# THE SEQUENTIAL CHANGE OF SERUM HEPCIDIN-25(HPC) LEVEL AND OTHER IRON METABOLISM MARKERS AFTER SINGLE INTRAVENOUS IRON ADMINISTRATION IN HEMODIALYSIS(HD) PATIENTS

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## BACKGRUOND

**Hepcidin-25 (HPC) is a crucial player of iron metabolism. Iron-overload and inflammation stimulate HPC production, whereas anemia, iron depletion inhibit HPC production. In our previous cross-sectional study, there was a significant positive correlation between serum ferritin and HPC in hemodialysis (HD) patients, and moreover, serum level of ferritin was the predictor of HPC level (Noriko Saito ASN2012). However, the sequential changes of HPC and other iron parameters are not elucidated in HD patients after intravenous iron administration (IVIA).**

## AIM OF THE STUDY

**To examine the relationship between HPC and other iron metabolism markers after IVIA in HD patients.**

## RESULTS

**1 . TSAT before IVIA was 20 (14-27)%, immediately increased and reached the peak at 0.5 hour as 81 (65-100)%, significantly decreased at 2 hours and returned to the level as same as before IVIA at 44 hours. In 6 (26%) patients, transferrin was oversaturated at 0.5 hour. (The data are indicated as medians (interquartile range ) or numbers (%).) (Figure 1)**
**Friedman test * $p<0.05$ vs 0 hour**

**2. HPC level before IVIA was 5.1 (0.6-20.3) ng/ml, significantly elevated after 4 hours at 15.1 (0.6-20.3) ng/ml ($p<0.05$), reached the peak after 20 hours at 36.5 (5.5-57.6) ng/ml and gradually decreased to 20.7 (3.6-41.3) ng/ml after 44 hours. (Figure 2) Friedman test * $p<0.05$ vs 0 hour**

**3. Ferritin level and 8 OHdG level before IVIA were 110 (49-216) ng/ml and 0.197 (0.120-0.268) ng/ml, significantly elevated after 20 hours at 151 (83-222) ng/ml ($p < 0.01$) and 0.290 (0.196-0.374) ng/ml ($p < 0.01$), respectively. The values of these parameters were unchanged at 44 hours. (Figure 3, 4)**
**Friedman test * $p<0.05$ vs 0 hour**

**4. Stepwise analysis indicated that HPC level at 4hours, 8OHdG at 0 hour and TSAT at 2 hours were predictor of ferritin level at 20 hours. (Table 1)**

## CONCLUSIONS

**In HD patients, after single IVIA, firstly TSAT and then, HPC level, and finally ferritin increased. Our sequential study had revealed the different kinetic patterns of iron parameters after IVIA in HD patients.**
**HPC, 8OHdG and TSAT could be the reliable predictor of ferritin level.**

**Figures: sequential changes of iron parameters after intravenous iron administration**

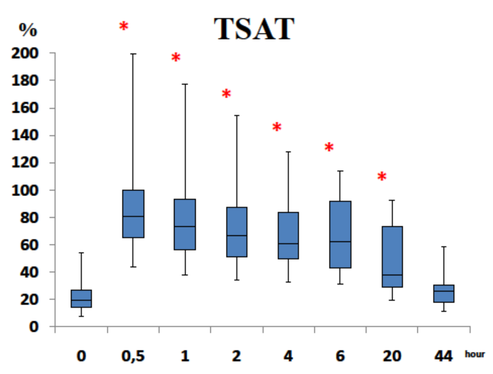


Figure 1

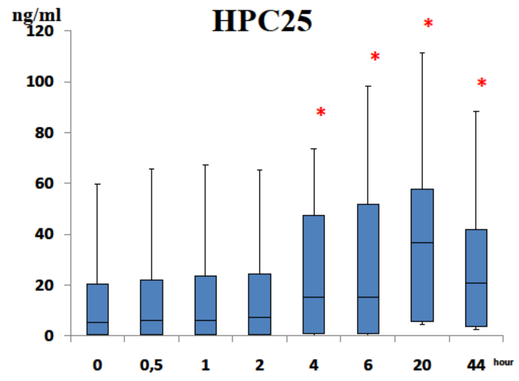


Figure 2

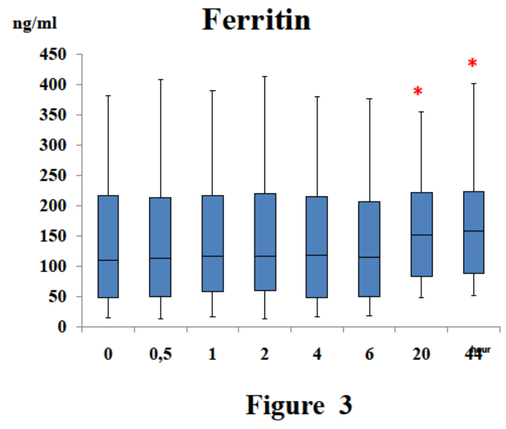


Figure 3

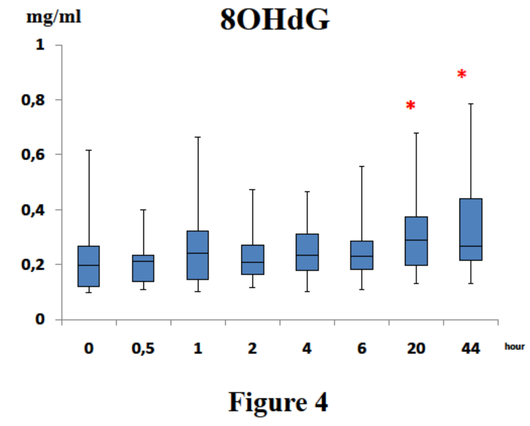


Figure 4

**Table 1. Stepwise multiple regression report for ferritin at 20 hours**

| Parameters | β | P Value | Adjusted $R^2$ |
|---|---|---|---|
| HPC25 at 4hours | 0.588 | <0.001 | 0.886 |
| 8OHdG at 0hour | 0.454 | <0.001 | |
| TSAT at 2hours | 0.225 | 0.006 | |

**B shows standard regression coefficient. $R^2$ shows coefficient of determination.**

## SUBJECTIVES and METHODS

23 HD patients were enrolled in the study. 83% of the patients received erythropoiesis-stimulating agents. (Table 2)
The laboratory data of HD patients before IVIA and healthy normal volunteers were compared. (Table 3)
HD patients were administered ferric oxide (Fe 40mg) intravenously after HD session. We evaluated the following markers before and at 0.5, 1, 2, 4, 6, 20 and 44 hours after IVIA : HPC, transferrin (Tf), 8-oxo-2'-deoxyguanosine (8-OHdG), soluble transferrin receptor(sTfR) and standard hematological parameters including high sensitive CRP (hs-CRP).
Serum HPC level was determined by LS-MS/MS. 8-OHdG was measured using ELISA.
Serum Tf and hs-CRP levels were measured by turbidimetric immunoassay and nephelometry, respectively.
The transferrin saturation (TSAT) value (%) was calculated from the serum iron and Tf values using the formula :
serum iron (μmol/L) / Tf (g/L) x 3.8. (Jaakko Parkkinen, Neprol Dial Transplant 2000:15;1827-1834.)

**Table2. Patient characteristics**

| | | | |
|---|---|---|---|
| Underlying renal disease | | | |
| Chronic glomerulonephritis | n=12 | | |
| Diabetic nephropathy | n=5 | | |
| Nephrosclerosis | n=5 | | |
| Congenital renal dysplasia | n=1 | | |
| Time on hemodialysis (years) | 14.6±13.3 | | |
| Dry weight (kg) | 45.3±8.5 | | |
| Dose of Erythropoiesis-stimulating agents | | | |
| darbepoetinα | n=12 | 43±36 | μg/week |
| epoetinβ | n=4 | 4313±3375 | IU/week |
| epoetinβ pegol | n=3 | 167±76 | μg/week |
| Intravenous iron therapy | n=0 | | |
| Oral iron administration | n=0 | | |

**Table 3 Baseline laboratory data of the HD patients before intravenous iron administration and normal control subjects**

| | Hemodialysis patients | | Control subjects | | p value |
|---|---|---|---|---|---|
| n(male/female) | 23(14/9) | | 20(9/11) | | 0.304 |
| Age(years) | 73.0 | (65.0-83.0) | 45.5 | (34.3-50.5) | <0.001 |
| RBC($10^4$/μl) | 355 | (300-387) | 464 | (417-502) | <0.001 |
| Hb(g/dl) | 10.9 | (9.1-12.2) | 14.5 | (13.2-15.2) | <0.001 |
| MCV(fl) | 91.2 | (88.6-96.1) | 93.1 | (88.7-95.9) | 0.836 |
| MCHC(%) | 33.6 | (32.5-34.5) | 33.5 | (32.5-34.2) | 0.864 |
| Iron(μg/dl) | 51 | (34-72) | 102 | (84-134) | <0.001 |
| UIBC(μg/dl) | 181 | (155-201) | 242 | (152-276) | 0.018 |
| TSAT(%) | 19.6 | (14.0－27.0) | 26.3 | (22.8－44.3) | 0.068 |
| transferrin(mg/dl) | 175 | (148-203) | 246 | (223-281) | <0.001 |
| Ferritin(ng/dl) | 110 | (49-216) | 67 | (26-94) | 0.056 |
| hs-CRP(ng/ml) | 2060 | (1170-5800) | 113 | (55-320) | <0.001 |
| Hepcidin25(ng/ml) | 5.1 | (0.6-20.3) | 9.5 | (2.7-12.7) | 0.626 |
| sTfR(nmol/l) | 23.5 | (17.5-31.0) | 14.9 | (11.3-19.9) | 0.002 |
| 8-OHdG(ng/ml) | 0.2 | (0.12-0.27) | 0.15 | (0.11-0.28) | 0.609 |

**Data are expressed as mean (interquartile range)**


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