

Association Between Breakfast Frequency and the Risk of Musculoskeletal Pain in Chinese college students – A Cohort Study

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Abstract. Background: Less breakfast frequency is a recognized risk factor for health. However, there is scarce epidemiological evidence regarding the relationships between the breakfast frequency and skeletal muscle pain. Therefore, we aimed to investigate the relationship between the breakfast frequency and the skeletal muscle pain in Chinese college students. Methods: A Cohort study was conducted among 2263 Chinese college students. Musculoskeletal pain and breakfast frequency were assessed with a self-reported questionnaire. Multiple logistic regression analysis was performed to testify the association between breakfast frequency and musculoskeletal pain. Results: After adjustment for potential confounding factors, the results showed significant differences in the risk of musculoskeletal pain with different breakfast frequency. Conclusions: Less breakfast frequency level was independently related to a higher self-reported prevalence of skeletal muscle pain in college students. The findings suggest that higher breakfast frequency may have a potentially beneficial effect on the prevention of skeletal muscle pain.

Keywords: Musculoskeletal Pain; Breakfast Frequency; Chinese; college students; A Cohort Study.

1. Introduction

Skeletal muscle pain is the most common disease in the modern society, surveys have shown that the prevalence of skeletal muscle pain varies from 4.2% to 13.3% across countries[1], Nationwide population surveys conducted in the Dutch reported that almost three-quarter (74.5%) of the Dutch population aged 25 years and over reported any musculoskeletal pain during the past 12 months, 53.9% reported musculoskeletal pain during the survey (point prevalence) and 44.4% reported musculoskeletal pain lasting longer than 3 months[2]. The surveys conducted by Ren among the college students in Chongqing showed that neck, shoulder, elbow, wrist/hand, and low back and waist pain was reported by 29.2%, 33.9%, 3.8%, 7.9% and 27.9%, respectively[3]. Obesity, sedentary, presence of fatigue, poor sleep, emotional disorder, high levels of psychological distress, individuals are more likely to suffer from skeletal muscle pain. In recent years, epidemiological study showed skeletal muscle pain has a major impact on sleep, depression and the quality of life[4][5][6][7]. In the U.S. alone, all forms of chronic pain are estimated to incur an economic burden of \$500 billion dollars annually[8]. Despite its high prevalence and a major impact on mental health and physical health, skeletal muscle pain remains poorly understood and available treatment regimens are largely insufficient.

higher breakfast frequency has long been recognized as a healthy dietary pattern[9]. The positive association between breakfast consumption and nutrition level[10]. Recent research has shown an association between regular consumption of breakfast and Coronary Heart Disease[11], Depression[12], obesity[13][14]. However, most college students do not realize the importance of breakfast. A cross-sectional study on Chinese college students shows that 27.5% of college students skip breakfast[15]. Another study on Chinese female college students found that 12.3% of female college students had breakfast less than three times a week[16]. Previous researches showed that dietary habits may increase the risk of skeletal muscle pain by having a hold on the nutrition intake of human body[17][18]. However, to date, studies regarding the negative effect of certain eating habits on skeletal muscle pain have primarily focused on simply investigating the association between diet selection and the risk of skeletal muscle pain; few studies on the association between breakfast frequency and skeletal muscle pain have been reported at this stage, and based on previous studies that found the association between breakfast frequency and nutritional level, chronic diseases, we speculated that there might be some association between breakfast frequency and skeletal muscle pain. Therefore, we designed a cohort study aiming to investigate the relationship between the breakfast frequency and the skeletal muscle pain in Chinese college students.

2. Materials And Methods

2.1 Study Population

Participants in this study were recruited between September 2021 and September 2022 from the Mian yang normal college cohort study, which was a prospective cohort study to assess the association between breakfast and Musculoskeletal Pain of college students in the Mian yang normal college. 2263 people were invited to participate in the study. All of the participants were asked to fill out a self-designed survey questionnaire that consisted of questions about demographic (e.g., gender, age, only one child, father education, mother education, parent's marital status, lifestyle and health-related habits (e.g. Mobile phone usage, sleep quality, Depression level)). All respondents have completed the questionnaire during the survey, and all are included in the study. Ethics approval was obtained from the Institutional Review Board of the College of Physical Education of Southwest University.

2.2 Measures

2.2.1 Assessment of Breakfast frequency

Breakfast frequency was determined by asking respondents the number of days per week on which they had consumed breakfast. The possible responses were no breakfast, 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, and every day. Participants were categorized as either 'occasionally' (0–3 times a week), 'frequent' (4–6 times a week) or 'daily' (7) breakfast consumers[19].

2.2.2 Assessment of Musculoskeletal Pain

The mNMQ was used to examine pain in six body regions[20][21]. The body parts measured by the mNMQ include the neck, shoulders, elbows, wrists or hands, low back and waist, and Hip leg. Respondents are asked if they have had any musculoskeletal trouble in the last 7 days which has prevented normal activity.

2.2.3 Relevant Covariates

Demographic variables and lifestyle factors including sex, age, one child (yes or no), parent's education (college or above), left-behind children (yes or no), Marital status of parents (first marriage, divorce, remarriage), Mobile phone usage (h/Day) (<1h, 1-2h, >2h).

Sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a 19-item self-reported questionnaire that evaluates sleep quality over the past month, which yields seven component scores: sleep latency, duration of sleep, habitual sleep efficiency, sleep disturbances, use of sleep medications, daytime dysfunction, and overall sleep quality. The sum of scores for these seven components yields the PSQI global score, with higher scores indicating poor sleep quality during the previous month. Based on the prior literature, PSQI global scores >7 were defined as “poor sleep quality”[22].

Depression and anxiety were assessed using the Beck Depression Inventory. The scale is a standard assessment tool, and its reliability and validity have been tested in the Chinese population. A higher score indicates a higher degree of mental disorder[23].

2.3 Statistical Analysis

All categorical variables were presented as proportions and were compared by logistic regression analysis. Each body part with musculoskeletal pain was used as a dependent variable and categories of breakfast frequency were used as independent variables. Multiple logistic regression analysis was also used to examine the relationship between categories of breakfast frequency and each body part with musculoskeletal pain. Model 1 was the crude univariate model; Model 2 the demographic variables of subjects adjusted include sex, age; only on child (yes or no), father education (High school degree or below, Bachelor degree or above), mother education (High school degree or below, Bachelor degree or above), parent's marital status (first marriage, divorce, remarriage), c Model 3: In addition to adjusting demographic variables, also adjusted the life habits of the subjects, including Mobile phone usage(h/Day)($<1h, 1-2h, >2h$), sleep quality(continuous variables), Depression level(continuous variables) And pain at baseline(yes or no); d Adjusted data are expressed as odds ratio (95% confidence intervals); eP were obtained using multivariate logistic regression analyses. All tests were performed using IBM SPSS Statistics 24.0 software (IBM SPSS Inc., Chicago, IL, United States)

3. Results

The participants' characteristics, according to categories of breakfast frequency at baseline period are shown in Table 1. Participants with higher frequencies of breakfast were reported to have higher proportions of females, lower levels of depression, a lower proportion of left-behind children and higher education with mother (P for trend: 0.001, 0.025, 0.005, 0.015, respectively). Participants with Low frequency breakfast also had high use of phone ($>2h/day$) (P for trend: 0.006). Other baseline characteristics did not differ significantly between categories. Among all participants at baseline period, neck, shoulder, elbow, wrist/hand, upper back/ waist and hip leg pain was reported by 30.5%, 34.7%, 3.8%, 8.1%, 30.3% and 13% respectively.

Table 2 Adjusted relationships between breakfast frequency and the risk of musculoskeletal Pain incidence during the 1-year follow-up period. The ORs (95% CIs) for neck pain in each breakfast frequency category (daily, frequent, occasional) in Model 3 were 1.000(Reference), 1.345(1.101, 1.643) and 1.820(1.392, 2.380), respectively (P for trends: < 0.001). The ORs (95% CIs) for shoulder pain in each Breakfast frequency category in Model 3 were 1.000(Reference), 1.463(1.209, 1.77) and 1.675(1.285, 2.184), respectively (P for trends: < 0.001). The ORs (95% CIs) for elbow pain in each Breakfast frequency category in Model 3 were 1.000(Reference), 3.152(1.818, 5.467) and 1.48(0.909, 2.41), respectively (P for trends: < 0.001). The ORs (95% CIs) for wrist/hand pain in each Breakfast frequency category in Model 3 were 1.000(Reference), 2.002(1.435, 2.793) and 2.073(1.33, 3.23), respectively (P for trend: < 0.001). The ORs (95% CIs) for upper back and waist pain in each Breakfast frequency category in Model 3 were 1.000(Reference), 1.377(1.126, 1.685) and 1.878(1.434, 2.459), respectively (P for trends: < 0.001). The ORs (95% CIs) for Hip leg pain in each Breakfast frequency category in Model 3 were 1.000(Reference), 1.482(1.141, 1.926) and 2.244(1.612, 3.123), respectively (P for trends: < 0.001).

The data analysis results show that with the decrease of breakfast frequency, the incidence of skeletal muscle pain also increases. Breakfast frequency is a risk factor for skeletal muscle pain.

TABLE 1 The participants' baseline characteristics according to frequency of consumption of breakfast

Characteristic		Breakfast frequency			
		Occasional (N=312)	Frequent (N=853)	Daily (N=1097)	P for linear Trend ¹
Sex(Female)%		49	60.3	53.9	0.001
Age (years)		21.34 (21.19, 21.50)	20.99 (20.91, 21.08)	21.28 (21.22, 21.35)	0.000
BMI(≥ 24)%		10.6	12.7	13.3	0.442
Only one child%		6.4	3.4	5.2	0.056
left-behind children%		16.3	9.8	10.3	0.005
Parents marital status%	first marriage	74.7	70.7	66.7	0.015
	divorce	8.7	13.4	13.6	0.063
	remarriage	16.7	15.9	19.7	0.085
Father education%	High school degree or below	82.4	86	84.3	0.175
Mather education%	High school degree or below	81.4	83.2	78	0.015
Mobile phone usage(h/Day) %	<1h	77.6	77.1	74.7	0.066
	1-2h	17.9	19.1	22.8	0.059
	>2h	4.5	3.8	2.6	0.006
sleep quality (≥ 8)%		17.6	15.1	15.1	0.527
Depression (≥ 24)%		14.7	10.3	9.4	0.025
¹ P for trends were assessed using multivariate logistic regression analyses. Significance of bold values is P < 0.05.					

TABLE 2 Adjusted relationships between breakfast consumption frequency and the risk of depressive symptoms incidence during the 1-year follow-up period.

	Total sample (n =2263)	Participants with skeletal muscle pain	Model 1 a	Model 2 b	Model 3 c
Neck					

Daily	312	125	1.000(Reference)d	1.000(Reference)	1.000(Reference)
Frequent	853	281	1.367(1.124,1.663)	1.336(1.095,1.630)	1.345(1.101,1.643)
Occasional	1097	290	1.860(1.43,2.42)	1.812(1.388,2.364)	1.820(1.392,2.380)
P for trende			P<0.001	P<0.001	P<0.001
Shoulders					
Daily	312	130	1.000(Reference)d	1.000(Reference)	1.000(Reference)
Frequent	853	340	1.439(1.193,1.735)	1.434(1.187,1.731)	1.463(1.209,1.77)
Occasional	1097	340	1.550(1.197,2.008)	1.552(1.198,2.01)	1.675(1.285,2.184)
P for trende			P<0.001	P<0.001	P<0.001
Elbows					
Daily	312	25	1.000(Reference)d	1.000(Reference)	1.000(Reference)
Frequent	853	37	1.509(0.923,2.443)	1.446(0.890,2.349)	3.152(1.818,5.467)
Occasional	1097	32	2.899(1.691,4.971)	2.985(1.738,5.126)	1.48(0.909,2.41)
P for trende			P<0.001	P<0.001	P<0.001
Wrists/hands					
Daily	312	34	1.000(Reference)d	1.000(Reference)	1.000(Reference)
Frequent	853	99	2.085(1.504,2.890)	2.031(1.461,2.824)	2.002(1.435,2.793)
Occasional	1097	65	1.942(1.256,3.001)	1.947(1.259,3.011)	2.073(1.33,3.23)
P for trende			P<0.001	P<0.001	P<0.001
upper back and waist					
Daily	312	120	1.000(Reference)d	1.000(Reference)	1.000(Reference)
Frequent	853	268	1.35(1.107,1.646)	1.36(1.113,1.661)	1.377(1.126,1.685)
Occasional	1097	276	1.841(1.412,2.401)	1.834(1.406,2.393)	1.878(1.434,2.459)
P for trende			P<0.001	P<0.001	P<0.001
Hip leg					
Daily	312	69	1.000(Reference)d	1.000(Reference)	1.000(Reference)
Frequent	853	140	1.448(1.120,1.873)	1.443(1.114,1.87)	1.482(1.141,1.926)
Occasional	1097	131	2.094(1.515,2.894)	2.094(1.515,2.896)	2.244(1.612,3.123)
P for trende			P<0.001	P<0.001	P<0.001

aModel 1: Crude; bModel 2: Adjusted for sex, age; Additionally adjusted for only on child (yes or no), father education (High school degree or below, Bachelor degree or above), mother education (High school degree or below, Bachelor degree or above), parent's marital status (first marriage, divorce, remarriage), c Model 3: Mobile phone usage(h/Day)(<1h, 1-2h, >2h), sleep quality(continuous variables), Depression level(continuous variables); d Adjusted data are expressed as odds ratio (95% confidence intervals); eP for trend were obtained using multivariate logistic regression analyses. Significance of bold values is $P < 0.05$.

4. Discussion

A Cohort Study was conducted in Chinese college to assess the relationship between breakfast frequency and the risk of musculoskeletal pain in different body parts. Multivariate logistic analyses showed that less breakfast frequency was significantly and independently related with higher risk of musculoskeletal pain in different body parts after adjusting for potential confounders.

The relationship between eating habits and skeletal muscle function has gained more and more recognition, Unhealthy eating behaviors are thought to predict, perpetuate, or underlie a variety of chronic musculoskeletal pain conditions. [24] for example, obesity occurs more frequently in patients with chronic pain, who all tend to have a dietary profile characterized by excessive calorie intake and high sugar, fat, sodium, and / or caffeine[25] In addition, studies have also found that intake of fewer vitamins (such as a, B12, D, e, K), calcium, magnesium, and folic acid, among others, can cause chronic musculoskeletal pain[26]. but few studies have been reported on the frequency of breakfast and the risk of muscle pain. Based on previous studies confirming a significant relationship between dietary habits and skeletal muscle function in college students, we speculate that breakfast frequency is associated with the risk of musculoskeletal pain in college students.

Although the exact etiology of the association between Breakfast frequency and musculoskeletal pain is not yet known, we explored a possible reasons. Regarding potential mechanisms underlying the relationship of the breakfast frequency with the risk of musculoskeletal pain, a plausible explanation is that the association is mediated by Micronutrient.

A study of U.S. military recruits by Fagnant[27] et al found that breakfast skipping was strongly associated with vitamin D deficiency (VDD) in recruits, and a study of Brazilian adolescents found that high-frequency breakfast intake significantly improved adolescent vitamin D intake Levels, Mielgo-Ayuso's survey of 1,058 European teenagers found that teens who skipped breakfast had significantly lower blood vitamin D and vitamin C concentrations than higher-frequency breakfast consumers[28]. Observational studies suggest[29] that adequate vitamin D levels are important for normal muscle function, muscle strength, and neuromuscular coordination. Studies have found that serum vitamin D levels are closely related to chronic back pain of unknown etiology, and vitamin D deficiency may lead to hyperalgesia and impaired neuromuscular function, increase susceptibility to pedicles, and lead to a decrease in the inflammatory pain threshold, which in turn triggers muscle pain. In animal experiments, vitamin D deficiency has also been shown to selectively alter target innervation, resulting in excessive skeletal muscle nociceptor innervation, which may lead to hypersensitivity and pain in muscles[30].

Mascarenhas R and Holick MF [31][32] proposed that when the body is insufficient in vitamin D, parathyroid hormone (PTH) secretion will increase, resulting in increased urinary calcium and phosphine excretion, resulting in hypocalcemia and hypophosphatemia. The collagen matrix of the periosteum is not properly mineralized, and collagen edema compresses the periosteum rich in sensory nerves and causes pain. In addition, studies found that higher levels of vitamin D intake reduced plasma levels of inflammation and pain-related cytokines, such as PGE2, tumor necrosis factor alpha (TNF- α) and leukotrienes B4 (leukotriene B4, LTB4), prostaglandin E2 (Prostaglandin E2, PGE2)[33][34][35][36]. Therefore, this study speculates that breakfast skipping may induce skeletal muscle pain by affecting students' blood vitamin D levels.

5. Conclusion

This prospective cohort study assessed the relationship between baseline breakfast consumption and the subsequent risk of muscle pain in the following year among Chinese college students. The results showed a significant relationship between breakfast frequency and an increased risk for Musculoskeletal Pain after adjustment for potential confounders. Findings from this study can help with the development of an effective intervention strategy against musculoskeletal pain. Future research using interventional or experimental studies is required to explore the causal relationship between the effects of breakfast frequency and musculoskeletal pain.

References

- [1] Ana, Filipa, Mouro, et al. Generalised musculoskeletal pain syndromes - ScienceDirect[J]. Best Practice & Research Clinical Rheumatology, 2010, 24(6):829-840.
- [2] Picavet H S J, Schouten J S A G . Musculoskeletal pain in the Netherlands: prevalences, consequences and risk groups, the DMC(3)-study[J]. Pain, 2003, 102(1-2):167-178.
- [3] Yang G, Cao J, Li Y, Cheng P, Liu B, Hao Z, Yao H, Shi D, Peng L, Guo L, Ren Z. Association Between Internet Addiction and the Risk of Musculoskeletal Pain in Chinese College Freshmen - A Cross-Sectional Study[J]. Front Psychol. 2019 Sep 3;10:1959.
- [4] Holley AL, Rabbitts J, Zhou C, Durkin L, Palermo TM. Temporal daily associations among sleep and pain in treatment-seeking youth with acute musculoskeletal pain[J]. Journal of Pain Official Journal of the American Pain Society. 2016;17(4):S1-S.
- [5] Meanschristensen AJ, Roybyrne PP, Sherbourne CD, Craske MG, Stein MB. Relationships among pain, anxiety, and depression in primary care[J]. Depression & Anxiety. 2010;25(7):593-600.
- [6] Tanaka M , Mizuno K , Fukuda S , et al. Relationships between dietary habits and the prevalence of fatigue in medical students[J]. Nutrition, 2008, 24(10):985-989.
- [7] Li Y , Nemoto T , Tobimatsu S , et al. Relationship between skipping breakfast and impaired fasting glucose along with cardiovascular and pre-diabetes condition risk factors in apparently healthy subjects[J]. Endocrinology Studies, 2011,1(2), e17.
- [8] Loeser J D . Relieving Pain in America[J]. Clinical Journal of Pain, 2012, 28(3):185.
- [9] Keski R A , Kaprio J , Rissanen A , et al. Breakfast skipping and health-compromising behaviors in adolescents and adults [J]. European journal of clinical nutrition, 2003(7):57.
- [10] Z Y, M T. Disordered Eating Behaviors and Food Addiction among Nutrition Major College Students. Nutrients[J]. 2016;8(11):673.
- [11] Kubota Y, Iso H, Sawada N, Tsugane S. Association of Breakfast Intake With Incident Stroke and Coronary Heart Disease: The Japan Public Health Center-Based Study[J]. Stroke. 2016;47(2):477-81.
- [12] Ferrer-Cascales R, Sánchez-SanSegundo M, Ruiz-Robledillo N, Albaladejo-Blázquez N, Laguna-Pérez A, Zaragoza-Martí A. Eat or Skip Breakfast? The Important Role of Breakfast Quality for Health-Related Quality of Life, Stress and Depression in Spanish Adolescents[J]. International Journal of Environmental Research and Public Health. 2018; 15(8):1781.
- [13] L. E. Cahill, S. E. Chiuve, R. A. Mekary et al., Prospective study of breakfast eating and incident coronary heart disease in a cohort of male US health professionals[J]. Circulation, 2013;128(4):337-343.
- [14] Deshmukhtaskar PR, Nicklas TA, O'Neil CE, Keast DR, Radcliffe JD, Cho S. The relationship of breakfast skipping and type of breakfast consumption with nutrient intake and weight status in children and adolescents: the National Health and Nutrition Examination Survey 1999-2006[J]. Journal of the American Dietetic Association. 2010;110(6):869-78.
- [15] Zhu Z , Cui Y , Gong Q , et al. Frequency of breakfast consumption is inversely associated with the risk of depressive symptoms among Chinese university students: A cross-sectional study[J]. PLoS ONE, 2019, 14(8):e0222014.
- [16] Zhang C, Zhang J, Wang Y, et al. Association between breakfast consumption frequency and the risk of irritable bowel syndrome among Chinese female college students: A cross-sectional study[J]. Medicine (Baltimore).2021 15;100(41):e27541.

- [17] Benson J, Wilson A, Stocks N, Moulding N. Muscle pain as an indicator of vitamin D deficiency in an urban Australian Aboriginal population[J]. *Med J Aust*. 2006;185(2):76-7.
- [18] Connolly D , Lauzon C , Agnew J , et al. The Effects Of A Vitamin C Supplement On Symptoms Of Delayed Onset Muscle Soreness[J]. *Medicine & Science in Sports & Exercise*, 2005, 37(5), S316.
- [19] Odegaard AO, Jacobs DR Jr, Steffen LM, Van Horn L, Ludwig DS, Pereira MA. Breakfast frequency and development of metabolic risk[J]. *Diabetes Care*. 2013;36(10):3100-6.
- [20] Crawford, J. O . The Nordic Musculoskeletal Questionnaire[J]. *Occupational Medicine*, 2007, 57(4):300-301.
- [21] Dol, K. Fatigue and pain related to internet usage among university students[J]. *JOURNAL OF PHYSICAL THERAPY SCIENCE*. 28(4), 1233–1237.
- [22] Ho R , Fong T . Factor structure of the Chinese version of the Pittsburgh Sleep Quality Index in breast cancer patients[J]. *Sleep Medicine*, 2014, 15(5):565-569.
- [23] Yu-Sen Peng, Chih-Kang Chiang, Kung-Yu Hung, et al. The association of higher depressive symptoms and sexual dysfunction in male haemodialysis patients[J]. *Nephrology Dialysis Transplantation*, 2007, 22(3), 857–861.
- [24] Elma O , Yilmaz S T , Deliens T , et al. Chronic Musculoskeletal Pain and Nutrition: Where Are We and Where Are We Heading?[J]. *PM & R: the journal of injury, function, and rehabilitation*, 2020(12):12.
- [25] Meleger A L , Froude C K , Walker J . Nutrition and Eating Behavior in Patients With Chronic Pain Receiving Long-Term Opioid Therapy[J]. *Pm & R*, 2014, 6(1):7-12.e1.
- [26] E. D. Batista, A. Andretta, R. C. de Miranda, J. et al. Food intake assessment and quality of life in women with fibromyalgia[J]. *Revista brasileira de Reumatologia*, 2016.56(2):105–110.
- [27] Fagnant H S, Lutz L J, Nakayama A T, et al. Breakfast Skipping is Associated with Vitamin D Deficiency among Young Adults entering Initial Military Training[J]. *JOURNAL OF THE ACADEMY OF NUTRITION AND DIETETICS* 2021,122(6),1114-1128.
- [28] Mielgo-Ayuso J , Valtue?A J , M Cuenca-García, et al. Regular breakfast consumption is associated with higher blood vitamin status in adolescents: The HELENA (healthy lifestyle in europe by nutrition in adolescence) study[J]. *Public Health Nutrition*, 20(8), 1393-1404.
- [29] Koundourakis NE, Avgoustinaki PD, Malliaraki N, Margioris AN. Muscular effects of vitamin D in young athletes and non-athletes and in the elderly[J]. *Hormones (Athens)*. 2016 ;15(4):471-488.
- [30] Tague SE, Clarke GL, Winter MK, et al. Vitamin D deficiency promotes skeletal muscle hypersensitivity and sensory hyperinnervation[J]. *J Neurosci*, 2011, 31: 13728 ~ 13738.
- [31] Mascarenhas R, Mobarhan S. Hypovitaminosis D induced pain[J]. *Nutr Rev*, 2004, 62:354 ~ 359.
- [32] Holick MF. Vitamin D deficiency: What a pain it is[J]. *Mayo Clin Proc*, 2003, 78:1457~1459.
- [33] Catalano A , Morabito M , Basile G, et al . Vitamin D reduces musculoskeletal pain after infusion of zoledronic acid for postmenopausal osteoporosis[J]. *Calcif Tissue Int* , 2012, 90:279 ~ 285.
- [34] Bertoldo F, Pancheri S, Zenari S, et al. Serum 25-hydroxyvitamin D levels modulate the acute-phase response associated with the first nitrogen-containing bisphosphonate infusion[J]. *JBMR*, 2010, 25: 447 ~ 454 .
- [35] Roelofs A J , Jauhiainen M , M?Nkk?Nen H , et al. Peripheral blood monocytes are responsible for $\gamma\delta$ T cell activation induced by zoledronic acid through accumulation of IPP/DMAPP[J]. *British Journal of Haematology*, 2009, 144(2):245-250.
- [36] Garcion E , Sindji L , Montero-Menei C , et al. Expression of inducible nitric oxide synthase during rat brain inflammation: regulation by 1,25-dihydroxyvitamin D3[J]. *Glia*, 2015, 22(3):282-294.