AN EXPLORATORY STUDY COMPARING BLOOD METAL CONCENTRATIONS BETWEEN STROKE AND NON-STROKE PATIENTS IN KOREANS

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ABSTRACT

Results from previous studies revealed that metal level in the body is related to certain types of diseases. For example. serum copper level with chronic heart failure, iron and transferrin in the blood serum with acute cerebral vascular diseases, Zn in the CNS, lead with neurotoxicity, hypertension, genetic damage, arsenic with cancer skin lesion, Al with neurobehavioral function (cognitive impairment and memory disorder), and etc. The rate of stroke has increased in recent years and several metals were found to be responsible for causing stroke. This study compared several blood metal concentrations between stroke and non-stroke patients. Patients with stroke (116 samples) and non-stroke (111 samples including lowback pain and others) participated in this study. Total of 227 blood samples were collected and participants completed questionnaires regarding age, gender, occupation, residence, alcohol, smoking, and etc. To be qualified into the stroke group, patients have never experienced stroke previously. Subjects only included ischemic stroke and intracerebral hemorrhage patients diagnosed by brain CT and brain MRI. Patients with high risk of metal exposure such as herbal intake and job related exposure were

excluded. 10ml of blood samples were analyzed by ICP-MS method at the Center of Nature and Science at Sangji University. Metal geometric mean (SD) concentrations in blood of study subjects showed higher values, 2.64-36.12%, than WHO reference values in Mn, Ni, Hg, Se, and As. Metal concentration in blood of stroke patients non-adjusted for potential confounders was higher except for Hg and also higher except for Ni in adjusted for potential confounders. Co was significantly higher in stroke patients (p=0.02) than non-stroke patients adjusted for potential confounders. Regression coefficient values of stroke patients was 0.17-8.25 in each metals. Odd ratio of stroke patients had 0.96 (Ni)-2.68 (Co) compared to non-stroke cases. This result means that Co increase of 1 raises the risk ratio of stroke by 2.86 times. Based on the results, metal concentration in blood seems to affect incidence of stroke.

Keyword

Exploratory Study, Blood Metal Concentrations, Stroke and Non-stroke Patients, Koreans

INTRODUCTION

- Relation of metal level and diseases reported.
  - Serum copper level with chronic heart failure
  - Iron and transferrin in the blood serum with acute cerebral vascular diseases
  - Zn in the central nervous system
  - Lead with neurotoxicity, hypertension, genetic damage
  - Arsenic to cancer skin lesion
  - Al to neurobehavioral function(cognitive impairment and memory disorder)
- Stroke rate in recent increase
- Several metals and stroke relation were found to be responsible
- Tried for comparison of several blood metal concentration between stroke and nonstroke patient

METHODS

- 10ml in blood samples
- ICP-MS; varian, Ultramass 700(USA. 1998)
- Center of Nature and Science at Sangji University, Korea

SUBJECTS

- New patient within 14 days
- Have never been experienced
- Include only ischemic stroke and intracerebrial hemorrhage patients by of use brain CT, brain MRI
- Exclude highly metal exposed patients

ex) Herbal intake, job related intensive exposure of heavy metals

OBJECTIVE CRITERIA OF STROKE

- Patients in one oriental medical hospital located in Wonju, Korea a between Sep/2000- May/2001
- Patients with stroke(116 samples) and nonstroke(111 samples, include low back pain, etc) participated in this study
- Total of 227 blood samples were collected when in hospital
- Questionnaires: Age, sex, job, residence, alcohol, smoking

RESULTS

Table 1. Comparison of general characteristics between stroke and nonstroke patients

	Stroke patients (N=116)		Nonstroke patients (N=111)		
Variable	No	Mean(SD) or %	No	Mean(SD) or %	P-value
Age	116	64 92 (11 72)	111	55 86 (19 22)	0 04
Sex					0 33
Male	48	41 38%	39	35 14%	
Female	68	58 62%	72	64 86%	
Job					0 002
Blue collar	21	18 10%	24	21 62%	
White collar	5	4 31%	7	6 31%	
Non-job	79	68 10%	47	42 34%	
Household	11	9 48%	21	18 92%	
Students	0	0 00%	6	5 41%	
No answer			6	5 41%	
Smoke					0.99
Never	89	76 72%	80	72 07%	
Post smoke	5	4 31%	5	4 50%	
Current smoke	22	18 97%	20	18 02%	
No answer			6	5 41%	
Alcohol					0 10
Never	88	75.86%	78	70 27%	
Post drink	5	4 31%	12	10 81%	
Current drink	23	19 83%	15	13 51%	
No answer			6	5 41%	
Residence					0 02
Urban	3	2 59%	0	0 00%	
Suburban	30	25 86%	43	39 64%	
Rural	83	71 55%	62	55 86%	
No answer			6	5 41%	
Education					0 02
Non	91	78 45%	60	54 05%	
Elementary	6	5 17%	12	10 81%	
Middle-high	16	13 79%	26	23 42%	
College and over	3	2 59%	7	6 31%	
No answer			6	5 41%	
Disease					0 00
Stroke	116	100%	0	0 00%	
Non stroke	0	0 00%	111	100%	
Blood pressure					
Systolic	116	139 57 (18 48)	111	131.06 (20 09)	0.001
Diastolic	116	88 88 (14 19)	111	83 94 (13 32)	0 009

Table 2. Geometric mean (SD), range (Min, Max) and % exceeding upper of WHO limit reference range in heavy metals concentration in blood of all patients (N=227)

Metal	Mean (SD)	Min	Max	% exceeding upper of limit reference	Reference values* (WHO)
As	1.99(1.54)	0	82.27	20 70	2-20
Cd	0.68(0.68)	0	18.92	6 61	0 3-4
Co	0 49(0.51)	0	14.90	2 64	5-10
Cu	242.26(0.50)	71.52	3295 70	3 08	800-1400
Hg	1.82(1.77)	0	1408.10	22.91	2-20
Mn	2.16(2.10)	0	561.16	36.12	8-12
Ni	1.19(1.67)	0	64.72	33 19	1-5(?)
Pb	3.97(2.48)	0	157.59	5.73	50-150
Zn	1339.43(0 47)	639.06	9743.60	3.02	6000-7000

- WHO (1996), Trace elements in Human Nutrition and Health. World Health Organization, Geneva. 258-9
- (?) is uncertain as reference value

Table 3. Geometric mean (SD) of heavy metal concentration in blood of stroke and nonstroke patients* (N=227)

Metal	Stroke	Nonstoke	P
As	2.16(1 57)	1.84(1 51)	0.38
Cd	0.71(0.65)	0.66(0.39)	0.29
Co	0.52(0.54)	0.47(0.48)	0.02
Cu	247.15(0 49)	235(0.51)	0.18
Hg	1.72(1.60)	1.95(1.97)	0.55
Mn	2.34(2.14)	1.97(2.08)	0.47
Ni	1.17(1.72)	1.14(1.62)	0.98
Pb	4.35(2.41)	3.46(2.53)	0 35
Zn	1339.43(0.47)	1326(0.46)	0.86

* Nonadjusted for potential confounder

Table 4. Adjusted geometric mean and SE of heavy metal concentration in blood of stroke and non-stroke patients*(N=227)

Metal	Stroke	Nonstoke	P
As	1 26(1 52)	1.13(1 39)	0 39
Cd	0 44(0 40)	0.42(0.49)	0 66
Co	0 44(0.39)	0.40(0 43)	0 05
Cu	156.02(0.38)	151.41(0 42)	0.41
Hg	3 82(0.46)	3.71(0.76)	0.91
Mn	1.52(0.62)	1.34(0.83)	0.62
Ni	0.78(0.46)	0.84(0.74)	0.73
Pb	1 04(1.20)	1 04(1 21)	0.84
Zn	1510 20(0.38)	1394 09(0 41)	0 81

*Note: Adjusted for sex, age, smoking, alcohol, blue color job, big city residence

Table 5. Regression Coefficient (SE) and odds ratios (SE) for stroke and nonstroke patients respectively, from multiple regression of heavy metal in blood (N=227)

Metal	Beta (SE)	P	Odds ratio(SE)	p
As	1.09(1.12)	0.37	1 10(0.11)	0 38
Cd	1.09(1.27)	0.37	1.10(0 26)	0 69
Co	2.64(1 67)	0.06	2.86(1.49)	0.04
Cu	1.23(1 62)	0.66	1.52(0.76)	0 40
Hg	1.00(1 09)	0 96	1.01(0.09)	0.92
Mn	1.04(1.08)	0.63	1.04(0.09)	0.64
Ni	0 96(1.11)	0.65	0 96(0.09)	0 68
Pb	1.05(1.08)	0 52	1.04(0 08)	0.62
Zn	1.23(1.82)	0.73	1.18(0.72)	0.78

Note: Adjusted for sex, age, smoking, alcohol, blue color job, big city residence.
Beta (SE), odds ratios (SE) values in Table 5 compared nonstroke patients group (control)

Table 6. Regression Coefficient (SE) and odds ratios (SE) for stroke and nonstroke patients who exposured multiple metal, from multiple regression of heavy metal in blood (N=227)

Multiple metal exposure	Beta(SE)	P	Odds Ratio	P
Co * Cu	0.51(0.31)	0 10	1.66(0 51)	0.10
Co * Pb	0.38(0.29)	0.19	1.47(0.43)	0.19
Cu * Pb	0.18(0.30)	0 55	1.20(0.36)	0.55
Co * Zn	0.51(0.31)	0 10	1.66(0 51)	0.10
Cd * Co	0.29(0.29)	0.33	1.33(0.39)	0.33
Co * Cu * Pb	0.38(0.29)	0.19	1.47(0.43)	0.19
Co * Cu * Zn	0.51(0.31)	0.10	1.66(0.51)	0.10
Cd*Co*Cu*Pb	0.21(0.32)	0.51	1.23(0.39)	0.51
Cd*Co*Cu*Zn	0.29(0.29)	0.33	1.33(0.39)	0.33
As*Hg*Mn*Pb*Cd	0.30(0.53)	0 57	1.35(0.71)	0.57
As*Cd*Co*Cu*Zn	0.20(0.30)	0.52	1.22(0.37)	0.52

Note: Adjusted for sex, age, smoking, alcohol, blue color job, big city residence.
Beta (SE), odds ratios (SE) values in Table 6 compared nonstroke patients groups (control)

CONCLUSIONS

- Metal geometric mean(SD) concentrations in blood of study subjects showed higher 2.64-36.12% than WHO reference values in Mn, Ni, Hg, Se, As.
- Metal concentration in blood of stroke patients nonadjusted for potential confounders was higher except Hg only and also higher except Ni only in adjusted for potential confounders. Co stroke patients(p=0.02) was significantly higher than nonstroke in adjusted for potential confounders.
- Regression coefficient values of stroke patients was 0.17-8.25 in each metals.
- Odd ratio of stroke patients had 0.96(Ni)-2.68(Co) compared to nonstroke. This result means that with a Co increase of 1, the risk ratio of stroke increases 2.86 times.
- Totally in these results, metal concentration in blood seems to affect incidence of stroke.
- Further study related to this study will be needed.