischemic models by carefully considering advantages and disadvantages listed above.

**Conclusion :** TTC staining seems to be effective since it reflects the histological damage sufficiently and quickly. It is hoped that researches focused on ischemic penumbra, which became popular recently, will be further carried on with use of NR staining, optical microscope and electron microscope.

**KEY WORDS :** Cerebral ischemic model · TTC · NR · H & E.

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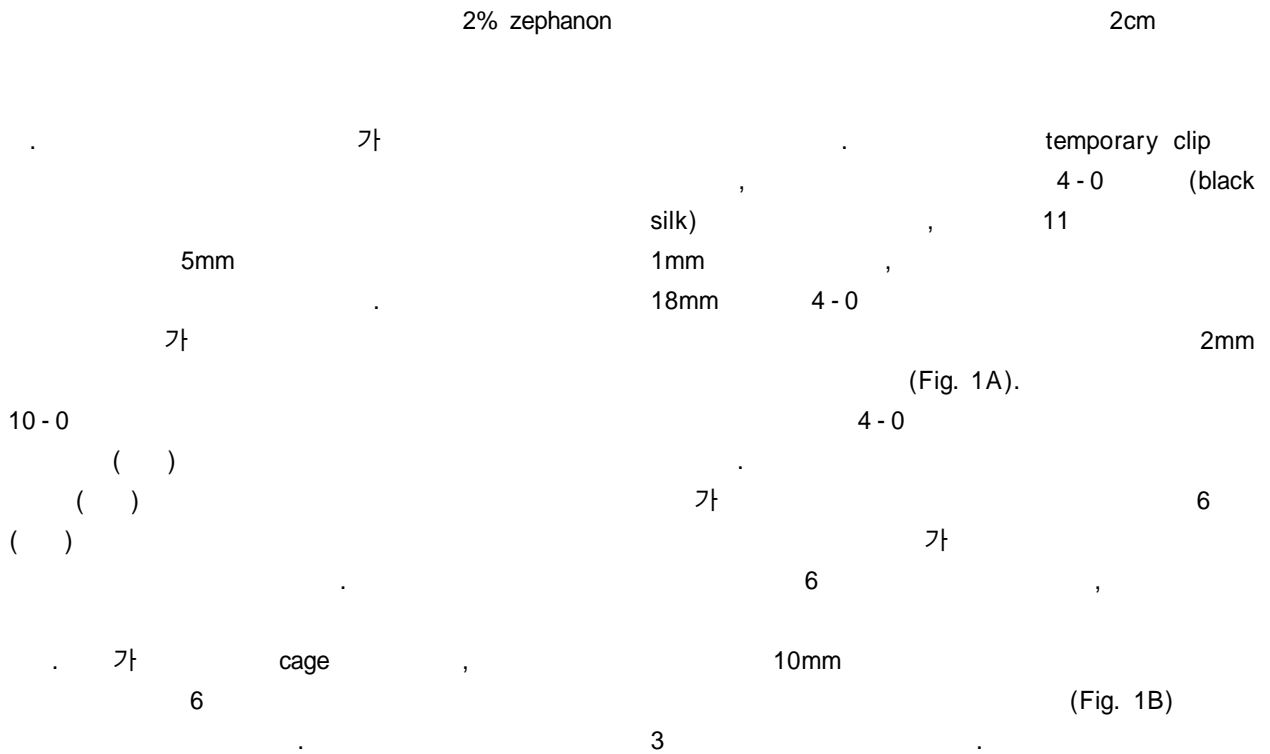
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19)21)

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3. 개두술을 이용한 뇌경색군



4. 나일론사를 이용한 뇌경색군

Nagasawa<sup>13)</sup> Yip<sup>24)</sup> 50cc

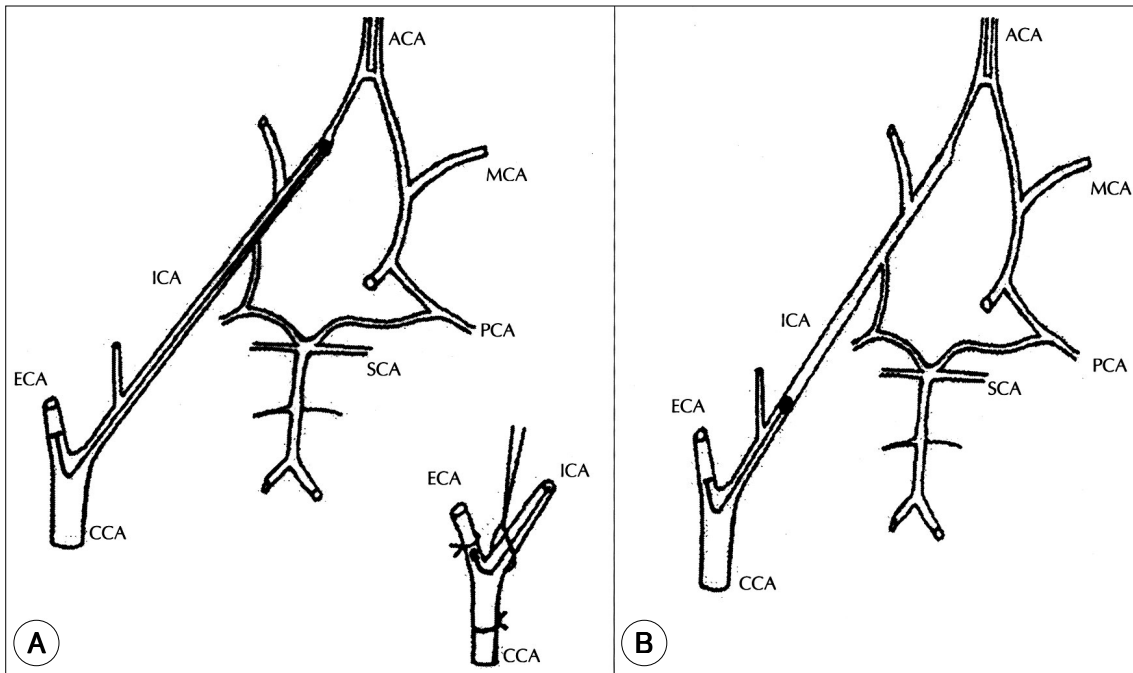


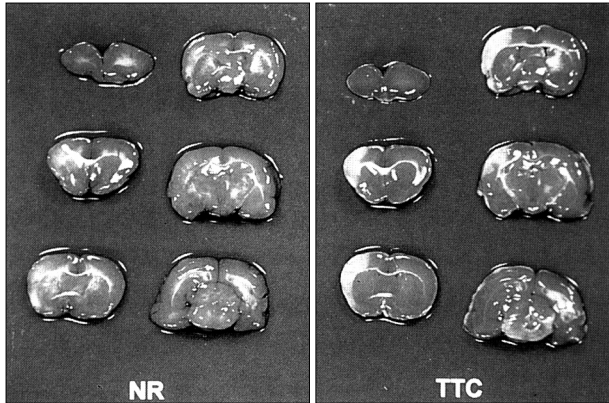
Fig. 1. A : Schematic representation of position of 4-0 nylon during occlusion of right middle cerebral artery. B : Reperfusion through MCA by withdrawal of 4-0 nylon to ICA proximal site. ECA : external carotid artery ; ICA : internal carotid artery ; CCA : common carotid artery ; ACA : anterior cerebral artery ; MCA : middle cerebral artery ; PCA : posterior cerebral artery ; SCA : superior cerebellar artery.

5. 뇌경색 범위의 측정  
 Chloral hydrate 2.5ml  
 buffered neutral red 10 4% phosphate bu -  
 6. 통계처리  
 one - way ANOVA test , p  
 0.05  
 2 3mm 7  
 8  
 37  
 1. 심폐 기능 측정치  
 2% TTC 10  
 30  
 10%  
 NR TTC  
 (Computer image analysis system)  
 (IBAS 2000, Kontron, West Germany)  
 Table 2  
 가

**Table 2.** Mean systolic arterial pressure, arterial blood gas analysis and temporal muscle temperature in experimental animals

Physiological parameter	Groups				
	1	2	3	4	5
MSAP(mmHg)					
Pre-ischemic	96 ± 3	113 ± 2	113 ± 2	96 ± 4	102 ± 3
Post-ischemic	103 ± 4	123 ± 3	96 ± 2	120 ± 5	118 ± 1
Post-reperfusion					107 ± 4
pH					
Pre-ischemic	7.39 ± 0.01	7.39 ± 0.03	7.38 ± 0.02	7.40 ± 0.02	7.39 ± 0.01
Post-ischemic	7.38 ± 0.01	7.37 ± 0.01	7.37 ± 0.01	7.37 ± 0.03	7.37 ± 0.03
Post-reperfusion					7.40 ± 0.01
PaCO <sub>2</sub> (mmHg)					
Pre-ischemic	42.5 ± 0.2	43.8 ± 0.3	43.5 ± 0.2	42.9 ± 0.1	43.7 ± 0.1
Post-ischemic	40.3 ± 0.1	40.5 ± 0.1	41.5 ± 0.3	40.2 ± 0.3	41.9 ± 0.2
Post-reperfusion					40.7 ± 0.2
PaO <sub>2</sub> (mmHg)					
Pre-ischemic	98.7 ± 0.1	98.7 ± 0.3	97.2 ± 0.2	97.8 ± 0.4	99.7 ± 0.2
Post-ischemic	99.7 ± 0.2	100.4 ± 0.2	100.3 ± 0.2	101.2 ± 0.2	101.7 ± 0.3
Post-reperfusion					102.8 ± 0.2
Hematocrit(mg%)					
Pre-ischemic	44.2 ± 0.2	42.8 ± 0.1	43.8 ± 0.3	43.8 ± 0.2	44.3 ± 0.1
Post-ischemic	43.2 ± 0.3	42.4 ± 0.1	43.2 ± 0.1	43.2 ± 0.4	43.7 ± 0.3
Post-reperfusion					43.5 ± 0.2
TM temperature( )					
Pre-ischemic	36.5 ± 0.2	36.5 ± 0.2	36.4 ± 0.2	36.6 ± 0.2	36.5 ± 0.2
Post-ischemic	36.4 ± 0.2	36.6 ± 0.2	36.5 ± 0.2	36.4 ± 0.2	35.4 ± 0.2
Post-reperfusion					35.5 ± 0.2

Values are expressed as the mean ± standard deviation MSAP : mean systolic arterial pressure ; TM : temporal muscle



**Fig. 2.** A gross photograph of the coronal section of a rat's brain with NR staining and TTC staining. The infarcted area of the brain was revealed as those area that had not stained into deep red by the NR or TTC. Infarct margin was more discrete in the brain stained with TTC than NR.

(acidosis)

가

가

36.5 ± 0.3

2. 육안 및 광학 현미경적 소견

( ) 가

(Fig. 1A).

NR

가

TTC

가

(Fig. 2).

H-E

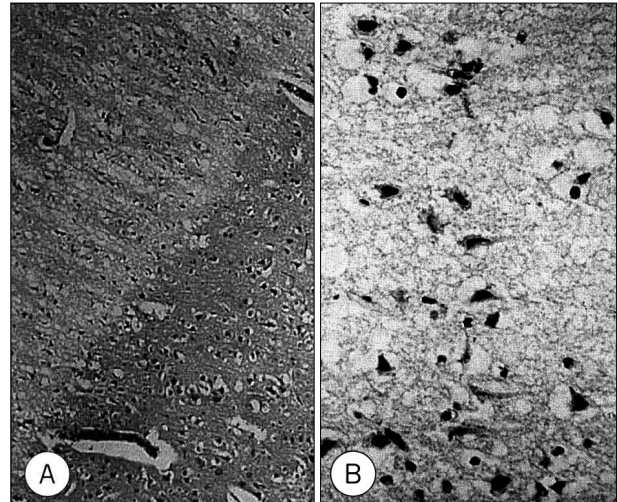
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(Fig. 3).

3. NR 염색과 TTC 염색 및 H-E 염색으로 측정된 뇌경색 범위의 차이

NR

6.35



**Fig. 3.** A : Microscopic finding of brain cortex shows the ischemic area(left upper) which is sharply demarcated from normal cortex(right lower)(H & E × 100). B : Microscopic finding of brain cortex shows ischemic injury of neurons consisting of nuclear angulation an hyperchromatism, loss of nucleoli and shrinkage of cytoplasm(H & E × 400).

**Table 3.** The infarct volume (%) in the experimental groups

Group	Stain		
	NR	TTC	H-E
	5.79 ± 2.33	2.72 ± 1.66	2.55 ± 1.64
	2.28 ± 1.21	0	0
	5.20 ± 2.65	1.71 ± 0.97	1.76 ± 1.07
	9.83 ± 4.13	4.11 ± 2.96	3.91 ± 2.87
	8.65 ± 4.77	1.32 ± 0.27	1.13 ± 0.26
Total	6.35 ± 1.43	2.00 ± 0.70*	1.87 ± 0.68*

Values are expressed as mean ± standard deviation

\* : significantly different from NR stain(p < 0.05)

NR : Neutral Red ; TTC : Triphenyltetrazolium chloride ; H-E : Hematoxylin-Eosin stain

± 1.43%

, TTC

2.00 ± 0.70%, H-E

1.87 ± 0.68%

NR

가 TTC

H-E

가

(p < 0.05) TTC

H-E

가 (Table 3).

가

TTC

2.72 ± 1.66%

H-E

2.55 ± 1.64%

TTC

4.11 ± 2.96%, H-E

3.91 ± 2.87%

가 가

가

TTC H-E

가

TTC H-E

1.32 ± 0.27%, 1.13 ±

0.26%

가

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가

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가

가 가

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### 고 찰

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19)21)

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30%

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5)13)

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가

13)14)22),

가 가

13).

가

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가

가

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18).

가

15

가

가

30

23)

ATP가

가

(anaerobic glycolysis)

(lactic acidosis) 가 6.35% TTC 2.00%  
<sup>12)17)</sup> 4.35%가 .  
 가  
 (ion) 가 가  
 가 <sup>2)</sup> (intervention) NR  
 가  
 가 TTC  
 Ca<sup>++</sup> 가 N - methyl - D - aspart -  
 ate(NMDA) 가 . TTC H - E  
 (ischemic penum -  
 bra) Astrup <sup>2)</sup> 가 10mL/  
 100g/min 가 .  
 (ischemic core)  
 가 ( 15 40mL/100g/min)  
 (surrounding or intermixed zone)  
 가  
 , Symon <sup>20)</sup> 결론  
 electrical failure가  
 가 가  
<sup>6)11)</sup>, Hoss - ( )  
 mann<sup>8)</sup>  
 가 가 가  
 ( , , )  
 NR -  
<sup>15)</sup> TTC deh -  
 ydrogenase  
 dehydrogenase  
 가 TTC H - E  
<sup>1)</sup> 가  
 (membrane pump) H - E  
 가 가 <sup>2)</sup> NR 가 . NR TTC 가  
 TTC (Isc - hemic penumbra)  
 NR

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- : 053) 620 - 3790, : 053) 620 - 3770  
E - mail : neuro@medical.yeungnam.ac.kr

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