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Klotho 基因多态性与脑梗塞的关系

王静雯 方丽君 刘迎梅 裴少芳 江玲玲
南京医科大学附属苏州医院神经内科 江苏 苏州 215008

【摘 要】: 勃◆ 吸伉娀媲 Klotho 佢伶伉峗吼佺暨CI暩匊尉侠log獷┥ 她彙慥▾ ㊦ナ偁分刜└ CI ㄉ壟她デ孳⇑ 方法: ▾ 80 fm CI 匊尉暨CI 宦暩丁 30 fm卻ㄣ⊡啌她ゃ丹■ 暨傚埡宦暩┳ 娀媲傚恥⇑ 扃壨戢屾シ瓮mV挹噱嚭偯 CI 宦丁傚埡宦┥ Klotho 佢伶她彙慥扉⇑ 慄慮响恥儳写勹峊壳嚂傚 Klotho 佢伶μs ㄩ偠(ㄖ)佚她(ㄨ)啓嶟截偁分刜暨rs192031暩甍彐乙伻⇑ 嗔侠謺慄慮㈜吤啌摽忯♠ Klotho 佢伶伻她乙儺搏塺吲kPa嫠μℓ Hardy-Weinberg 翀录⇑ kℓ呀謺乙哑╗ Klotho 嫽♪佢伶丁佢伶偁分刜└ CI ㄉ壟塺她デ孳⇑ CI 宦匊尉侠log獷┥ Klotho 她廛奶彙慥嚶翀呉呜♫╝ 傚埡宦暨P<0.05暩⇑ 个憃§ 圍▲唚翀录乙哑呜婗謺Klotho 佢伶偁分刜暨rs192031暩嫠μℓ懂⌂翀录乙儺暨P>0.05暩⇑ 佢╝ 佢伶她デ屾乙哑彙呉謺rs192031 偁分刜丁嫽♪佢伶└ CI 她ㄉ壟妠デ暨P<0.05暩⇑ Klotho 佢伶偁分刜 rs192031 她 TT 佢伶伻她 CI 匊尉她叵尅㊣丁撣傎異峏廛奶岮任戰呉呜撣╝ 傚埡宦匊尉暨P<0.05暩⇑

【关键词】: Klotho暻峗吼佺暻佢伶偁分刜

Relationship Between the Klotho Gene Polymorphism and Cerebral Infarction

Jingwen Wang Lijun Fang Yingmei Liu Shaofang Pei Lingling Jiang

Department of Neurology Suzhou Hospital Affiliated Nanjing Medical University Jiangsu Suzhou 215008

Abstract: We aimed to study the expression of Klotho gene in peripheral blood of patients with cerebral infarction (CI) and the relationship between its polymorphisms and the occurrence of CI. Methods: 80 CI patients (CI group) and 30 healthy people (control group) who received physical examination were selected as the research objects. The expression of Klotho gene in CI group and control group was determined by enzyme-linked immunosorbent assay. The single nucleotide polymorphism (rs192031) in the promoter region of the Klotho gene was typed by conformational difference gel electrophoresis. In addition, whether the distribution frequencies of Klotho genotypes conformed to Hardy-Weinberg equilibrium was assessed by chi-square test. At the same time, the relationship between Klotho alleles and gene polymorphisms and the incidence of CI was analyzed. The protein expression level of Klotho in peripheral blood of CI group was significantly lower than that of control group (P<0.05). Hardy-Weinberg equilibrium analysis showed that the Klotho gene polymorphism (rs192031) conformed to the genetic equilibrium distribution (P>0.05). Gene-based association analysis showed that rs192031 polymorphisms and alleles were associated with the occurrence of CI (P<0.05). The systolic blood pressure and high-density lipoprotein cholesterol of CI patients with TT genotype of Klotho gene polymorphism rs192031 were significantly higher than those of control patients (P<0.05).

Keywords: Klotho; Cerebral infarction; Gene polymorphism

1 引言

峗(ㄖ)┥ 吲┆ 宦▾ 峗懹尔獷㊦ㄒ獷刜卞 ⅄ 失堳┳ ┳ 徥┳ 六彙墇她夬夼謺┳ 六┐ 尔獷刜峗(ㄖ)┥ ㄉ夼塺慆揮謺滿兡咾壯╝ 撣獷㊣↩孨傻夼▾ ㊦ㄩ峹孛唗娥卄嫽佢娘夬夼她ㄉ壟ㄉ慢謺峗(ㄖ)┥ 她忴噤揖┳ 她┤ 僿她俾岪⇑ 懹乙偕尉慄慮侧扉偁┥ 处她伱搵刜乙哑娀媲忤偳謺暉獷㊣↩獷孨▸ 恮写兑⇐撣獷峏嫽佢娘夬夼傝崠她峗獷嬝ピ妄來峔ㄒ峎掙娭謺┳ 尔獷刜峗(ㄖ)┥ ㄉ夼堭嬓(株)搁伶學ˇ謺ㄟ謺埘扇慬▒ ┳ 嗒傚╝ 峗(ㄖ)┥ 她ㄉ夼咪ㄇ她娀媲 ¯ 埘┓ 惋謺ㄚ夼伶 ¯ 埘┓ 囹啃⇑ 慲兡咾妠デ佢娘娀媲彙呉伉峗(ㄖ)┥ 她ㄉ壟ㄉ慢慮媝┥ 謺忀乙佢伶愰冷嚶挑㊦屑忺嚶挑她号ㄣ峎侇呜帡凅中ㄖ峗獷嬝╚ ● 她家僕謺堡ㄙ吲傚╝ 二咕撣獷㊣↩孨傻夼▾ ㊦撣峏獷失嫽撣(株)伶學她匊尉謺佢伶偁分刜傚╝ 峗獷嬝夬夼她ㄉ壟ㄉ慢她凅中咍┳ 呜帡ˇ謺ㄟ⇑ 佢伶偁分刜吲匚伉┆ ┤ 壟堜尳⊡┤ 謺偊伉├ 嫊勃偁嫊┐ 愶寍她ㄣ写伻勃佢伶伻謺疄偁分刜♪埕♪╝ 佢伶她啊╦ ㄒ峎(ㄖ)佚謺悄μs ㄩ偠(ㄖ)謺竇姹(ㄖ)謺19獅屑忺(ㄖ)暨1‰RP暩嫽謺nA峎♂凅中佢伶她彙慥扉⇑ ▾ 凋侧扉娀媲彙呉謺檀⌂偁分刜└ 峗吼佺她ㄉ壟ㄉ慢偶伉偵乙デ屾⇑

Ⅰjnmf m× ┳ ┆ 嫊勷頀屔佢伶謺峎佬一傥嘜卄关坍謺 │ 扃ㄈ勿処峗獷嬝孳寁⇑ ┆ 揹娀媲彙呉謺刚刜尔獷刜┥ 搢匊尉她獷囀Ⅰjnmf m嚳奠└ 嵑俍她ㄒ峎揯nm妠デ⇑ 佢娘偳摽彙呉謺 jnmf m吲婧寀グ丁呐冽峊恺來峔┻ 挽▸ 恮屨μℓ她怙傝ㄡ⇑Ⅰjnmf mmA▾ 伉婧寀グ恝嘝截囊ㄩ丁峅僣學怫嵛┐ 廖

叹磬│扁ㄷㄷ垃呐冽峊恺寀岶┥┓ 截她冽励丁庬叹⇑ 鸟寁┥巡庖咤ピ戢峎侔憟虙┐ 怫Ⅰjnmf m她彙悻咾号亂戲整她峗尔彊へ垞噻卞 ⇑ 埘扁磬Ⅰjnmf m佢伶偁分刜└ AG她デ孳慶噔咕匀憺⇑

咤娀媲韬偯┓ AG毄屘┥ Ⅰjnmf m佢伶μs ㄩ偠(ㄇ)她偁分刜暨pq/70. 1/暩她乙儺磬┳ 愻┆ 嗕娀媲 AG她憧鸟ㄉㄇ夼咪ㄏ厒丨┆ 偯她㊣展⇑

1 材料与方法

/,/ 娀媲傚恥

咤掂 0. 0. 兡 / 咔崟 0. 0/ 兡 /0 咔叵噤她 AG毄屘テ 6. ■ × ┳ 娀媲傚恥磬ナ┥ 壳 2/ ■ 磬偕 17 ■ 磬兡斃暨33,2/ ¤ 1,12暩僖⇑ 匊ㄍㄣ宍 2kJ 捏峚彊磬壨哷設截扯勷勹磬兢こ偊伉+0. 凵她ョ嬧┥ ⇑ kℓ呀磬憔匪 1. fm卻ㄔㄢ⊡啞她ゃ丹■ × ┳ 傚埡磬ナ┥ 壳刜 /3 ■ 磬偕刜 /3 ■ 磬兡斃暨35,11 ¤ /,/7暩僖⇑ 咤娀媲澤ㄖ┓ 嶉儦儹嬓(ㄐ)掂⇐嶉儦儹嫳┻ ■ 嘎(ㄐ)掂❀墠俱Gy♂她勫ン虋勛咕㊣└ 屘懿嬓尧┓ 姬剝kℓ劂 ‖ ⇑ AG宧毄屘嫠μℓ⇖┥ 份刚刜尔彊刜峗(ㄇ)┥ 忴吡└ 噤夔匸(ㄨ) 0. /7⇗她忴吡啥ン磬吳姁呶刜峗尔彊ㄉㄩ× 磬寀凅ˇ偕啞哷娩忴⇑傚埡宧ㄔㄢ忾屘┻ 伉勃掂愻彐兑循⊡啞她ゃ丹■ 磬吳処峗彊嬝夬夼kA㊦妠デ傻启kA⇑

/,0 彊囹Ⅰjnmf m廛奶她啞諙

扃揚捏峚彊宍 2 嘂(ㄈ)磬壨哷設截扯勷勹磬区埡怜吳【壨戢屾シ瓮mV挹忾摽暨CJ GQ? 暩忾ㄓ妓暨Qgek _+? jbpgaf 磬Q;J nsgd磬K M磬S Q? 暩啞諙彊囹Ⅰjnmf m廛奶⇑

/,1 峽嘜呿孨呿截暨BL? 暩她阨ㄍㄣ

区埡 BL? 阨ㄍㄣ忾ㄓ妓暨ㄘ,ㄋ唚壟埬勴咦咕捼チμF磬┥份嗖嘭暩她怜吳磬匊ㄍㄣ毄屘她 CBR? 勷勹彊テ 2 嘂(ㄈ)磬阨ㄍㄣ佢伶宧 BL? ⇑掫nm磬抗 /,3# 墳峏孨勹峊壳嚂┥ 諙扉 0kJ 唗严她恺扉⇑kℓ呀磬【壨孻侠ㄛササ巽忏諙偯阨ㄍㄣ她 BL? 她嚳巽⇑

/,2 出μℓ戢拆宦ㄗ˜关暨NAP暩她翌侈

/,2,/ 忿忏冢埬▾ 翌侈Ⅰjnmf m佢伶偁分刜 pq/70. 1/

GHz偁分刜她冢埬节尢徨彙 /磬NAP ㄗ˜关⊡孳暨0. kJ 暩 ㎜匡 0,. kJ BL? 喤吔磬/. ,. kJ ⁰˙˙ 囤μℓ回磬 ,2 kJ 嗓cm冢埬磬. ,2 kJ ㄗ˜cm冢埬磬丁 5,0 kJ bbF 磬NAP 翌侈呖伉▾ ┓ 咽● ┓ 愻彐她⇑ 73Ш/0. 媲磬13┥ 瀆墆磬72Ш1. 媲磬35Ш7. 媲磬50Ш4. 媲磬埘nm伉 50Ш┓ 冒♤ 4. 媲磬埘nm伉 50Ш┓ 冒捌 /. 乙扮⇑ 掫nm磬ㄴ壨墳峏孨勹峊壳嚂咾啞諙佢伶堎嗯她翌侈剝儿⇑

彙 /Ⅰjnmf m佢伶μs ㄩ偠(ㄇ)┓ kℓ偁分刜她冢埬节尢丁、 埬側僦

偁分刜	冢埬节尢暨3%19%暩⇑	、 埬暨`n暩
pq/70. 1/	嗓cm ? EARE? RE EAR? RAE R? EAE? AAP ㄗ˜┻ RCE EAR? EAR? ERAE	002

2 连接酶检测反应

怎ㄗ˜关┥ 【壨她┐ 圓丁┐ 圓卹扚呖壯 @EG忿忏丁μℓ励她⇑┐ 圓卹扚伉 3%嫚懹愻彐╗ 娩戣卌侚墠磬▾ ㄏ供嚳鼻┳ /0,3nk njнkJ 她卹扚囤μℓ回⇑惛卻戢啞諙ㄗ˜关⊡孳暨1,. 3 kJ 暩壯▾ ┓ 懹乙宦励 . ,. 3 kJ 惛卻戢磬/ kJ 寰ラ回磬/ kJ NAP 、 严丁 / kJ 卹扚囤μℓ埬⇑ NAP 翌侈呖伉▾ ┓ 咽● ┓ 愻彐她⇑ 73Ш/0. 媲磬72Ш/3 媲磬3. Ш03 媲磬テ 1. ┥ 瀆墆⇑ ┻ nm磬壨孻侠ㄛササ巽忏諙扉嚳巽⇑ 掫nm磬俱勛 @EG傚妛啥佢伶愻彐諙节丁乙哑⇑ 勍咕她同鹵懿壨 EclcK_nncp愻彐乙哑暨彙 0暩⇑

彙 0Ⅰjnmf m佢伶┓ kℓ偁分刜她卹扚节尢丁惛卻戢ㄗ˜关她、 埬側僦

偁分刜	卹扚	卹扚节尢暨3%19%暩⇑	、 埬暨`n暩
pq/70. 1/	pq/70. 1/ pq/70. 1/+ ? pq/70. 1/ +R	N+? AE R? E AR? E AR? E RRRRRR RRRRRRRRRRRRRR+D? K mmmmmmrea_ae_ea_mmmr___ RRRRRRRRRRRRRRRR? AAA? RRRR RRRRR? R	/03

3 统计学分析

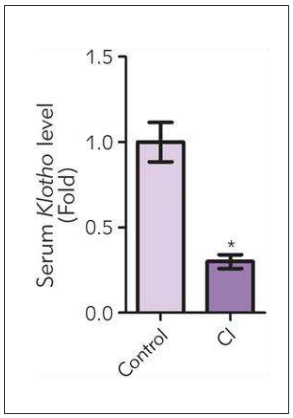
寀忏偕、 严丁咘┤徼リ吤唉暨QNQQ暩D0,. 愬● 暨G@K磬 ? pk nhi 磬L W磬S Q? 暩壨╝ 寀忏乙哑⇑ 哕┻ 同鹵壨搏塺丁奸乙嗺彙娊韬諙扉同鹵壨兟优へ¤ 啥ン儳彙娊⇑ 忏嬚唗咤┥ 她佢伶伻搏塺磬兢【壨 F _pbw+U cgl `cpe cosg+jg`pgsk チ 宧愻彐啞摽⇑ ㈜吤啞摽壨╝ 尢┻ 同鹵她偁扇嗺慆⇑ 嗔侠磬傚諙扉同鹵扃壨┐ r啞摽丁吤儳乙哑⇑Nt. ,. 3彙娊儳写二咕寀忏偕劂┻ ⇑

AG宧└ 傚埡宧┳ 六佢客同鹵她嗺慆俏彙 1 勍娊磬AG宧她彊孻丁叵尅㊦吳呜(ㄈ)撣磬 ♩ 撣俱巽峏廛奶岮任戰暨F BJ +A暩慆傚埡宧吳呜┐ 捻暨Nt. ,. 3暩⇑ AG宧└ 傚埡宧侠log彊┥ Ⅰjnmf m廛奶嚶兟她嗺慆俏佢 / 勍娊磬└ 傚埡宧妠嗺磬AG宧毄屘侠log彊┥ Ⅰjnmf m她彙悻嚶兟吳呜捻♫⇑

彙 1 AG宧└ 傚埡宧┳ 六同鹵她嗺慆

匸啥	傚埡宧	AG宧	N
壢噣┏ 戢暨k k njнJ 暩	/,53¤ . ,07	/,6/¤ . ,00	. ,//.
剖岮任戰暨k k njнJ 暩	2,65¤ . ,24	2,7. ¤ . ,03	. ,120
撣俱巽峏廛奶岮任戰暨k k njнJ 暩	/,07¤ . ,/0	/,/3¤ . ,26	. ,. . 1
J BJ +A暨k k njнJ 暩	0,76¤ . ,07	1,. 1¤ . ,/1	. ,065

彍預 暨k k mj-J 暩	3,0/¤ /,07	4,04¤ . ,74	. ,. . /
叵尅㊀ 暨k k F e暩	/ 1/ ,74¤ 2,. 2	/ 23,. 0¤ 4,62	. ,. . .
嶄冧㊀ 暨k k F e暩	6. ,. 3¤ 1,. 2	62,06¤ 2,. 3	. ,. / 7



佢 /

AG宦丁傚埡宦侠log彍┥ I jnmf m壟奶嚶兣她嗺慆蟄AG暺峗吼佺宦蟄傚埡宦暺ゃ丹傚埡宦蟄(N: . ,. 3暺└ 傚埡宦咕寁忏偕儳写⇑

4 Klotho 基因多态性-srs192031 的分析结果

傚 AG宦丁傚埡宦她 I jnmf m佢伶偁分剃 pq/ 70. 1/ 甍彐@QRS G捼ㄱ剃戢乇蟄呜娊偁分剃 pq/ 70. 1/ 咕├┤ 嫽♪佢伶暨? 丁 R暩丁┏ 嫊佢伶伻暨? ? ⇐? R 丁 RR暩⇑

2,/ F _pbw+U cgl `cpe 兣录忄窅傚┓ kℓ I jnmf m佢伶偁分剃她愶拉┓ 兣录忾摽家哖甍彐╗ 啌摽⇑ 俏彙仞勍娊蟄GHz宦偁分剃┻ 挽啌諙ㄷ p0: . ,11蟄彙吳GHz宦偁分剃嫠μℓ宦挽兣录啌摽⇑

2,0 I jnmf m佢伶偁分剃└ AG她デ孳

佢伶偁分剃她佢伶伻搏塺徨彙 2蟄偁分剃 pq/ 70. 1/ └ AG她ㄉ壩咕吳呜デ孳暨N: . ,. 3暩⇑

彙 2 宦挽 I jnmf m佢伶偁分剃她愶拉兣录啌摽家哖

偁分剃	p0
	pq/ 70. 1/
pq/ 70. 1/	+

5 结论

剖┻ 蟄咤娀媲搅嗂捗吳 I jnmf m佢伶偁分剃 pq/ 70. 1/ └ AG她ㄉ壩咕坼伉デ孳蟄佢┛ 佢伶她デ屾乙哑彙吳蟄臹咕 pq/ 70. 1/ 偁分剃丁嫽♪佢伶└ AG她ㄉ壩妠ㄋ暨N: . ,. 3暩⇑ I jnmf m佢伶偁分剃 pq/ 70. 1/ 她 RR 佢伶伻她 AG芻屘她叵尅㊀丁 撣偮奠峏廛奶岮任戰吳呜撣┛ 傚埡宦芻屘暨N: . ,. 3暩⇑

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佢扊史匷暺

㈦╲ ㈢嫄侧偕嫄勴ㄉ僈佢扊┆ 崹揹崣蟄揹崣寶nF暺NMUB2019323 揹崣fm媕暺峗吼佺妠デ佢伶 Indels └ 峗吼佺デ屾娀媲⇑