IMPACTS OF QUERCETIN SUPPLEMENTATION POST-EXERCISE

IMPACTOS DA SUPLEMENTAÇÃO DE QUERCETINA PÓS-EXERCÍCIO

IMPACTOS DE LA SUPLEMENTACIÓN DE QUERCETINA DESPUÉS DEL EJERCICIO

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ABSTRACT

Introduction: Quercetin (Q) is a flavonoid that has been shown to be an antioxidant in vitro. A current review is necessary to evaluate whether Q can improve biochemical damage markers following exercise-induced muscle damage (EIMD) and delayed onset muscle soreness (DOMS). Objective: Specify the impact of Q supplementation on EIMD, DOMS, and inflammatory cytokines (IL-6, IL-10, and TNF-α) after exercise. Methods: Participants (n=28) were randomly assigned to Q (1000 mg/day) and placebo (PLA). Intake was done 48 hours before EMID to 96 hours after EMID (one week). Before EIMD (PRE) and 24, 48, 72, and 96 hours after EIMD, blood samples were collected for CK and measurement of inflammatory cytokines. ANOVA test was used for data analysis with a significance P > 0.05. Results: Peak DOMS was seen 48 hours after EIMD, regardless of the DOMS combination. Q had a significant reducing effect on CK response at 24 hours (-43%), 48 hours (-48%), 72 hours (-56%), and 96 hours (-67%) after EIMD compared to placebo. IL-10 and IL-6 did not change statistically for the applied sample size. TNF-α was lower by Q intake significantly at 24 hours (-24%), 48 hours (-22%), and 96 hours (-22%) compared to PLA. Furthermore, the TNF-α trend was lower with Q intake at 72 hours (-19%). Conclusion: Q supplementation decreased biological inflammation during post-IMD recovery but not quadriceps DOMS. ***Level of Evidence: Therapeutic Studies – Investigating Treatment Outcomes.***

Keywords: Quercetin; Soft Tissue Injuries; Myalgia; Creatine Kinase.

RESUMO

Introdução: A quercetina (Q) é um flavonóide que provou ser um antioxidante in vitro. Fez-se necessária uma revisão atual projetada para avaliar se a Q pode melhorar os marcadores bioquímicos de dano após o dano muscular induzido pelo exercício (EIMD) e a dor muscular de início retardado (DOMS). Objetivo: O objetivo da revisão atual foi especificar o impacto da suplementação Q sobre EIMD, DOMS e citocinas inflamatórias (IL-6, IL-10 e TNF-α) após o exercício. Métodos: Os participantes (n=28) foram alocados em Q (1000 mg/dia) e placebo (PLA) aleatoriamente. Fez-se ingestão 48 horas antes da EMID a 96 horas após a EMID (uma semana). Antes da EIMD (PRE) e 24, 48, 72 e 96 horas após a EIMD, amostras de sangue coletadas para CK e medição de citocinas inflamatórias. O teste ANOVA foi usado para análise de dados com significância P > 0,05. Resultados: O pico DOMS foi visto em 48 horas após EIMD, independentemente da combinação de DOMS. Q teve um efeito de redução significativo na resposta CK em 24 horas (-43%), 48 horas (-48%), 72 horas (-56%) e 96 horas (-67%) após a EIMD em comparação com placebo. IL-10 e IL-6 não mudaram estatisticamente para o tamanho da amostra aplicada. TNF-α foi menor pela ingestão de Q significativamente às 24 horas (-24%), 48 horas (-22%), e 96 horas (-22%) em comparação com o PLA. Ademais, a tendência TNF-α foi menor com a ingestão de Q às 72 horas (-19%). Conclusão: A suplementação de Q diminuiu a inflamação biológica durante a recuperação pós EIMD, porém não os DOMS do quadríceps. ***Nível de evidência: Estudos Terapêuticos – Investigando os Resultados de tratamento.***

Descritores: *Quercetina; Lesões dos Tecidos Moles; Mialgia; Creatina Quinase.*

RESUMEN

Introducción: La quercetina (Q) es un flavonoide que ha demostrado ser un antioxidante in vitro. Por ello, es necesaria una revisión actual diseñada para evaluar si la Q puede mejorar los marcadores bioquímicos de daño tras el daño muscular inducido por el ejercicio (EIMD) y el dolor muscular de aparición retardada (DOMS). Objetivo: El objetivo de la presente revisión fue especificar el impacto de la suplementación con Q en el EIMD, el DOMS y las citoquinas inflamatorias (IL-6, IL-10 y TNF-α) después del ejercicio. Métodos: Los participantes (n=28) fueron asignados aleatoriamente a Q (1000 mg/día) y a placebo (PLA). La ingesta se realizó desde 48 horas antes de la EMID hasta 96 horas después de la misma (una semana). Antes de la EMID (PRE) y 24, 48, 72 y 96 horas después de la EMID, se tomaron muestras de sangre para la CK y la medición de citoquinas inflamatorias. Se utilizó la prueba ANOVA para el análisis de los datos con una significancia P > 0,05. Resultados: El pico de DOMS se observó en las 48 horas posteriores a la EIMD, independientemente de la combinación de DOMS. Q tuvo un efecto significativamente reductor en la respuesta de la CK a las 24 horas (-43%), 48 horas (-48%), 72 horas (-56%) y 96 horas (-67%) después de la EIMD en comparación con el placebo. La IL-10 y la IL-6 no cambiaron estadísticamente para el tamaño de muestra aplicado. El TNF-α se redujo significativamente con la ingesta de Q a las 24 horas (-24%), a las 48 horas (-22%) y a las 96 horas

(-22%) en comparación con el PLA. Además, la tendencia del TNF-α fue menor con la ingesta de Q a las 72 horas (-19%). Conclusión: La suplementación con Q disminuyó la inflamación biológica durante la recuperación después de un IMD, pero no el DOMS del cuádriceps. ***Nivel de evidencia: Estudios terapéuticos –Investigación de los resultados del tratamiento.***

Descriptores: *Quercetina; Traumatismos de los Tejidos Blandos; Mialgia; Creatina Quinasa.*

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INTRODUCTION

Many research articles focused on the resistance exercise induces increase in production of reactive oxygen species (ROS), which may be involved in muscle damage and muscle force reduction within the training. Exercise-induced muscle damage (EIMD) starts an inflammatory response related to remodeling and secondary muscle damage. Furthermore, the inflammatory response might amplify delayed onset muscle soreness (DOMS), reduce muscle performance, accelerate the fatigue onset and postpone muscle recovery.[1]

The inflammation reaction to EIMD happens in two main steps. Through the first step, macrophages and neutrophils can diffuse ROS and clear debris by phagocytosis. Moreover, byproducts of ROS and cytokines from the damaged muscle are diffused into the blood, involving in oxidative stress and low-grade systemic inflammation, elevating blood TNF-α levels, and changing glutathione redox status.[2] Overall, the pro-oxidant and pro-inflammatory procedures may enforce secondary damage to the muscle, extending amelioration and restoration procedures within the chronic inflammation step.

Wide assays have been performed on anti-inflammatory and antioxidant features of these nutrients in relevance to exercise. There is growing evidence revealing that Q has considerable therapeutic potential in the various chronic diseases prevention and treatment, including cardiovascular diseases, as well as cancer.[3]

Recent studies suggested that Q reduced expression of inflammation cytokines of TNF-α, IL-6, IL-8 and IL-10 and transcription of macrophages cultured in humans, that are suggested relate to secondary muscles damages. The primary result of the current review is on EIMD markers to evaluate the supposition which 7 days of Q administration could not only suppress the muscle damage induced via eccentric exercise, but likewise could enhance the inflammation in the 4 days following the damage.

METHODS

Study population

The study participants were informed about this work and they signed the Free and Informed Consent Form (EHIC) for this work. The following criteria were accepted for inclusion: (1) sedentary to or untrained participants; (2) aged between 18 to 30 years; and (3) healthy participants that checked by a questionnaire of general health. The criteria for exclusion were: (1) chronic inflammatory injury or symptoms and history of orthopedic, endocrine or metabolic diseases; (2) undertaking routine resistance exercise in the last six months; (3) Physical Activity Readiness Questionnaire negative response. About study duration, subjects were requested to maintain their nutritional diet and habitual exercise. Furthermore, from 48 hours beforehand and within one-week study duration subjects asked to refrain from Q consumption and other nutrients featuring antioxidants, supplementation, regular NSAIDs, ergogenic aids and some situation which could inhibit the weaker performance of physical activity. Our observation showed about 29 percent non-compliance in present assay and 28 participants finished the whole process (Table 1).

Table 1. Subjects characteristics.

Characteristic	Quercetin (n=16)	Placebo (n=12)
Gender (# F)	11	7
Age (y)	19 ± 2	20 ± 1
Height (M)	1.69 ± 0.09	1.71 ± 0.1
Weight (kg)	64.2 ± 11.1	64.8 ± 10.9
BMI	22.8 ± 2.9	22.1 ± 1.9
Body fat (%)	23.9 ± 8.6	22.9 ± 11.5
Muscle strength (1RM)	182 ± 39	195 ± 57
Total load lifted during EIMD (kg)	9211 ± 2541	10325 ± 4052

This study was conducted in accordance with the Declaration of Helsinki principle. The participants signed the Free and Informed Consent Form (EHIC) for this work.

Supplementation

During the first session 48 hours before EIMD, participants engaged in a pre-treatment assessment (PRE). After that, subjects were allocated to Q or placebo (PLA) randomly using a double-blind approach. Stratification applied to allocate subjects to supplement group to certify same male and female numbers and an equivalency according to basic strength among groups. Beginning from the next day, for 7 continuous days, volunteers took 2 capsules with 500 mg of Q one after rising in the morning and one after 12 hours to attain 1000 mg dose daily. Capsules with PLA were indiscernible in appearance and taste from Q capsules. Compliance of subjects observed daily by the study staff.

EIMD protocol

Participants finished 6 sets of leg press training with 10 repetitions at 110 percent of their 1 repetition maximum (1RM) as load set. Participants were requested to hold a 5 seconds contraction with a metronome on leg press. Five seconds contraction elected to increase the contraction in EIMD consequently. If some volunteers were incapable for the five seconds contraction holding, the weight decreased two kilograms.

Quadriceps DOMS

We measured DOMS on anterior thigh and applied them as other leg muscles indicative. Briefly, a standard force over the aimed anatomical part in the seated situation was used. Participants were prepared ten centimeter line without visual indicator except anchors in end and required to show DOMS degree by drawing a line in spot they perceived correlated to their pain. For soreness grade specification, the same investigator recorded. Three rate for every quadriceps summed up to specify overall pain grades of quadriceps for the left and right legs.

Collection of blood samples

Venous blood samples were obtained from all participants PRE EIMD and 24, 48, 72, and 96 hours after EIMD applying standard phlebotomy technique from an antecubital vein. Plasma samples were collected from clotted blood after centrifuging.

Serum creatine kinase and serum cytokines measurement

CK concentration were measured using ELISA method, based on the manufacturers' protocol. In brief, serum aliquots analyzed duplicate applying multiplex assay with high-sensitivity, based on the manufacturers' protocol. Obtained data applied to assess unknown levels by Software of Milliplex Analyst.

Statistical analyses

For evaluating significance, data were analyzed applying a 2 (Q or PLA) by 5 (PRE, 24, 48, 72, and 96 hours) analyses of variance with frequent measurements on the 2nd item. Measures are reported as mean ± SE and $p < 0.05$ was used as the significance level. Significant α measures adjusted by the Huynh–Feldt way to compute for the frequent measurements design. Significance impacts location specified applying t-tests with Bonferroni modification for multiple comparisons.

RESULTS

Quadriceps DOMS

We observed a significant impact in time in relation with DOMS on right quad (Figure 1. A), left quad (Figure 1. B) and mixed quad (Figure 1. C). Top DOMS was seen at 48 hours post EIMD without the DOMS combination.

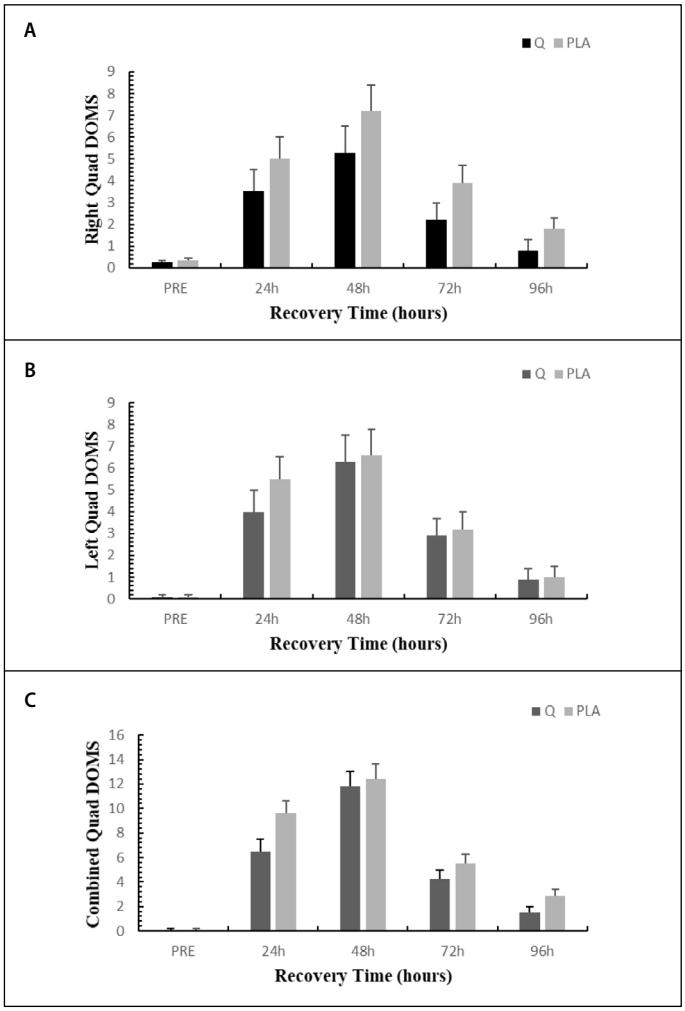

Figure 1. Quadriceps DOMS was consistently used to assess perceived muscle soreness using a visual analog scale. Measurements were made PRE, 24, 48, 72, and 96 hours following EIMD (Exercise-Induced Muscle Damage; 60 reps at 110% of the 1RM, eccentric only). There was no significant difference in muscle soreness between treatment conditions.

Plasma creatine kinase

Q had a significant reduction effect on CK response (Figure 2) at 24 hours (–43%), 48 hours (–48%), 72 hours (–56%), and 96 hours (–67%) after EIMD compared to placebo. Both groups represented an increase in CK after EIMD significantly; as regards, the Q group had a lower blunted elevation in CK significantly that came back to PRE measures at 48 hours after EIMD.

Serum cytokines

We observed significant effects for Q supplementation on TNF--α (Figure 3. A); as regards, changes in IL-6 (Figure 3. B), and IL-10 didn't touch significant point statistically for the participants number (Figure 3. C). TNF-α was decreased by Q administration significantly at 24 hours (–24%), 48 hours (–22%), and 96 hours (–22%) compared to control group. Also, TNF-α tendency was being smaller by Q administration at 72 hours (–19%).

DISCUSSION

The main finding was that Q consumption (1000 mg/day) significantly reduced serum DOMS, CK and TNF-α levels after EIMD during recovery.

Despite decreased aforementioned inflammation marker, we noticed no significant decrease in IL-6 and IL-10 with Q compared to placebo. Consistent with Trombold et al. (2010) suggestion [4], we found no significant increase in blood collected every 24 hours for 96 hours after exercise. Although some articles have suggested alteration in IL-10 and IL-6 at same time spots post exercise,[5] others have not.[6]

As expected the delayed peak of CK, we detect increased CK concentrations every 24 hours for 96 hours after exercise for both Q and PLA groups. Because of this, we evaluated CK plasma levels in the days' post EIMD, and we detected that when subjects consumed Q, the elevation in CK was lesser in comparison to control group. When myocytes are seriously injured and cell membrane is damaged, myocytes leave necrotic, sarcoplasm proteins leakage from cell membrane and enter to blood flow . In addition, HMB has been widely applied as a supplement for EIMD and DOMS inhibition, improves skeletal muscle hypertrophy and exercise performance.[7] Phosphorylation or esterification to CoA derived carbons for cholesterol synthesis, as a membranes basic components. Thus, decreased myocellular protein effluxes, as like as CK and LDH, out of cells. Moreover, some assays has indicated that HMB can motivate synthesis of protein and suppress the pathway of ubiquitin-proteasome proteolytic (Ub) as a basic pathway of intracellular protein wasting away.[8] We hypothesis these mechanisms for CK reduction with Q administration in statistical analysis, that Q could have improved membranes cells consistency and thereby reduced proteins release.

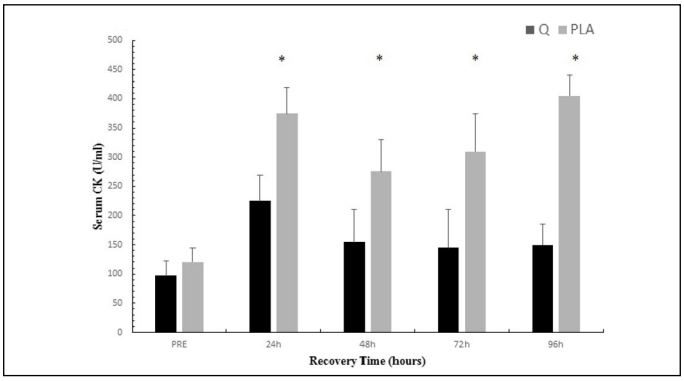

Figure 2. CK measured PRE, 24, 48, 72, and 96 hours after EIMD (Exercise-Induced Muscle Damage; 60 reps at 110% of the 1RM, eccentric only). * indicated a difference between Q and placebo groups ($P < 0.05$).

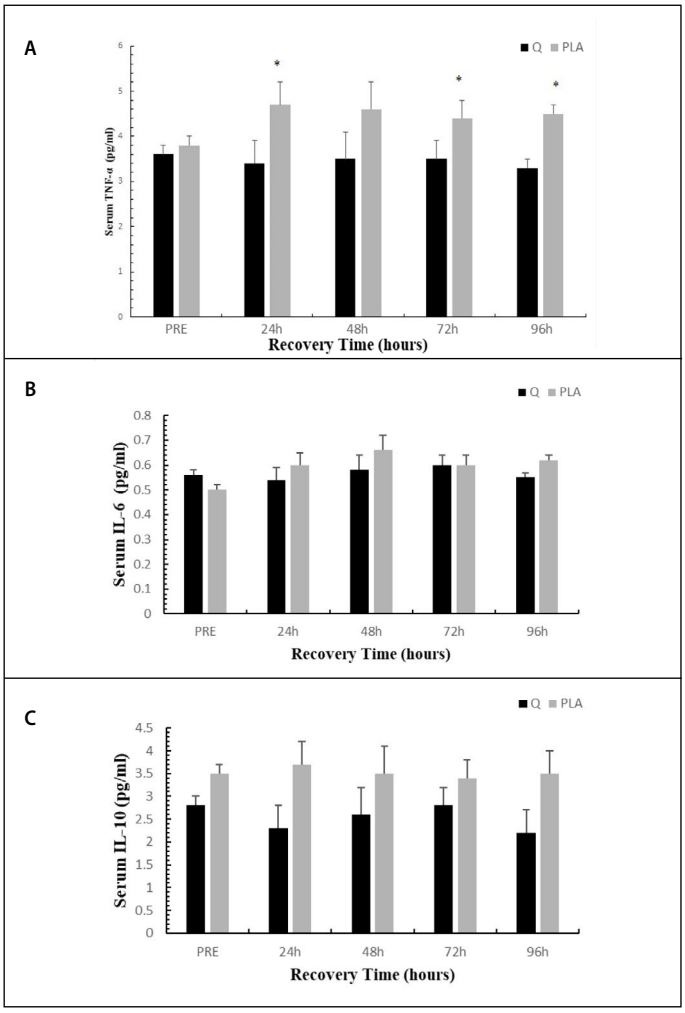

Figure 3. Serum cytokines (TNF-α (A), IL-6 (B), and IL-10 (C)) measured PRE, 24, 48, 72, and 96 hours after EIMD (Exercise-Induced Muscle Damage; 60 reps at 110% of the 1RM, eccentric only). * indicated a significant difference between Q and placebo groups ($P < 0.05$).

Reduction in function is the main feature of EIMD and create DOMS that occur when micro trauma started in myocytes by stress generated during exercise and get worse by the inflammatory responses subsequently.[9]

The potential mechanisms of Q's regulation of inflammation have not been indicated. Based on previous investigations, various mechanisms suggested for Q inflammation reduction, which may aid to clarify its health meliorating specification.[10] First, evidence shows that Q suppresses the nuclear factor- kB (NF-kB) transfer in to nucleus, which different pro-inflammatory cytokines are generated and the reaction of inflammation is more reinforced. Furthermore, Q supplementation could antagonize NF-kB transcriptional activation indirectly via enhancing peroxisome proliferator-activated receptor γ (PPARγ) activation. Moreover, Q may decrease inflammatory factors via intervening with the pathway of AMPK/ SIRT1.[11] So, by NF-kB signals and inhibition of COX-2 upregulation, Q suppressed generation of prostaglandin, implying that Q consumption might reduce vascular permeability. It could be that Q fixates cells membranes, which should be relate to moderated elevation in plasma CK acting.

Strength and Limitations

Short periods of Q consumption appear not to be suitable for different biological effects of Q since the estimated elimination rate is less than 24 hours in humans.[12] The basic present study limitation is that we didn't assess Q bioavailability during the supplementation.

CONCLUSION

The outcomes within the current study indicate that Q ingestion seems beneficial for reducing DOMS and EIMD which happens post exercise. Further assays with various dose of Q is required to assess the best dose and duration for best recovery. At last, we concentrate on main indices correlated to post exercise recovery, consist of CK levels and DOMS indices.

The author declare no potential conflict of interest related to this article

AUTHORS' CONTRIBUTIONS: The execution of this work, its knowledge content and writing of the manuscript is completed by Weiyuan Ying.

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