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Original article

Risk factors for herpes zoster reactivation in maintenance hemodialysis patients

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ABSTRACT

Objective: Herpes zoster (HZ) reactivation is common in immunocompromised patients. Advanced renal failure is also reportedly associated with impairment of cellular immunity. There is not any study yet assessing risk factors of HZ reactivation in hemodialysis patients.

Methods: All patients undergoing maintenance hemodialysis for more than 3 months and who developed HZ between 2000/01/01 and 2009/12/31 in a tertiary referral medical center were identified, and matched 1:1 to hemodialysis patients without HZ by age and gender. Multivariate-adjusted conditional logistic regression model was constructed to determine possible risk factors.

Results: Out of a total of 126 maintenance hemodialysis patients (65.3% female), 63 belonged to the HZ reactivation group and 63 to the age/sex matched control patients. Conditional logistic regression model linked corticosteroid use with heightened risk (odds ratio [OR] 20.2, 95% confidence interval [CI] 3.5–125.6; $p = 0.002$), while iron therapy and 1α-hydroxylated vitamin D were associated with significantly lower likelihood of developing HZ (OR 0.12, 95%CI 0.0–0.6; $p = 0.01$, and OR 0.06, 95% CI 0.0–0.4; $p = 0.005$ respectively).

Conclusions: Use of iron preparations and 1α-hydroxylated vitamin D is potentially associated with less risk of developing HZ reactivation in maintenance hemodialysis patients.

1. Introduction

Herpes zoster (HZ), or shingles, is a painful reactivation of latent varicella zoster virus (VZV), presenting with grouped vesicles on an erythematous base along defined dermatomal area, visceral organ damage (hepatitis), or central nervous system involvement (encephalitis) [1]. HZ reactivation is associated with increased mortality in hospitalized patients, owing to their immunocompromised background [2]. Shingles is also found to increase mortality in immunocompetent elderly patients [3]. Most people acquire such infection during early childhood, with viral latency in the sensory root ganglions. Reactivation occurs when host immunity wanes and HZ virus cruises along peripheral nerve with resultant symptoms.

Patients with advanced renal failure are immunosuppressed. In vitro evidence suggests that uremia impairs proliferative response of T-cell to mitogen and decreases downstream effector function [4,5]. Clinically, end-stage renal disease (ESRD) patients have a 6–50 fold higher risk of acquiring tuberculosis infection compared to the general population, and the mortality from sepsis in ESRD patients is also higher in ESRD [6,7]. However, literature is sparse regarding HZ reactivation and the associated features. The factors associated with HZ reactivation in ESRD patients have not been elucidated before. We hypothesized that ESRD patients with HZ reactivation may harbor predisposing factors entailed by uremia. Therefore we conducted this matched case–control study to investigate the characteristics and the associated risk factors of ESRD patients under maintenance hemodialysis predisposing to HZ reactivation.

2. Materials and methods

National Taiwan University Hospital (NTUH) is a tertiary medical referral center, with a patient population coming from all over the country. The dialysis unit is composed of fifty dialysis beds, which provide dialysis treatments to both in-patients and outpatients, with an average 250 patients undergoing maintenance hemodialysis. All dialysis patients aged 20 years or more who received in-patient or out-patient medical service in NTUH between 2000/01/01 and 2009/12/31 were identified by ICD-9-CM (International Classification of Diseases, Ninth edition, Clinical Modification) diagnostic codes of 585.x (chronic renal failure), 403.x (hypertensive renal disease), 404.x (hypertensive renal and heart disease) and V45.11 (renal dialysis). We performed a retrospective chart review to verify these patients' dialysis status. Those who received dialysis due to acute renal failure, who were dialyzed for less than 3 months, who had history of solid organ transplantation, and those with concomitant pregnancy were excluded. From this cohort, we further recruited patients with herpes zoster reactivation, through cross-matching with ICD-9-CM diagnostic code of 053.x (herpes zoster).

Subsequent chart reviews were performed to evaluate the detail of HZ events, including confirmation of diagnosis, the dialysis vintage during

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the event, the dermatomal distribution, the allocated treatment, and treatment related adverse event or drug overdose. Treatment related overdose was defined as any adverse effect occurring within one week of drug use, with symptoms compatible with overdose. Cutaneous HZ was diagnosed by dermatologists with the characteristic grouped vesicles within dermatomal distribution, with or without Tzanck smear. Patients' demographic profiles including age, sex, other concomitant comorbidities (diabetes mellitus [DM], hypertension, congestive heart failure [CHF], coronary artery disease [CAD], hepatic disease, any malignancy, and cerebrovascular event [CVA]), primary renal pathology leading to ESRD, and concurrent medication regimen were recorded. Hypertension was defined as blood pressure higher than 140/90 mm Hg pre-dialysis on more than two occasions, or use of any anti-hypertensive medications. DM was defined according to fasting blood glucose higher than 126 mg/dL at any time, serum glycated hemoglobin value higher than 6.5%, or use of any anti-diabetic agents. CHF was diagnosed with symptoms and echocardiographic findings. Diagnosis of CAD was based on ischemic symptoms and image findings. Hepatic disease included liver cirrhosis or chronic active hepatitis (B or C). CVA was defined as history of any cerebrovascular events occurring during the past year. Primary renal pathology was established through biopsy or appropriate clinical setting. Concomitant medication, either through oral, intravenous or subcutaneous route, was defined as the use of such medication starting at least 1 month before the index event. Drug compliance was established with thrice weekly dialysis clinic visits and pill counts. We described treatment related overdose as any adverse effect occurring with clinically inappropriate antibiotic or analgesic dosage. Otherwise the adverse events were attributed to treatment related adverse effects. Monthly laboratory data were also collected, and the most recent results before the date HZ occurred were recorded.

Literature review suggests that demographic profiles such as age and gender play an important role in determining the incidence of HZ reactivation [8]. In light of this, we conducted this study with a case–control design using one-to-one pairwise matching to identify potential factors associated with HZ reactivation in uremic patients other than age and gender. Without knowledge of the potential influential factors and study design, an independent researcher randomly selected the control subjects without development of HZ from our hemodialysis unit during the entire recruitment period (2000/01/01–2009/12/31). These control patients were selected based upon matching with cases in age (+/- 3 years) and gender. Varicella zoster serology was not obtained due to the high local seroprevalence rate [9]. All variables including comorbidities, primary renal pathologies, concurrent medications and laboratory profiles were recorded in the same manner as in HZ group patients. We analyzed the HZ and control group with respect to the potentially associated factors. The protocol of this study was approved by the local institutional review board (National Taiwan University Hospital Research Ethics Committee) (Registration no. 201108039RC). The data were independently processed and were not released to the researchers. This study did not involve therapeutic interventions or diagnostic tests but retrospective chart and record reviews, and the National Taiwan University Hospital Research Ethics Committee specifically waived the need for informed consent from the study subjects.

The results were analyzed statistically using SPSS software version 18 (SPSS Inc., Chicago, IL). The distributional properties of continuous variables were expressed as median (interquartile range [IQR], 25th–75th percentile), whereas categorical variables were presented as frequencies and percentages. The variables we collected did not follow normal distribution, such that characteristics between groups were compared with Wilcoxon signed rank test in case of continuous variables, or McNemar test in dichotomic variables. We performed a univariate analysis to identify the possible factors associated with HZ reactivation. Factors with a p-value <0.1 were entered into multivariable-adjusted conditional logistic regression model for further analysis. All statistical results with a p-value <0.05 were considered significant.

3. Results

A total of 63 ESRD patients experiencing HZ reactivation were identified through the aforementioned process. Another 63 age- and sex-matched control patients were also selected. Among HZ group, one patient developed two cutaneous HZ episodes during the observation period, while only the first one was included in the analysis reported. Disseminated herpes zoster infection was not reported. The characteristics of all patients are summarized in Table 1.

The median age of HZ and control groups were 62 and 63 years respectively, and nearly one-third of patients from both groups were male. Dialysis vintage was similar between groups (HZ group vs. control, 2.0 vs. 3.2 years; $p=0.233$). Compared to control, HZ group had significantly more cerebrovascular accidents in the past (HZ group vs. control, 19% vs. 4.8%; $p=0.022$), and it was more likely to use corticosteroids within the past month before the index event (HZ group vs. control, 14.3% vs. 1.6%; $p<0.001$). However, HZ group was less likely to have received iron preparations and 1α-hydroxylated vitamin D treatment continuously within the past month (for iron preparations, HZ group vs. control, 10.5% vs. 47.6%; $p=0.021$; for vitamin D, HZ group vs. control, 5.4% vs. 46.0%; $p<0.001$). There was no difference in the percentage of liver cirrhosis or chronic active hepatitis between groups. HZ group also had significantly higher C-reactive protein (CRP) levels ($p<0.001$) and ferritin levels ($p=0.002$), but lower hemoglobin ($p=0.041$) and intact parathyroid hormone (iPTH) values ($p=0.021$). Significantly more HZ patients had hypertension as their primary renal disease (HZ group

Table 1
Demographic profiles of ESRD patients with and without herpes zoster reactivation.

	With HZ (n = 63)	Without HZ (n = 63)	p Value
Age (yr)	62.0 (27.0–85.0)	63.0 (29.0–88.0)	0.893
Sex (male/female)	22/41	22/41	1.000
Dialysis vintage (yr)	2.0 (0.5–5.0)	3.2 (0.8–6.7)	0.233
Comorbidities			
Hypertension	51 (81.0)	51 (81.0)	1.000
Diabetes mellitus	16 (25.4)	19 (30.2)	0.678
Heart failure	11 (17.5)	8 (12.7)	0.607
Coronary artery disease	13 (20.6)	13 (20.6)	1.000
Hepatitis or cirrhosis	8 (12.7)	2 (3.2)	0.109
Cerebrovascular accident*	12 (19.0)	3 (4.8)	0.022
Malignancy	11 (17.5)	15 (23.8)	0.541
Etiology of renal diseases			
Diabetes mellitus	16 (25.4)	19 (30.2)	0.426
Hypertension	12 (19.0)	3 (4.8)	0.013
Glomerulonephritis	24 (38.0)	29 (45.9)	0.371
Others	12 (19.0)	12 (19.0)	1.000
Medications			
Corticosteroids	9 (14.3)	1 (1.6)	<0.001
Immunosuppressants	5 (7.9)	0 (0.0)	0.063
ACEI/ARB	15 (27.3)	24 (38.1)	0.345
Iron therapy	6 (10.5)	30 (47.6)	0.021
Erythropoietin	49 (84.5)	59 (93.7)	0.267
Statins	5 (8.9)	13 (20.6)	0.146
1α-hydroxylated vitamin D	3 (5.4)	29 (46.0)	<0.001
Laboratory profiles			
Hemoglobin (g/dL)	9.8 (6.8–14.0)	10.7 (5.7–14.6)	0.041
Albumin (g/dL)	4.1 (2.2–5.1)	4.1 (3.4–4.6)	0.211
Creatinine (mg/dL)	6.2 (4.5–11.4)	7.8 (6.5–12.3)	0.092
Calcium (total) (meq/L)	2.3 (1.9–3.5)	2.3 (1.9–3.7)	0.381
Phosphorus (mg/dL)	4.5 (1.8–9.6)	4.7 (2.5–10.5)	0.242
Intact PTH (pg/mL)	140.0 (1.1–1363)	282.0 (5.1–3000.0)	0.021
CRP (mg/dL)	1.6 (0.0–20.8)	0.3 (0.0–16.1)	<0.001
Ferritin (ng/mL)	483 (67.2–7720.0)	326.0 (16.6–1058)	0.002
ISAT (%)	26.0 (12.0–94.0)	23.0 (7.0–56.0)	0.211

Data are expressed as median (25/75th percentile) for continuous variables or number of subjects with percentage in parenthesis for categorical variables.
Abbreviations: ACEI, angiotensin converting enzyme inhibitor ; ARB, angiotensin receptor blocker ; CRP, C-reactive protein ; ESRD, end-stage renal disease ; HZ, herpes zoster ; ISAT, iron saturation ; PTH, parathyroid hormone.
* History of cerebrovascular accident within the past year.

vs. control, 19 vs. 4.8%; p = 0.013), but there was no difference between groups regarding other primary renal disease etiologies.

The dermatome distributions are as follows: 44.4% thoracic nerves, 20.6% cranial nerves, 19.0% cervical nerves, 14.3% lumbar nerves and 1.6% sacral nerves. Patients with HZ were commonly managed conservatively without antivirals (42.9%). Approximately one-third of patients (34.9%) developing HZ were not given any analgesia, and even if analgesia were provided, most were ineffective (acetaminophen 41.3%). One out of six patients (17.5%) developed treatment-related overdose or adverse effects, characterized mostly by consciousness disturbances and seizures.

Factors associated with HZ reactivation in maintenance hemodialysis patients are listed in Table 2. A univariate analysis of all variables listed in Table 1 shows that history of CVAs (odds ratio [OR] 5.5, 95% confidence interval [CI] 1.2–24.8; p = 0.027), use of corticosteroids (OR 9.0, 95%CI 1.1–71.0; p = 0.037) and elevated CRP (OR 1.36, 95%CI 1.0–1.8; p = 0.035) as well as ferritin levels (OR 1.002, 95%CI 1.001–1.003; p-0.009) were associated with more HZ reactivation, while iron supplements (OR 0.08, 95%CI 0.0–0.3; p = 0.001), use of 1α-hydroxylated vitamin D (OR 0.08, 95%CI 0.0–0.3; p = 0.001) and higher iPTH levels (OR 0.999, 95%CI 0.99–1.0; p = 0.047) were associated with less likelihood of HZ activation. We further constructed a multivariate-adjusted conditional logistic regression model by stepwise variable selection, with variables whose p-value was <0.1 in the univariate analysis. Corticosteroid administration for more than 1 month was significantly associated with more severe HZ reactivation (OR 20.2, 95% CI 3.5–125.6; p = 0.002). On the other hand, iron and 1α-hydroxylated vitamin D administrations were linked to a lower percentage of HZ reactivation (OR 0.12, 95% CI 0.0–0.6; p = 0.01 and OR 0.06, 95% CI 0.0–0.4; p = 0.005 respectively). A re-analysis excluding patients with SLE using corticosteroids or those with liver diseases did not influence our results significantly.

4. Discussion

In the present study, utilizing a well-matched cohort of patients with HZ, we demonstrated the important association between the use of iron supplementations, 1α-hydroxylated vitamin D, corticosteroids and development of HZ reactivation in ESRD patients.

Our HZ patients are unique, in that two-thirds of these are female. A further analysis of gender distribution based on different age strata shows a significant increase of female patients in advanced age subgroups. Similar findings have been documented previously [10,11]. Chidiac and coworkers, in a nationwide primary care service survey, showed that the female predominance in HZ patients emerged gradually as age rose [10]. In the older-than-75 subgroup, female patients with HZ accounts for nearly 100% of the annual incidence. Our data is consistent with their findings, and this suggests that female sex as a risk factor for HZ may also apply to the ESRD population.

Table 2
Univariate and multivariate conditional logistic regression analysis of variables associated with herpes zoster reactivation.

Variables	Univariate analysis		Multivariate analysis	
	O.R. (95% CI)	p Value	O.R. (95% CI)	p Value
Hepatitis or cirrhosis	4.00 (0.8–18.8)	0.08		
Cerebrovascular accident	5.50 (1.2–24.8)	0.027		
Use of iron therapy	0.08 (0.0–0.3)	0.001	0.12 (0.0–0.6)	0.010
Use of corticosteroids	9.0 (1.1–71.0)	0.037	20.2 (3.5–125.6)	0.002
Use of statins	0.33 (0.1–1.2)	0.099		
Use of 1α-hydroxylated vitamin D	0.08 (0.0–0.3)	0.001	0.06 (0.0–0.4)	0.005
CRP	1.36 (1.0–1.8)	0.035		
Intact PTH	0.999 (0.99–1.0)	0.047		
Ferritin	1.002 (1.001–1.003)	0.009		

Abbreviations: CI, confidence interval; CRP, C-reactive protein; OR, odds ratio; PTH, parathyroid hormone.

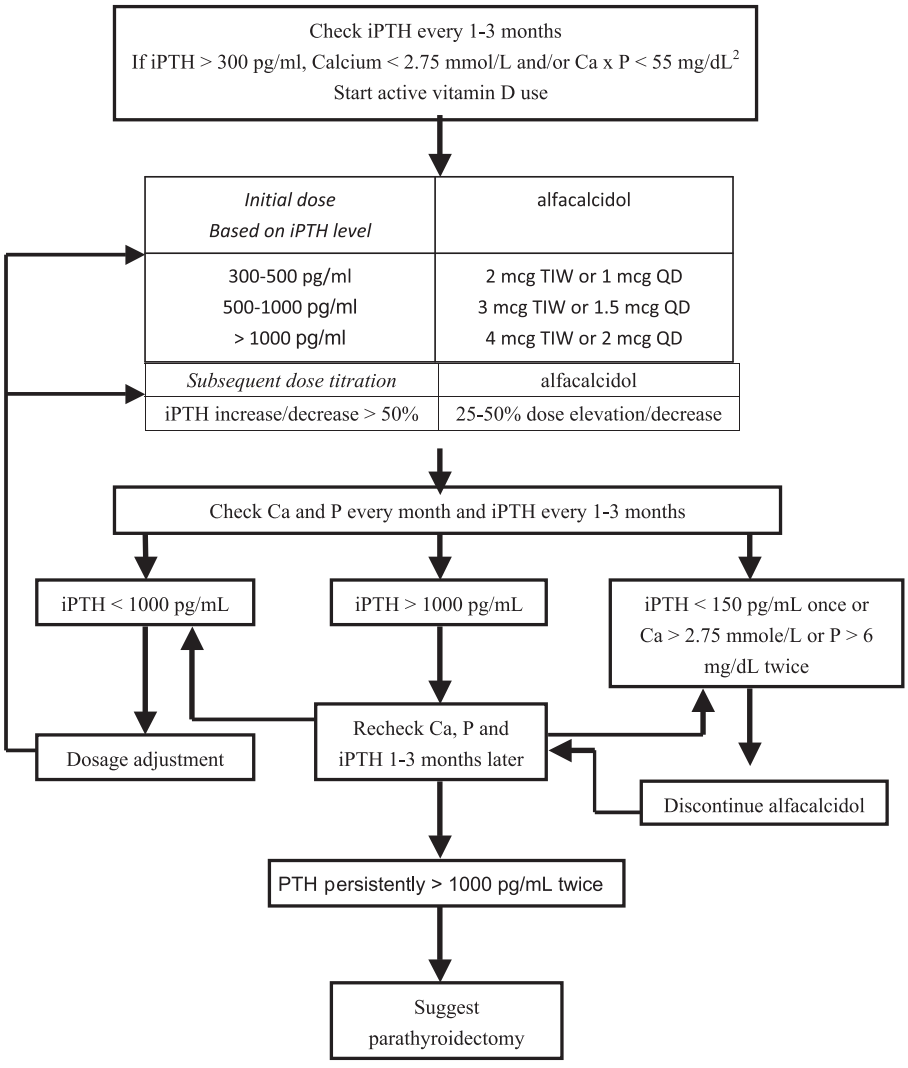
In the current study, the dermatomal distributions of cutaneous HZ in our hemodialysis patients were compatible with the traditional patterns [12]. Most analgesic agents offered to these HZ patients were ineffective (acetaminophen, non-steroidal anti-inflammatory agents). The behavioral factors leading to these inappropriate regimens might need further elucidation.

In univariate analysis, percentage of patients with a history of CVAs was higher in HZ group. The neurologic complications of VZV infection may rarely include myelitis, optic neuritis, meningitis/encephalitis, or vasculopathy with stroke-like presentations [13]. These symptoms can also occur without any cutaneous rashes (zoster *sine herpete*) [14]. It could be then difficult to differentiate between atherosclerotic stroke, HZ-induced vasculopathy with stroke-like symptoms and parenchymal encephalitis in adult patients, without cerebrospinal fluid (CSF) sampling [13,14]. Acute encephalomyelitis caused by VZV usually occurs in the elderly (with immune-senescence), and presents with fever, consciousness change or meningeal signs [15,16]. Vascular lesions on neuroimaging studies are infrequent, with low percentages of abnormal CNS findings [15,16]. VZV vasculopathy is characterized by large vessel unifocal arteritis or small vessel multifocal vasculopathy, with a preceding zoster event by weeks to months [13]. Findings of neuroimaging studies in VZV vasculopathy are similar to those of atherosclerotic strokes. In our patients, although lumbar punctures were not performed, we did identify several lines of evidence suggesting atherosclerotic strokes as the origins of their stroke-like events rather than VZV vasculopathy or encephalitis. The 15 patients with a history of CVAs all presented with focal neurologic symptoms without fever or consciousness disturbance, and neuroimaging studies reported typical focal parenchymal infarcts on magnetic resonance imaging/computed tomography, arguing against encephalitis. Although viral vasculopathy is a concern, we suggest that this is less likely. The index zoster events were preceded by the CVAs by months, quite unusual for VZV vasculopathy [13]. Nonetheless, a definite conclusion can only be made with CSF studies for VZV DNA or specific antibodies [14].

The subsequent multivariate analysis revealed that use of 1α-hydroxylated vitamin D was associated with significantly less HZ reactivation in hemodialysis patients (OR 0.06, 95% C.I. 0.0–0.4). In our unit, active vitamin D is used per protocol (Table 3) to suppress secondary hyperparathyroidism and to treat renal osteodystrophy. To further explore this connection, indication, duration of use and dosage of 1α-hydroxylated vitamin D in each group was analyzed (Table 4). HZ group patients received on average significantly lower dosage and shorter duration of 1α-hydroxylated vitamin D. This further suggests a potential biologic relationship between a lower percentage of active vitamin D use and the development of herpes zoster. A sensitivity analysis using a concurrent medication definition of at least 2 months only attenuated the association mildly (OR 0.1, 95% C.I. 0.0–0.4).

For ESRD patients, vitamin D is utilized for suppression of secondary hyperparathyroidism or correction of hypocalcemia, and it is frequently given in "active" form (1α-hydroxylated), which does not require renal activation but requires hepatic activation. The dosage is usually higher than that used for nutritional replacement [17]. Previous works demonstrated that vitamin D deficiency correlates with higher risk of respiratory tract infection and tuberculosis [18,19], and multiple studies suggested that vitamin D possesses non-classical immunomodulatory effects [20]. For HZ, vitamin D reportedly modulates T-cell repertoires and induces antimicrobial peptide (beta defensin) production, potentially associated with anti-viral activity [21,22]. This lends support to our epidemiologic findings. In addition, an uneven distribution of hepatic diseases causing drug activation defect is unlikely to affect our results, since a sensitivity analysis excluding these patients did not significantly alter the results. However, our study findings should be interpreted cautiously. First, different forms of vitamin D between previous studies and ours preclude a head-to-head comparison and the drawing of conclusions. Second, use of 1α-hydroxylated vitamin D in ESRD patients could, on the contrary, represent a marker of concurrent secondary hyperparathyroidism, and the associated lower HZ

Table 3
Active vitamin D prescription protocol.



prevalence may be the effect of hyperparathyroidism rather than drug use per se. Uremic hyperparathyroidism had been found to be associated with dysregulated B and T cell proliferation as well as immunoglobulin production [23]. Our control group did have significantly higher iPTH values than HZ group (HZ group vs. control, 140.0 vs. 280.0 pg/mL; $p = 0.021$). In addition, the higher dosage and longer duration of active vitamin D use in control group underlies the possibility of severer osteodystrophy. A comparison of serum alkaline phosphatase levels also supported our theory that control group had higher iPTH levels and severer bone diseases, necessitating more active vitamin D therapies (HZ group vs. control, 412 vs. 322 IU/L; $p = 0.042$). Active vitamin D might have a collateral effect on the incidence of HZ reactivation in addition to the suppression of hyperparathyroidism in control group. Though the similar serum calcium and phosphate levels between HZ and control group seem to argue against a strong vitamin D effect, they could also be influenced by the use of phosphate binders or dietary content in uremic patients. Nonetheless, the interplay between use of active vitamin D, secondary hyperparathyroidism, renal osteodystrophy, and lower percentage of HZ events is complicated but interesting. We believe that our findings are important and may warrant more detailed mechanistic research. Further large-scale clinical studies are awaited for confirmation.

The role of iron in susceptibility to infection or suppression of infection is currently unclear. Our finding of a protective role against HZ by iron preparations seems counter-intuitive, since intravenous iron formula is potentially oxidizing, and free irons may induce tissue damages and provide substrates for microbial survival [24]. Iron overload also reportedly leads to more bacterial infection in patients on maintenance hemodialysis [25]. By contrast, iron therapy has been shown to inhibit hepatitis C virus replication in vitro [26]. There are currently few reports investigating the relationship between iron supplementations and the probability of infection. Several observations in our patients suggest that this association should be interpreted alternatively: Our HZ group had higher CRP and ferritin levels but lower hemoglobin values than control, with similar percentages of erythropoietin use ($p = 0.267$). All patients in our analysis did not receive blood transfusions in the preceding 3 months before the index HZ events. It is then likely that the inflammatory condition of HZ group patients was more intense (higher CR and, ferritin levels), and consequently displayed lower hemoglobin levels. This chronic inflammation might pave the way toward immune dysregulation and underlie the susceptibility to HZ reactivation. Iron-use per se does not "lower the risk of HZ incidence", but alternatively, it is the elevation of risk in the less-iron-use group that produces

Table 4
Dosage, duration and indication of the drugs implicated in multivariate analysis.

	Indication		Dosage		Duration	
	HZ (n)	Control (n)	HZ	Control	HZ	Control
Corticosteroids	Lupus (6) SS (1), MPA (1), AI (1)	Lupus (1)	Prednisolone 14.7 (7.8–38.2) mg/day	Prednisolone 5 mg/day	43.7 (5.4–88.2) mo	84 (9.8–102.6) mo
Active vitamin D	SHPT (3)	SHPT (29)	Alfacalcidol 2.3 (1.2–3.3) μg/wk[a]	Alfacalcidol 3.9 (0.7–9.2) mcg/wk	3 (1.4–4.5) mo[a]	8.4 (3–22) mo
Iron therapy	Anemia (6)[b]	Anemia (30)[b]	Ferric chloride 120 mg/wk[c]	Ferric chloride 120 mg/wk	3 (1.3–6.5) mo[a]	9 (1.4–11.1) mo

Continuous data are expressed in arithmetic mean, with 25% and 75% range in parenthesis.
Abbreviations: AI, adrenal insufficiency; HZ, herpes zoster; MPA, microscopic polyangiitis; SHPT, secondary hyperparathyroidism; SS, Sjogren Syndrome; mo, month; wk, week.
[a] $p<0.05$ with Student's *t*-test.
[b] Hemodialysis patients with inadequate ferritin level and under concurrent erythropoietin therapy were given iron for hemoglobin correction.
[c] Intravenous iron therapy was given as a standard formula of 120 mg ferric chloride per week in hemodialysis patients in authors' institution.

this paradoxical result. Physicians are falsely prompted to lower or discontinue their iron prescriptions in HZ group by inflammation-induced hyperferritinemia. Use of iron therapy, in this regard, may simply be a "marker" of the uneven distribution of inflammation extent between groups, rather than the effect of iron therapy per se.

Our study has its strengths. This is the first study to investigate the risk factors of HZ reactivation in ESRD patients, and the novelty of our findings may stimulate further researches. However, its limitations include inadequate case numbers, its retrospective nature, and the potential missing of cases by limiting the definition of continuous medication use to 1 month (patients using these medications intermittently would not be recruited). Finally, we did not measure the serum 25-OH vitamin D level, and the true biologic nature of vitamin D therapy cannot be determined accordingly.

In conclusion, in our age and sex-matched ESRD patients, use of 1α-hydroxylated vitamin D and iron preparations is associated with fewer HZ reactivation in ESRD population, while use of corticosteroids is related to more HZ events. Further study is warranted to delineate the whole pictures of herpes zoster in the maintenance hemodialysis populations.

5. Learning points

- Herpes zoster reactivation occurs more commonly in female patients with end-stage renal disease.
- Adverse effects occur in 17.5% of treatment for patients with end-stage renal disease during hemodialysis developing herpes zoster.
- Use of active vitamin D and iron supplement is potentially associated with a lower incidence of herpes zoster in maintenance hemodialysis patients.

6. Funding

None declared.

7. Conflict of interests

None declared. The authors state that they have no conflicts of interest.

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