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A Comparative Estimation of Aldolase - A and Creatine Kinase-Muscle Levels in Arthritis Patients and Snail Consuming Subjects

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Abstract: The people consumed snails, the prevalence of arthritis was lower as per the reducing levels of biomarkers viz. Aldolase A (Aldo-A) and Creatine kinase muscle (CK-MM). The objective of this study was to estimate the level of Aldo-A and CK-MM in arthritis patients compared to subjects who consumed snails. A total of 100 subjects, half of the patients were presented with OA (group A) and rest subjects did not show OA (group B) who consumed snails in the diet. For Aldo-A (U/L) and CK-MM (µg/L), the significant (P<0.03 and P<0.002) reducing levels were observed in group B (3.98 \pm 1.15 and 36.00 \pm 12.23) when compared to group A (4.48 \pm 1.18 and 45.72 \pm 18.04). In conclusion, these natural products of edible snails are preventing oxidative stress and well-known anti-inflammatory, immunemodulatory and wound healing capacity, which is due to decreasing values of Aldo-A and CK-MM.

Keywords: Aldo-A, Arthritis, Biomarkers, CK-MM, Edible snail

1. Introduction

Aldolase is an enzyme involved in synthesizing glucose and breaking it down into products of energy. Elevated serum aldolase levels may indicate damage to different organ systems. Reference ranges for aldolase are as follows: [1]

Adult: 3-8.2 Sibley-Lehninger units/dL or 22-59 mU/L at 37°C (SI units).

Elevated aldolase A (Aldo-A) levels may be seen in several disorders such as damage to the skeletal muscle (trauma), dermatomyositis, polymyositis, muscular dystrophy, nonspherocytic haemolytic anaemia, osteosarcoma, etc. [2]

Measurement of Aldo-A can also help differentiate between muscle versus neurological myopathy. If aldolase A is elevated, the primary cause of myopathy may be related to an inflammatory state of the muscle. Aldolase is a cytoplasmic enzyme involved and fructose in glucose metabolism. It specifically catalyzes the reversible reaction converting fructose 1,6-bisphosphate dihydroxyacetone phosphate (DHAP) and glyceraldehydes 3phosphate. [3]

The enzyme works on six reversible reactions in gluconeogensis and glycolysis. In gluconeogenesis, aldolase catalyses the reduction of phosphoenolpyruvate to fructose 1,6-bisphosphate. In glycolysis, aldolase catalyzes fructose 1,6-bisphosphate to phosphoenolpyruvate through an oxidative reaction. [4,5]

Creatine kinase (CK) is a dimeric enzyme that catalyses the reversible phosphorylation of creatine by ATP. [6] In 1966, CK isoenzymes were identified in various tissues. [7] The isoenzymes of CK are dimers of either type B or type M polypeptide chains, BB isoenzymes are found in the central nervous system, and MM isoenzymes are a principal component in adult skeletal muscles. [8] The myocardium has 15% CK-MB isoenzyme and 85% CK-MM [9] while skeletal muscles contain about 1-3% of CK-MB. [10] The level of creatine kinase-muscle (CK-MM) could be estimated through the measurement of CK-MM isoforms, [11,12] which is also expressed in many muscle disorders. The standard value of CK-MM was established of about <168 U/L. [13] Another parameter like Aldo-A estimation was also documented by many researchers (reference value is <7.6 U/L) in patients with various diseases, such as skeletal muscle damage. [14-

Ganguly [13] reported that the induction of CK-MM and Aldo-A levels are suitable biomarker after confirming with radiological imaging in the case of OA. This study emphasized that CK-MM and Aldo-A from the patient's serum could be recognized accurately to know the considerable inflammation, degeneration of muscle and skeletal tissues during the early stage of OA. This analysis helps quickly and in affordable low cost to determine OA where sometimes no pain or discomfort or deformities observed in the joints prior to focus as per the radiological images.

CK-MM is a muscle enzyme, which participated in the phosphocreatine circuit for energy supply to muscles, [17] while Aldo-A is a glycolytic enzyme abundantly expressed in muscles. [18] It was noted from earlier study by Wu and Perryman [19] that the elevation of serum CK (hyperCKemia) and Aldo-A level is regard as a biomarker of muscle damage resulting to a seepage of these cytosolic enzymes into the blood.

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Several bioactive compounds from natural sources of plants and animals have capable towards therapeutic efficacy as potential related to anti-inflammatory, antioxidant, and tissue protective properties [20-25] These natural compounds could be regulated the inflammatory processes and metabolic pathways involved in OA, thereby inhibiting the symptoms and potentially slow down the disease progression. [26] So, investigating the efficacy of the natural products in the treatment of OA encounters a growing demand for natural health remedies, but also creates novel opportunities for the therapy of an elevated prevalent age-related disorders. [27]

In a study by Ibrahim et al. [25] evaluated on antioxidant and anti-inflammatory effects of *Eremina desertorum* snail mucin in which several stress biomarkers were inhibited to prevent oxidative stress and inflammation. Recently, Ganguly and Banerjee [28] reported regarding the importance of Aldo-A and CK-MM among KOA adult patients in which they stated that these two markers are suitable to predict OA.

In the present study, it was estimated to know the level of Aldo-A and CK-MM in arthritis patients compared to subjects who consumed snails.

2. Materials and Methods

In the present study, subjects were included and categorised into 2 groups. Among total 100 participant, 50 patients of arthritis as group A and 50 subjects as healthy controls who were consumed snail and mussels as group B. As per history of inflammatory joint disorders and muscle damage in patients, the biomarker especially Aldo-A and CK-MM for group A and group B separately were estimated. The Aldo-A and CK-MM concentrations were expressed in terms of U/L by using Kit (SKU: AD189, Randox and E-EL-H1433, Cell Biologics). Categorical variables were taken and expressed in percentage frequency distribution and continuous variable expressed as Mean ± SD and comparison were made between group A and group B patients as per student 't' test by using statistical tool. P value less than 0.05 considered as significant.

3. Results

Table 1 evaluates the frequency distribution of Aldo-A in serum of group A and B participants. The majority of patients were observed >5.0 U/L (17, 34.0%) when compared to group B (10, 20.0%).

Table 1: Aldo-A distribution

Aldo-A (U/L)						
Group A	Frequency	%	Group B	Frequency	%	
< 5.0	33	66.0	< 5.0	40	80.0	
>5.0	17	34.0	>5.0	10	20.0	
Total	50	100.00	Total	50	100.00	

Table 2 evaluates the frequency distribution of muscle creatine kinase (CK-MM) in serum of group A and B participants. In group A, majority of patients were observed $>50 \,\mu\text{g/L}$ (34, 68.0%) when compared to group B (5, 10.0%).

Table 2: CK-MM distribution

CK-MM (µg/L)						
Group A	Frequency	%	Group B	Frequency	%	
< 50	16	32.0	< 50	45	90.0	
>50	34	68.0	>50	5	10.0	
Total	50	100.00	Total	50	100.00	

Table 3 describes comparative analysis of mean \pm SD of Aldo-A (U/L) and CK-MM (µg/L) between arthritis patients (group A) and snails and mussels consumed (group B) subjects. For Aldo-A (U/L), a significant (P<0.03) decreased level was observed in group B (3.98 \pm 1.15) when compared to group A (4.48 \pm 1.18). For CK-MM (µg/L), a significant (P<0.002) reduced level was observed in group B (36.00 \pm 12.23) when compared to group A (45.72 \pm 18.04).

Table 3: Comparative analysis of mean Aldo-A and CK

Mini between group A and group B							
Parameters	Group A	Group B	P-				
$(Mean \pm SD)$	(n = 50)	(n = 50)	value				
Aldo-A (U/L)	4.48 ± 1.18	3.98 ± 1.15	0.03				
CK-MM (µg/L)	45.72 ± 18.04	36.00 ± 12.23	0.002				

4. Discussion

Generally, Aldo-A and CK-MM was observed a decreasing trend among non-RA group while these were exceeded among RA patients, which is supported by Ganguly. [13]. Moreover, similar findings were observed in our study participants who consumed snails regularly revealed lower value.

In another study by Ganguly and Banerjee [28] estimated serum level of Aldo-A and CK-MM after receiving Jumpstart Nutrition® dietary supplement for 12 weeks among OA patients compared to the control group (without supplementation), 47.06% of patients used glucosamine, chondroitin sulfate, and diacerein (SYSADOA) and 52.94% of the patients used other alleviative medicines. They found a significantly (P<0.0001) reducing levels of Aldo-A and CK-MM in OA group when compared to the control group.

Some studies exhibited that CK-MM and Aldo-A levels are closely associated with age-associated connective tissue damage, bone erosion, and skeletal muscle damage. [29] Interestingly, the reduction of Aldo-A and CK-MM in the subjects of consumed snails due to the presence of collagen when compared to OA patients, who did not consume snails. It is well-known fact that the orally administered hydrolyzed collagen peptides are suitable for improving skeletal muscle health and performance. [30]

Several earlier studies emphasized the potential benefit of collagens in food supplementation. Zdzieblik et al. [31] reported that collagen peptide supplementation increased the muscle strength in elderly sarcopenic men. Oertzen-Hagemann et al. [32] investigated the beneficial efficacy collagen peptide supplementation in combination on the protein composition of skeletal muscle.

Prabhakar and Roy [33] reported that the flesh of *Bellamia* (*Viviparous*) bengalensis is used as a traditional medicine against arthritis in the people of north Bihar. In another experimental study by Sarkar et al. [20] reported that an in

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vivo method with rat model with OA groups, ankle/knee swellings were significantly reduced after treatment with *Viviparous bengalensis* flesh extract.

Our study confirms that snail consumed patients did not observe OA. Our study also stated that there was improved the Aldo-A and CK-MM among the subjects who consumed snails.

5. Conclusions

The present study indicates that the prevalence of arthritis was significantly lower as per the reduction level of Aldo-A and CK-MM among subjects who consumed natural bioactive compounds especially snails and mussels. It is evidenced that these natural products of edible snails and mussels are preventing oxidative stress and well-known anti-inflammatory, immune-modulatory and wound healing capacity, which is due to decreasing values of Aldo-A and CK-MM observed improved in the snail consumed subjects (group B).

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Conflict of interest

As per authors no conflict of interest is declared.

References

- [1] Pagana KD, Pagana TJ, Pagana TN. Mosby's Diagnostic & Laboratory Test Reference. 14th ed. St. Louis, Mo: Elsevier; 2019.
- [2] Long F, Cai X, Luo W, Chen L, Li K. Role of aldolase A in osteosarcoma progression and metastasis: in vitro and in vivo evidence. Oncol Rep. 2014;32(5):2031-2037.
- [3] Anastasopoulou C. Aldolase. Medscape. 2019. Retrieved from: https://emedicine.medscape.com/article/2087158-overview?form=fpf#a4
- [4] Siebers B, Brinkmann H, Dorr C, et al. Archaeal fructose-1,6-bisphosphate aldolases constitute a new family of archaeal type class I aldolase. J Biol Chem. 2001;276(31):28710-28718.
- [5] Szekrenyi A, Soler A, Garrabou X, Guérard-Hélaine C, Parella T, Joglar J, et al. Engineering the donor selectivity of d-fructose-6-phosphate aldolase for biocatalytic asymmetric cross-aldol additions of glycolaldehyde. Chemistry. 2014;20(39):12572-12583.
- [6] Moghadam-Kia S, Oddis CV, Aggarwal R. Approach to asymptomatic creatine kinase elevation. Cleve Clin J Med. 2016;83(1):37-42.
- [7] van der Veen KJ, Willebrands AF. Isoenzymes of creatine phosphokinase in tissue extracts and in normal and pathological sera. Clin Chim Acta. 1966;13(3):312-316.
- [8] Dawson DM, Eppenberger HM, Kaplan NO. Creatine kinase: evidence for a dimeric structure. Biochem Biophys Res Commun. 1965;21(4):346-353.

- [9] Lee TH, Goldman L. Serum enzyme assays in the diagnosis of acute myocardial infarction. Recommendations based on a quantitative analysis. Ann Intern Med. 1986;105(2):221-233.
- [10] Tsung JS, Tsung SS. Creatine kinase isoenzymes in extracts of various human skeletal muscles. Clin Chem. 1986 Aug;32(8):1568-1570.
- [11] Uji Y, Karmen A, Sugiuchi H, Okabe H, Hata K, Miura M. Simultaneous automated measurement of serum total CK and CK-MM isoform ratio in serum. J Clin Lab Anal. 1994;8(5):273-276.
- [12] Armbruster DA. The genesis and clinical significance of creatine kinase isoforms. Laboratory Medicine. 1991;22(5):325-334.
- [13] Ganguly A. Levels of C-reactive protein, creatine kinase-muscle and aldolase A are suitable biomarkers to detect the risk factors for osteoarthritic disorders: A novel diagnostic protocol. Caspian J Intern Med. 2019;10(1):25-35.
- [14] Burtis CA, Ashwood AR, Burns DE, editors. Tietz text book of clinical chemist and molecular Diagnostic. 5th ed. USA: Elsevier Saunders; 2012. pp. 572-577.
- [15] Apple FS, Rogers MA, Ivy JL. Creatine kinase isoenzyme MM variants in skeletal muscle and plasma from marathon runners. Clin Chem. 1986 Jan;32(1 Pt 1):41-44.
- [16] Clarkeon PM, Apple FS, Byrnes WC, McCormick KM, Triffletti P. Creatinekinase isoforms following isometric exercise. Muscle Nerve. 1987; 10:41-44.
- [17] Saks V. The phosphocreatine-creatine kinase system helps to shape muscle cells and keep them healthy and alive. J Physiol. 2008;586(12):2817-2818.
- [18] Taguchi K, Takagi Y. [Aldolase]. Rinsho Byori. 2001; Suppl 116:117-124.
- [19] Wu AH, Perryman MB. Clinical applications of muscle enzymes and proteins. Curr Opin Rheumatol. 1992;4(6):815-820.
- [20] Sarkar A, Datta P, Gomes A, Das Gupta SC, Gomes A. Anti-osteoporosis and anti-osteoarthritis activity of fresh water snail (*Viviparous bengalensis*) flesh extract in experimental animal model. Open Journal of Rheumatology and Autoimmune Diseases. 2013;3;10-17.
- [21] Srinandhinidevi KM, Viveka S. Evaluation of in vitro anti-inflammatory activity of freshwater snail. Uttar Pradesh Journal of Zoology. 2021;42(24);597-601.
- [22] Lee H, Zhao X, Son YO, Yang S. Therapeutic single compounds for osteoarthritis treatment. Pharmaceuticals (Basel). 2021;14(2):131.
- [23] Rocha J, Peixe L, Gomes NCM, & Calado R. Cnidarians as a source of new marine bioactive compounds--an overview of the last decade and future steps for bioprospecting. Marine Drugs. 2011; 9:1860-1886.
- [24] Kang H, Kim B. Bioactive compounds as inhibitors of inflammation, oxidative stress and metabolic dysfunctions via regulation of cellular redox balance and histone acetylation state. Foods. 2023;12(5):925.
- [25] Ibrahim AM, Morad MY, El-Khadragy MF, Hammam OA. The antioxidant and anti-inflammatory effects of *Eremina desertorum* snail mucin on experimentally induced intestinal inflammation and testicular damage. Biosci Rep. 2022;42(10):BSR20221020.

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- [26] Pérez-Lozano ML, Cesaro A, Mazor M, Esteve E, Berteina-Raboin S, Best TM, et al. Emerging natural-product-based treatments for the management of osteoarthritis. Antioxidants (Basel). 2021;10(2):265.
- [27] Maouche A, Boumediene K, Baugé C. Bioactive compounds in osteoarthritis: Molecular mechanisms and therapeutic roles. Int J Mol Sci. 2024;25(21):11656.
- [28] Ganguly A, Banerjee S. Biomonitoring the skeletal muscle metabolic dysfunction in knee osteoarthritis in older adults: Is Jumpstart Nutrition® Supplementation effective? Caspian J Intern Med. 2023;14(4):590-606.
- [29] Lee YT, Yunus MHM, Ugusman A, Yazid MD. Natural compounds affecting inflammatory pathways of osteoarthritis. Antioxidants (Basel). 2022;11(9):1722.
- [30] Zhang L, Li T, Wang R, Xu J, Zhou L, Yan L, et al. Evaluation of long-time decoction-detoxicated *Hei-Shun-Pian* (Processed *Aconitum carmichaeli* Debeaux lateral root with peel) for its acute toxicity and therapeutic effect on mono-iodoacetate induced osteoarthritis. Front Pharmacol. 2020;11:1053.
- [31] Buhrmann C, Brockmueller A, Mueller AL, Shayan P, Shakibaei M. Curcumin attenuates environment-derived osteoarthritis by Sox9/NF-kB signaling axis. Int J Mol Sci. 2021;22(14):7645.
- [32] Oertzen-Hagemann V, Kirmse M, Eggers B, Pfeiffer K, Marcus K, de Marées M, et al. Effects of 12 weeks of hypertrophy resistance exercise training combined with collagen peptide supplementation on the skeletal muscle proteome in recreationally active men. Nutrients. 2019;11(5):1072.
- [33] Prabhakar AK, Roy SP. Ethno-medicinal uses of some shell fishes by people of Kosi River Basin of North-Bihar, India. Ethnomedicine. 2009;3(1):1-4.