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Determination of Lactate (Lactic Acid) and Lactate Dehydrogenase (LDH) in Synovial Fluid of Arthritis Patients for Differential Diagnosis of Septic and Non Infectious Arthritis

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Abstract: Lactate (Lactic acid) and lactate dehydrogenase (LDH) determination in synovial fluid (especially lactate) are being considered as significant tests to differentiate between septic arthritis and other forms of arthritis. The presented study reported the determination of lactate and LDH in synovial fluids of male and female arthritis patients, to substantiate differential diagnosis between sepsis and non-infectious arthritis. Sixty five females and forty five males' arthritis patients were selected in the study with age groups of 32-80 yrs in females and 41-84 yrs in males, subdivided into four age groups each, respectively. Lactate and LDH were determined in synovial fluid of all selected patients by L-Lactate PAP (4-amino-antipyrine) colorimetric and DGKC methods, respectively. Results: In female groups, n = 14 (21.53%) and in male groups, n = 16 (35.55%) patients showed significantly elevated lactate and LDH concentrations. High percentage of patients that showed elevated lactate levels [46.10 ± 10.90 mg/dl] were in the age group of 51-60 yrs in females (27.77%, n = 5/18) and 56-66 yrs [44.40 ± 8.10 mg/dl] in males (38.46%, n = 5/13). LDH levels corresponded with the elevated concentration of estimated lactate in respective female and male groups with highest LDH levels were noted in age group 51-60 yrs in females (390.10 ± 30.20 U/L) and age group 56-66 yrs in males (350.50 ± 31.25 U/L). Elevated lactate and LDH levels in synovial fluid of arthritis patients were consistent with bacterial culture findings that manifested growth of Pseudomonas aeruginosa, Staphylococcus aureus and Enterococci species. In conclusion: It is suggest that lactate and LDH determination should be included in chemical analysis of synovial fluids, when arthritis patients were suspected of sepsis or synovium bacterial infections.

Key words: Synovial fluids · Lactate · Sepsis · L-Lactate PAP (4-amino-antipyrine) · Lactate dehydrogenase · LDH

INTRODUCTION

Lactate (Lactic acid) and lactate dehydrogenase (LDH) determination in synovial fluid is being considered as a significant test to differentiate between septic arthritis and other forms of arthritis [1-5]. Presence of lactate and LDH in synovitis has long been known as obligatory to metabolism of synovium by bacterial infections [4, 6-10], thus resulting in septic arthritis. Although analysis of synovial fluid, since long, has been recommended as a mandatory test for the diagnosis of arthritis [2, 11-14], recent and past studies suggest lactate assessment in synovial fluid as an exceptional diagnostic test to differentiate septic arthritis from gout and other forms of arthritis and/or peri-prosthetic joint infections [1-4]. The present study describes determination of lactate and LDH in synovial fluids of male and female arthritis patients, to assess the presence of sepsis or commonly suggested bacterial infectious arthritis.

MATERIALS AND METHODS

Patients Selection and Grouping: A total of 140 male and female patients's were screened and confirmed for the presence of arthritis, through clinical and diagnostic evaluations during April 2014 to April 2015.

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Out of 140, n = 65 females and n = 45 males were selected for final inclusion in the study. The patients were within the age groups of 32-80 yrs in females and 41-84 yrs in males, subdivided into four age groups each, respectively.

Determination of Lactate and Lactate Dehydrogenase (LDH): Lactate was determined in synovial fluid by L-Lactate PAP (4-amino-antipyrine) colorimetric method of Randox (Rx Monza, Randox Laboratories, UK). The principle was based in the conversion of lactate into H_2O_2 and then to a purple colored end product after addition of TOOS (N-ethyl 2-OH-3-Sulphopropyl m-toluidine). Color intensity is directly proportional to increased lactate concentration in synovial fluids. Normal concentration of lactate in synovial fluid is similar to plasma lactate levels of < 20 mg/dl. LDH was estimated by DGKC method 15] on Hitachi 912 chemistry analyzer where decrease in NADH level is directly proportional to the concentration of LDH activity. Normal LDH concentration in synovial fluid is Less than 240 U/L.

Statistical Analysis: The data is presented in mean ± SD and considered significant when $P < 0.05$. Data was analyzed using SPSS version 15 (USA) and compared among various age groups and gender.

RESULTS

Results are summarized in Table 1 to 4. In present study synovial fluids of 65 females and 45 males patients' were analyzed for lactate and LDH to determine whether the patients were suffering from septic arthritis or non-infectious arthritis. Both gender group of patients were further divided into age groups as 32-50 yrs (n = 15), 51-60 yrs (n = 18), 61-71 (n = 20) and 72-80 yrs (n = 12) in females and 41-55 yrs (n = 10), 56-66 yrs (n = 13), 67-77 yrs (n = 16) and 78-84 (n = 4) in males, respectively. In female groups, n = 14 (21.53%) patients showed significantly elevated lactate concentration out of 65 (Table 1), whereas in male groups, n = 16 (35.55%) patients showed significant elevation of lactate levels (Table 2). High percentage of patients that showed elevated lactate levels [46.10 ± 10.90 mg/dl] were in the age group of 51-60 yrs in females (27.77%, n = 5/18) (Table 1) and 56-66 yrs [44.40 ± 8.10 mg/dl] in males (38.46%, n = 5/13) (Table 2). The normal lactate levels were in the range of 10.20 ± 2.86 mg/dl to 15.50 ± 3.50 mg/dl in female groups and 10.00 ± 2.10 mg/dl to 13.90 ± 5.25 mg/dl in male groups. Similarly LDH levels also corresponded with the elevated concentration of estimated lactate in respective female and male groups (Table 3, 4). Highest LDH levels were noted in age group 51-60 yrs in females (390.10 ± 30.20 U/L) and age group 56-66 yrs in males (350.50 ± 31.25 U/L) (Table 3 and 4). Bacterial culture studies reported *Pseudomonas aeruginosa, Staphylococcus aureus* and *Enterococci* species as the main organisms indentified in the synovial fluids of both male and female patients that exhibited elevated lactate and LDH levels. Interestingly, bacterial cultures of synovial fluids of certain patients that exhibited positive growth of organisms manifested normal lactate levels, suggestive of prophylactic antibiotic therapy.

Table 1: Lactate Levels In Synovial Fluids Of Female Arthritis Patients (N = 65)

Age groups	Total number of patients in each age-group	Number of patients with normal lactate levels	Normal Lactate levels Mean ± SD mg/dl	Number of patients with elevated lactate levels	Elevated Lactate levels Mean ± SD mg/dl
32-50 yrs	15	12	12.15 ± 2.40^{b}	3	$30.00 \pm 8.10^{a,b}$
51-60 yrs	18	13	15.50 ± 3.50^{d}	5	$46.10 \pm 10.90^{d,b}$
61-71 yrs	20	17	13.60 ± 3.10^{c}	3	$43.40 \pm 7.60^{a,b,d}$
72-80 yrs	12	9	10.20 ± 2.86^{a}	3	$39.40 \pm 5.20^{a,b,c}$
	65 (100%)	51 (78.46%)		14 (21.53%)	

Statistical significance a = P < 0.0001, b = P < 0.001, c = P < 0.01, d = P < 0.05

Results are expressed as mean ± SD

Table 2: Lactate levels in Synovial fluids of male arthritis patients (n = 45)

Age groups	Total number of patients in each age-group	Number of patients with normal lactate levels	Normal Lactate levels Mean ± SD mg/dl	Number of patients with elevated lactate levels	Elevated Lactate levels Mean ± SD mg/dl
41-55 yrs	10	6	$10.00 \pm 3.50^{a,b,d}$	04	$33.20 \pm 8.60^{a,b}$
56-66 yrs	13	8	13.90 ± 5.25^{d}	05	$44.40 \pm 8.10^{b,d}$
67-77 yrs	18	13	10.50 ± 2.10^{a}	05	$39.45 \pm 5.26^{a,c}$
78-84 yrs	04	02	10.00 ± 1.50	02	$40.25 \pm 7.00^{a,c}$
	45 (100%)	29 (64.44%)		16 (35.55%)	

Statistical significance a = P < 0.0001, b = P < 0.001, c = P < 0.01, d = P < 0.05

Results are expressed as mean ± SD

Table 3: Lactate dehydrogenase (LDH) levels in Synovial fluids of female arthritis patients (n = 65)

Age groups	Total number of patients in each age-group	Number of patients with normal LDH levels	Normal LDH levels Mean ± SD U/L	Number of patients with elevated LDH levels	Elevated LDH levels Mean ± SD U/L
32-50 yrs	15	12	160.30 ± 10.20[b]	3	290.20 ± 25.10[a,b]
51-60 yrs	18	13	180.20 ± 20.15[d]	5	390.10 ± 30.20[d,b]
61-71 yrs	20	17	130.50 ± 15.20[c]	3	310.50 ± 28.50[a,b,d]
72-80 yrs	12	9	135.10 ± 14.70[a]	3	301.75 ± 25.60[a,b,c]
	65 (100%)	51 (78.46%)		14 (21.53%)	

Statistical significance a = P < 0.0001, b = P < 0.001, c = P < 0.01, d = P < 0.05

Results are expressed as mean ± SD

Table 4: Lactate dehydrogenase (LDH) levels in Synovial fluids of male arthritis patients (n = 45)

Age groups	Total number of patients in each age-group	Number of patients with normal LDH levels	Normal LDH levels Mean ± SD U/L	Number of patients with elevated LDH levels	Elevated LDH levels Mean ± SD U/L
41-55 yrs	10	6	170.15 ± 11.50[a,b,d]	04	301.10 ± 26.45[a,b]
56-66 yrs	13	8	182.25 ± 12.60[d]	05	350.50 ± 31.25[b,d]
67-77 yrs	18	13	133.50 ± 14.90[a]	05	310.60 ± 30.10[a,c]
78-84 yrs	04	02	140.65 ± 14.10[d]	02	295.45 ± 30.50[c,d]
	45 (100%)	29 (64.44%)		16 (35.55%)	

Statistical significance a = P < 0.0001, b = P < 0.001, c = P < 0.01, d = P < 0.05

Results are expressed as mean ± SD

DISCUSSION

Present study described analysis of lactate and LDH in synovial fluid of around 110 patients; 65 females and 45 males, aged between 32-84 yrs, all suffering from arthritis. The results showed that 21.53% of female patients showed higher lactate and LDH levels, whereas 35.55% of males exhibited similar pattern. Elevated lactate and LDH levels were also correlated with bacterial cultures of synovial fluid, which showed the growth of *Pseudomonas aeruginosa, Staphylococcus aureus* and *Enterococci* species as the suspected sepsis causing agents. Previous studies of septic arthritis reported *S.aureus*, *P. aeruginosa* and *S. epidermidis* and in some cases meningococcal infections as the causative etiology [12]. Other arthritis patients in both gender groups exhibited normal (less than 20 mg/dl) levels of lactate and LDH ranging from less than 15.50 ± 3.50 mg/dl and 180.20 ± 20.15 U/L in females to less than 13.90 ± 5.25 mg/dl and 182.25 ± 12.60 U/L in males, respectively.

Furthermore, it was advocated that diagnosis of septic arthritis should be urgent that treatment could be initiated for effective outcome [16]. Moreover, D-lactate was suggested as rapid diagnostic test to rule in bacterial synovitis, where 85% of synovial fluid samples tested positive for lactic acid (lactate) [2]. Similarly, it was noted that lactic acid determination in sequential synovial samples was diagnostically important to evaluate response to therapy [16]. More recently, using lactate as a synovial inflammatory biomarkers to differentiate between infectious arthritis and gout-arthritis, reported to be successful, manifesting significant diagnostic potential of AUC-0.901 with sensitivity of 89.5% [3]. Furthermore, C-reactive protein, WBC, % polymorpho-nuclear cells, along with lactate were recently been suggested to be best inflammatory marker to predict septic conditions [4].

Significant interest in determination of Lactate and in many cases LDH, as a diagnostic tool to distinguish between septic and non infectious (non-septic) arthritis has been shown in several recent and past studies on the detailed report (DR) of synovial fluids [2-5, 11, 13, 14, 17]. It is reported that septic arthritis in adult needed to be diagnosed promptly to differentiate it from rheumatic arthritis in order to initiate therapy, which eventually improves morbidity [17].

CONCLUSION

Present study described evaluation of lactate in synovial fluid of arthritis patients, in order to differentiate between patients with septic arthritis and those with no synovial infectious. Elevated lactate and LDH levels in the study were corresponded with bacterial culture outcomes that manifested growth of *Pseudomonas aeruginosa, Staphylococcus aureus* and *Enterococci* species. It is strongly suggested that lactate determination should be included in chemical analysis of synovial fluids, when arthritis patients were suspected of sepsis or synovium bacterial infections.

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