

Chronic nonspecific musculoskeletal pain in adults with special reference to serum uric acid levels

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Introduction: Increased serum uric acid levels have been found to be variably associated with chronic nonspecific musculoskeletal pain in different subgroups of population. Tresent study is aimed knowing association increased serum uric acid levels in adult population with chronic nonspecific musculoskeletal pain. Primary outcome measure was to know levels of serum uric acid levels in patients with chronic nonspecific musculoskeletal pain and, secondary outcome measure was to know effect of Hypouricemic agents Febuoxastat in patients with hyperuricemia. **Methods:** One hundred and twenty five (n=125) adult patients (M: F-63:62) having chronic nonspecific musculoskeletal pain of ≥ 6 weeks duration were included in study and, their serum uric acid levels were estimated. An eleven points (0-10) Numerical Rating Scale (NRS) was used to assess level of chronic musculoskeletal pain in study participants. Patients with hyperuricemia were given oral Hypouricemic drug febuoxastat. Study was conducted for period one year. **Results:** Serum uric acid levels were raised in a significant proportion (p value <0.0001) of patients (70.4%) with chronic nonspecific musculoskeletal pain. Mean serum uric acid level was 8.3mg/dl in 70.4% (n=88) patients and 5.6 mg/dl in 20 %(n=25) patients. Mean serum uric acid level was below 2.0mg/dl (1.85±0.10mg/dl) in the remaining 9.6% (n=12) patients. Among the 88 patients having higher mean serum uric acid levels 39.2% (n=49) were female and 31.2 %(n=39) were male patients. **Conclusion:** Increased serum uric acid levels have an important role in development and pathogenesis chronic non specific musculoskeletal pain in adults. Both increased and decreased serum uric acid levels can cause symptomatic chronic nonspecific musculoskeletal pain.

Keywords: Uric Acid, Chronic Musculoskeletal Pain, Adults, Hyperuricemia, Hypouricemia

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Introduction

Body pain is one of the most important qualitative parameters for evaluating patients' quality of life [1]. Chronic nonspecific musculoskeletal pain, reported commonly among different communities, is defined as pain of at least 1-6 months duration without any identifiable cause [2, 3, 4, and 5]. The common causes of Chronic musculoskeletal pain are inflammatory and collagen diseases, osteoarthritis, post fracture pain, renal bone disease, and ischemic bone pain, endocrine and metabolic disorders, autoimmune disorders, chemotherapeutic drugs, primary malignancies/secondaries, mental disorders, and arthritis including the Gout syndrome. Diagnosis of chronic nonspecific musculoskeletal pain is usually made after carefully excluding all the above mentioned diseases. Widespread musculoskeletal pain has earlier been associated with increased serum uric acid levels [6] and, Studies have shown that chronic musculoskeletal pain has been significantly and independently associated with hyperuricemia [7]. Normal physiological value of serum uric acid is 2.0-7.0 mg/dl for males and 2-6.5 mg/dl for females. Women have usually been reported to complain of myalgia and men usually have lower back pain [8].

The mechanism of pain modulation has been described differently in different studies [9, 10]. Eisinger et al associated fibromyalgia with hyperuricemia and disturbed carbohydrate metabolism [11]. It was seen that multiple pain localization had worst effect on pain and general health and these patients had increased serum uric acid levels [8]. Studies have reported high mean serum uric acid levels in patients with musculoskeletal pain as compared to pain free population [12]. The present study is focused to determine the profiles of serum uric acid levels in patients with chronic nonspecific musculoskeletal pain.

Material and Methods

This is a prospective longitudinal study carried out after the institutional ethical committee approval. A written informed consent was obtained from all the participants of the study. The study included 125 adult patients with, chronic nonspecific musculoskeletal pain of ≥ 6 week's duration and, in whom the common causes of musculoskeletal

Pain were ruled out. Normal serum uric acid level was set between 2.0-7.0mg/dl for men and 2.0- 6.5mg/dl for women. Blood samples for serum uric acid levels were collected in the morning before breakfast to

minimize the confounding variables that may cause alter serum uric acid levels. An 11 points (0-10) unidimensional pain assessment tool, the Numerical Rating Scale [19] was used to assess the level of chronic musculoskeletal pain in the study participants [Figure 1]. An NRS score of ≥ 4 was set to define the presence of musculoskeletal pain in the study participants. Patients with malignancy, on cytotoxic drugs and certain other medications that could confound the serum uric acid measurement, known cases of gout, and other autoimmune disorders were all excluded from the study. Detailed history was taken up on prescribed performance regarding the patients' current illness and history of chronic musculoskeletal pain. The site and number of tender points were recorded. Physical examination of all the participants was done for weight, height, temperature, blood pressure, anemia, presence/absence of joint swelling, pain localization, deformity and functional disability and any other relevant finding. Subsequent baseline hematological and biochemical data was collected for all patients participating in the study. All other relevant investigations were done to rule out the common causes of chronic musculoskeletal pain in the study participants.

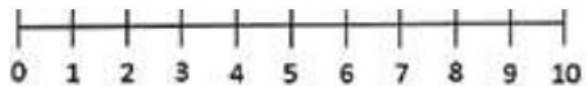


Figure 1: Numerical Rating Scale (NRS) score for Assessment of chronic musculoskeletal pain. Here, 0 means no pain and 10 means worst possible pain.

Those patients having hyperuricemia with chronic musculoskeletal pain were managed by oral febuxostat 80mg/day tapered to 40mg/day along with other symptomatic medication and dietary restriction of high protein diet. Normouricemic and Hypouricemic patients were given only symptomatic management.

Results

A total of 125 patients (63 female and 62 male) participated in our study. Baseline demographic characteristics are defined in table 1. Majority (70.4%) of patients with

Unidentified chronic musculoskeletal pain had increased mean serum uric acid levels of 8.3 ± 0.76 mg/dl in both male (n=39) and female (n=49) groups [Table 4]. Based on the serum uric acid levels all the patients were categorized into three different groups. Patients of unidentified chronic musculoskeletal pain with hyperuricemia (n=88) were categorized into Group I, those with hypouricemia (n=12) into Group II, and the Group III patients were normouricemic (n=25) patients.

Table 1: Basic demographic characteristics of study subjects

Sex of patient	Mean Duration of complaints (wks)	No. of patients	Age (years) Mean \pm SD	Height (cm) Mean \pm SD	Weight (kg) Mean \pm SD
Female	52 \pm 15	63	41.34 \pm 1.70	158.32 \pm 1.25	58.60 \pm 2.34
Male	44 \pm 20	62	38.21 \pm 1.54	164.00 \pm 1.85	63.78 \pm 2.89

Distribution of pain location in the study subjects is shown in table 2. We can infer from the table 2 that maximum numbers of male patients with chronic nonspecific musculoskeletal pain were having low and upper back pain. Whereas maximum number of female patients were having heel pain and generalized bodyache.

Table 2: Regional distribution of pain in study subjects

S.No	Site of pain	No. of Male patients	No. of Female patients	Total	Percentage (%)
1	Low back pain	30	8	38	30.4
2	Upper back pain	12	6	18	14.4
3	Isolated elbow pain	4	5	9	7.2
4	Isolated heel pain (unilateral)	3	10	13	10.4
5	Isolated heel pain (bilateral)	1	19	20	24.0
6	Generalized muscle pain	7	13	20	8.0
7	Isolated arm pain between shoulder and elbow	5	2	7	5.6
Total		63	125	100	

Table 3: Mean serum uric acid levels and corresponding NRS scores in study subjects

Serum uric acid level (mg/ml) Mean \pm SD	NRS score in male patients Mean \pm SD (n=62)	NRS score in female patients Mean \pm SD (n=63)
8.3 \pm 0.76	6.83 \pm 1.56	7.12 \pm 1.46
5.6 \pm 0.45	5.34 \pm 1.21	5.46 \pm 1.32
1.85 \pm 0.10	5.38 \pm 1.15	5.46 \pm 1.41

Hyperuricemic patients with unidentified chronic musculoskeletal pain have higher mean Numerical Rating Scale NRS) score in both male and female patient groups

Table 4: Distribution of serum uric acid levels in male and female patients

Category/Group of patients	Mean Serum uric acid \pm SD (mg/dl)	No. of female patient (n)	No. of male patient (n)	Total no. of patient (n)	Percentage (%)	P value
Hyperuricemic (Group I)	8.3 \pm 0.76	49	39	88	70.4	<0.0001
Normouricemic (Group III)	5.6 \pm 0.45	6	19	25	20	<0.0001
Hypouricemic (Group II)	1.85 \pm 0.10	8	4	12	9.6	<0.0002
Total		63	125	100		

A small proportion of patients 9.6% (n=12) with chronic musculoskeletal pain had an unexplained lower mean serum uric acid levels [Table 4]. Out of 88 Patients with hyperuricemia who were given oral Hypouricemic drug Febuxostat, 81.8% Patients (n=72) had lowered serum uric levels on subsequent follow up and their decreasing trends of serum uric acid levels were followed by decreasing NRS scores.

Discussion

Chronic nonspecific musculoskeletal is one of the commonly reported problem form various communities with the reported incidence varying from 11.2% to as high as 50% [3]. Uric acid, which is produced via the action of Xanthine oxidase on Xanthine is, a weak acid. The plasma concentration of uric acid is under tight control through different physiological mechanism taking place at the level of kidney. The biochemical homeostasis of uric acid level is maintained by the uric acid production and excretion and, any derangement in these mechanism can lead to either hyper or hypouricemia. Uric Acid has a tendency to undergo crystal formation when the plasma concentration exceeds 6.0 mg/dl.

Abnormalities in serum uric acid levels are highly prevalent and gradually increasing public health issue with its prevalence ranging from 2.6 to 47.2% in different population [14]. Although a direct relation between chronic noninflammatory musculoskeletal pain and biomarkers has

Not been established, some relationship has been found between abnormal serum uric acid and chronic pain by few authors as mentioned above.

Based on the consequences on health and disease of both hyperuricemia and hypouricemia, a deranged serum uric acid level is called a double edged sword [13]. In our study also, although majority (70.4%) patients with chronic usculoskeletal pain had an increased serum uric acid, however there was a small proportion (9.6%) of patients with similar complaints who rather had a decreased serum uric acid levels. Low serum uric acid levels predispose the individual to poor handling of oxidative stress and subsequent neurodegenerative disorders; however its exact role in chronic musculoskeletal manifestations has not been studied. The exact pathomechanisms of hypouricemia leading to chronic musculoskeletal pain are not clear to us and need further exploratory research on this issue.

In our study majority of patients (70.4%) with chronic unidentified musculoskeletal pain were having hyperuricemia, a finding that has been repeatedly confirmed by several authors. Out of 88 patients with hyperuricemia 49(55.6%) were female in our study. Authors like Naeema Afzal have also concluded in their study that female patients are more prone to develop hyperuricemia [15]. In our study we observed that frequently repeated musculoskeletal problems were backache in male and heel pain female patients. Therefore we strongly recommend that in adults with unexplained backache and heel pain serum uric acid levels should be checked and managed accordingly.

In the present study the patients with hyperuricemia with chronic musculoskeletal pain; treated by oral febuoxastat, a novel nonpurine Xanthine oxidase inhibitor showed a decreasing trends in their serum uric acid levels and NRS scores. In our study those patients who had their serum uric acid levels below 5.5mg/dl had maximum pain relief on subsequent follow-up. Srivastava and gaur et al [16] in a similar study treated patients with allopurinol/colchicines and reported 96.2% response rate. However, the response rate in our study treated with oral febuoxastat is lower (81.8%), compared to Srivastava and gaur et al. A lower response rate to Hypouricemic drug Febuoxastat in our study may be explained on the basis of different mechanism

Of action of the two drugs, patient compliance to drugs, failure to stick to dietary restrictions etc.

Conclusion

The study concludes that hyperuricemia is an important factor underlying the pathogenesis of unidentified chronic usculoskeletal pain in adults. Further research is warranted to determine the role of hypouricemia in the development of different musculoskeletal manifestations.

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