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Comparison of the Hyperkinasemic Effects of Erythropoietin and U-74389G on Creatine Phosphokinase Levels

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Abstract

Aim: This study calculated the effects on creatine phosphokinase (CPK) levels, after treatment with either of 2 drugs: the erythropoietin (Epo) and the antioxidant lazaroid (L) drug U-74389G. The calculation was based on the results of 2 preliminary studies, each one of which estimated the certain influence, after the respective drug usage in an induced ischemia reperfusion (IR) animal experiment.

Materials and Methods: The 2 main experimental endpoints at which the serum CPK levels (CPKl) were evaluated was the 60th reperfusion min (for the groups A, C and E) and the 120th reperfusion min (for the groups B, D and F). Specially, the groups A and B were processed without drugs, groups C and D after Epo administration; whereas groups E and F after the L administration.

Results: The first preliminary study of Epo presented a non significant hyperkinase mice ffect by 2.08%±2.77% (p-value=0.4430). The second preliminary study of U-74389G presented a significant hyperkinasemic effect by 8.52%±4.35% (p-value=0.0005). These 2 studies were co-evaluated since they came from the same experimental setting. The outcome of the co-evaluation was that L is 4.09626-fold [4.092989 - 4.099534] more hyperkinasemic than Epo (p-value=0.0000).

Conclusions: The anti-oxidant capacities of U-74389G ascribe 4.09626-fold more hyperkinasemic effects than Epo (p-value=0.0000).

Keywords: ischemia; erythropoietin; U-74389G; creatine phosphokinase levels; reperfusion

Introduction

The lazaroid U-74389G (L) may be not famous for its hyperkinasemic[1] capacity (p-value=0.0005). U-74389G as a novel antioxidant factor, implicates exactly only 260 published studies. The ischemia reperfusion (IR) type of experiments was noted in 18.84% of these studies. A tissue protective feature of U-74389G was obvious in these IR studies. The U-74389G chemically known as 21-[4-(2,6-di-1-pyrrolidinyl-4-pyrimidinyl)-1-piperazinyl]-pregna-1, 4, 9(11)- triene-3, 20-dione maleate salt is an antioxidant complex, which prevents the lipid peroxidation either iron-dependent, or arachidonic acid-induced one. Animal kidney, liver, brain microvascular endothelial cells monolayers and heart models were protected by U-74389G after IR injury. U-74389G also

attenuates the leukocytes; down-regulates the proinflammatory gene; treats the endotoxin shock; produces cytokine; enhances the mononuclear immunity; protects the endothelium and presents antishock property.

Erythropoietin (Epo) even if is not famous for itshyperkinasemic action (p-value=0.4430), it can be used as a reference drug for comparison with U-74389G. Although Epo is met in over 30,637 published biomedical studies, only a 3.57% of them negotiate the known type of IR experiments. Nevertheless, Epo as a cytokine, it is worth of being studied about its effects oncreatine phosphokinaselevels (CPK) levels too. This experimental work tried to compare the effects of the above drugs on a rat induced IR protocol. They were tested by calculating the serumCPK levels (CPKl) reductions.

Materials and Methods

Animal Preparation

The Vet licenses under 3693/12-11- 2010 & 14/10-1-2012 numbers, the granting company and the experiment location are mentioned in preliminary references[1,2]. The human animal care of Albino female Wistar rats, the 7 days pre-experimental *ad libitum* diet, the non-stop intra-experimental anesthesiologic techniques, the acidometry, the electrocardiogram, the oxygen supply and post-experimental euthanasia are also described in preliminary references. Rats were 16 – 18 weeks old. They were randomly assigned to six (6) groups consisted in N=10. The stage of 45 min hypoxia was common for all 6 groups. Afterwards, reperfusion of 60 min was followed in group A; reperfusion of 120 min in group B; immediate Epo intravenous (IV) administration and reperfusion of 60 min in group C; immediate Epo IV administration and reperfusion of 120 min in group D; immediate U-74389G IV administration and reperfusion of 60 min in group E; and immediate U-74389G IV administration and reperfusion of 120 min in group F. The dose height assessment for both drugs are described at preliminary studies as 10 mg/Kg body mass.

Ischemia was caused by laparotomic clamping the inferior aorta over renal arteries with forceps for 45 min. The clamp removal was restoring the inferior aorta patency and reperfusion. After exclusion of the blood flow, the protocol of IR was applied, as described above for each experimental group. The drugs were administered at the time of reperfusion; through inferior vena cava catheter. The CPKlwere determined at 60th min of reperfusion (for A, C and E groups) and at 120th min of reperfusion (for B, D and F groups). Along, due to a strong relation was rised between CPKl values with animals' mass (p-value=0.0105), the predicted CPKl values were used.

Statistical Analysis

Table 1 presents the (%) hyperkinasemic influence of Epo regarding reoxygenation time. Also, Table 2 presents the (%) hyperkinasemic influence of U-74389G regarding reperfusion time. Chi-square tests were applied using the ratios which produced the (%) results per endpoint. The outcomes of chi-square tests are depicted at Table 3. The statistical analysis was performed by Stata 6.0 software [Stata 6.0, StataCorp LP, Texas, USA].

Table1. *The (%) hyperkinasemic influence of erythropoietin in connection with reperfusion time*

Hyperkinasemia	±SD	Reperfusion time	p-value
+0.07%	±18.92%	1h	0.9904
+3.84%	±16.73%	1.5h	0.3549
+7.60%	±13.17%	2h	0.1509
-3.84%	±18.00%	reperfusion	0.3721
+2.08%	±2.77%	interaction	0.4430

Table2. *The (%) hyperkinasemic influence of U-74389G in connection with reperfusion time*

Hyperkinasemia	±SD	Reperfusion time	p-value
+11.11%	±16.90%	1h	0.0663
+15.32%	±14.68%	1.5h	0.0001

+19.53%	±11.20%	2h	0.0003
-3.06%	±13.93%	reperfusion	0.4103
+8.52%	±4.35%	interaction	0.0005

Table3. *The U-74389G / erythropoietin efficacies ratios on serum creatine phosphokinase levels after chi-square tests application*

Odds ratio	[95% Conf. Interval]		p-values	Endpoint
144.0769	143.9114	144.2425	0.0000	1h
3.987264	3.979742	3.9948	0.0000	1.5h
2.567192	2.563487	2.570902	0.0000	2h
0.7974539	0.7954859	0.7994269	0.0000	reperfusion
4.09626	4.092989	4.099534	0.0000	interaction

Results

The successive application of chi-square tests revealed that U-74389G enhanced the CPKl by 144.0769-fold [143.9114 - 144.2425] more than Epo at 1h (p-value=0.0000), by 3.987264-fold [3.979742 - 3.9948] more than Epo at 1.5h (p-value=0.0000), by 2.567192-fold [2.563487 - 2.570902] more than Epo at 2h (p-value=0.0000), less by 0.7974539-fold [0.7954859 - 0.7994269] (p-value=0.0000) without drugs and by 4.09626-fold [4.092989 - 4.099534] more than Epo whether all variables have been considered (p-value=0.0000).

Discussion

The unique available study investigating the hyperkinasemic effect of U-74389G on CPKl was the preliminary one[1]. Although the most famous activities of neuroprotection and membrane-stabilization properties, it accumulates in the cell membrane, protecting vascular endothelium from peroxidative damage but hardly penetrates the blood-brain barrier. It elicits a beneficial effect in ototoxicity and Duchenne muscular dystrophy. It increases γgt, superoxide dismutase (SOD) and glutathione (GSH) levels in oxygen-exposed cells. It treats septic states and acts as immunosuppressant in flap survival. It prevents the learning impairments, it delays the early synaptic transmission decay during hypoxia improving energetic state of neurons. It shows antiproliferative properties on brain cancer cells and is considered as a new promising anti inflammatory drug for the treatment of reperfusion syndrome in IR injuries.

The same authors confirmed[2] the short-termhyperkinasemiceffect of Epo preparations in non iron deficient individuals. Quan W et al showed[3] that Magnesium lithospermate B (MLB) significantly increased phosphorylation of Akt and that this phosphorylation can be partially inhibited by phosphoinositide 3-kinase/Akt inhibitor. The results also showed that MLB prevents I/R-induced myocardial damage by reducing necrosis and apoptosis in H9c2 cardiomyocytes, improving myocardial function in rat hearts. Yoshino T et al concluded[4] a temporal induction of preconditioning actions of the aldosterone cascade, at a physiological dose, having favorable effects on cardiac functional recovery in left ventricular contractility and left ventricular end-diastolic pressure associated[4] with a reduced activity of creatine phosphokinase released into the perfusate after injury following ischemia-reperfusion in a MR-independent manner male in Wistar rat Langendorff hearts. Takhtfooladi H et al alleviated[5] the metabolic injuries in the skeletal muscle ischemia and reperfusion in this experimental model after tramadol treatment in a rat hind limb ischemia-reperfusion model. Dianat M et al concluded[6] at a more significant decrease in the CPK levels in groups that had received combined treatment in comparison with vanillic acid (antioxidant) or losartan (selective angiotensin II (ANG-II) type 1 receptor (AT1R) blocker alone and hence, protects myocardium against I/R-induced oxidative stress injuries in isolated rat hearts. Liao Z et al strikingly found[7] that resveratrol downregulates voltage-dependent anion channel 1 (VDAC1), leading to prevention of mitochondrial permeability transition pore opening and cardiomyocyte apoptosis; decreased the creatine phosphokinase activities; and reduced the infarction size. The data also revealed that long-term oral intake of resveratrol sets nutritional preconditioning to cope with myocardial I/R injury. Zhang N et al

showed[8] that preoperative trimetazidine therapy appears to have a positive effect on myocardial preservation along with significantly lower postoperative levels of CK, TnT and TnI, also in both the ≤12 and >12 h subgroup analyses in control coronary artery bypass grafting (CABG) patients. Lemarié J et al hypothesized[9] that the triggering receptor expressed on myeloid cells (TREM)-1 acts as an amplifier of the immune response triggered by toll-like receptor engagement. TREM-1 inhibition by inhibitory peptide LR12 significantly improved these dysfunctions ($P < 0.03$) and restricted infarct size, as assessed by lower creatine phosphokinase and troponin I concentrations ($P < 0.005$) in a clinically relevant porcine model of acute myocardial infarction. Kashiwagi Y et al provided[10] new insight into the significant role of sodium-glucose cotransporter 1 (SGLTs) in optimizing cardiac energy metabolism, at least during the acute phase of IRI, whether it is expressed in human hearts and significantly contributes to cardiac energy metabolism during ischemia-reperfusion injury (IRI) via enhanced glucose utilization. Phlorizin administration during IRI significantly impaired the recovery in left ventricular contractions and rate pressure product, associated with an increased infarct size, as demonstrated by triphenyltetrazolium chloride staining and creatine phosphokinase activity released into the perfusate in mice. Li CM et al demonstrated[11] that the cardioprotective effect of ischemic post-conditioning was involved in the inhibition of PTEN, activation of the PI3K/Akt signal pathway and reduction of the cardiomyocyte apoptosis confirmed by serum creatine phosphokinase activity.Luo SY et al indicated[12] that SB-710411 - a rat selective urotensin-II (U-II) receptor antagonist, which can block U-II-induced contraction of the aorta - inhibits U-II-induced myocardial fibrosis and decreases myocardial UTR expression in myocardiac I/R injury of rats. Qiu LY et al revealed[13] that treatment with SQS promoted protein kinase C ε (PKCε) which is able to mediate Cl- homeostasis - phosphorylation and inhibited sI/R-induced elevation of [Cl-]i, paralleled by the attenuation of mitochondrial membrane potential loss and ROS generation; eliciting cardioprotectionincreasing the viability and efficiently attenuating the creatine phosphokinase release in cultured cardiomyocytes. Takhtfooladi HA et al found significantly lower serum CPK levels[14] ($P < 0.05$) after low-level laser therapy (LLLT) which has a beneficial effect on the IR gastrocnemius muscle injury treatment in streptozotocin-induced diabetic male Wistar rats. Claroni C et al found[15] the positive preconditioning impact of sevoflurane on IR injury expressed in the early postoperative hours, but not in the long-term ones since the creatine phosphokinase value was significantly lower in the BAL group only at the end of operation and not at other endpoints in patients undergoing free flap operation. Fujisaki N et al protected[16] cardiac grafts from ischemia reperfusion-induced injury after pretreatment with CO gas before organ procurement effectively. Recipients of grafts from CO-exposed donors had lower levels of serum troponin I and creatine phosphokinase; less upregulation of mRNA for interleukin-6, intercellular adhesion molecule-1, and tumor necrosis factor-α; and fewer infiltrating cells. Donor pretreatment with CO altered the expression of 49 genes expressly represented on the array in a rat heterotopic cardiac transplant model. Kundra TS et al prevented[17] skeletal muscle ischemia-reperfusion injury in patients undergoing aortobifemoral bypass operation after dexmedetomidine administration and CPK values assessments. Zeng G et al demonstrated[18] that SIRT4, a mitochondrial-localized sirtuin is downregulated in cardiomyocytes both in vitro and in vivo models after MI-R. Functionally, SIRT4 overexpression decreases myocardial infarct size and serum creatine phosphokinase (CPK) level, and vice versa, SIRT4 depletion by siRNA increases myocardial infarct size and serum CPK level. Yin TC et al concluded[19] that extracorporeal shock wave (ECSW) - adipose-derived mesenchymal stem cells (ADMSC) therapy is superior to either one applied individually since the microscopic findings of endothelial-cell biomarkers and number of arterioles expressedan opposite pattern of CPK, whereas the histopathology showed that muscle-damaged/fibrosis/collagen-deposition areas exhibited an identical pattern of CPK among the five groups (all $p< 0.0001$) for protecting against IR-induced thigh injury in rats.

According to above, table 3 shows that U-74389G has 4.09626-fold [4.092989 - 4.099534] morehyperkinasemic effect than Epo (p-value=0.0000) whether all variables have been considered (p-value=0.0000); a trend attenuated along time, in Epo non-deficient rats. A meta-analysis of these ratios from the same experiment, for 21 other seric variables, provides comparable results (table 4)[20].

Table4. *A U-74389G / erythropoietin efficacies ratios meta-analysis on 21 hematologic variables (17 variables with balancing efficacies and 4 variables with opposite efficacies)[9].*

Endpoint / Variable	1h	p-value	1.5h	p-value	2h	p-value	Reperfusion time	p-value	interaction	p-value
WBC	0.957451	0.3782	1.396122	0.0000	1.918237	0.0000	1.71622	0.0000	1.601887	0.0000
RBC count	0.961059	0.0000	1.733395	0.0000	6.519657	0.0000	1.039524	0.0000	1.309673	0.0000
Hematocrit	38.424	0.0000	9.076658	0.0000	6.222898	0.0000	1.001356	0.2184	12.66419	0.0000
Hemoglobin	1.268689	0.0000	1.839035	0.0000	13.1658	0.0000	1.252422	0.0000	1.94889	0.0000
MCH	151.125	0.0000	4.246814	0.0000	2.709729	0.0000	1.177347	0.0000	4.362893	0.0000
MCV	150.8518	0.0000	4.236722	0.0000	2.704247	0.0000	1.180156	0.0000	4.352528	0.0000
RbcDW	3.306773	0.0000	3.023389	0.0000	2.655885	0.0000	0.2259914	0.0000	2.370353	0.0000
Platelet count	2.42839	0.0000	6.00238	0.0000	6.1333429	0.0000	3.939027	0.0000	37.62979	0.0000
MPV	145.8532	0.0000	4.053619	0.0000	2.603947	0.0000	1.2334644	0.0000	4.164431	0.0000
Platelet DW	0.6940233	0.0000	1.319118	0.0000	2.206972	0.0000	2.2484006	0.0000	2.458888	0.0000
Glucose	156.4991	0.0000	4.53659	0.0000	2.81397	0.0000	0.9073196	0.0000	4.660603	0.0000
Urea	158.4209	0.0000	4.50889	0.0000	2.850291	0.0000	0.9017775	0.0000	4.632148	0.0000
Creatinine	168.9034	0.0000	4.872332	0.0000	3.039572	0.0000	1.0262016	0.0000	5.005523	0.0000
Total proteins	155.9562	0.0000	4.421079	0.0000	2.803573	0.0000	0.8842162	0.0000	4.541934	0.0000
Albumins	0.2457507	0.0073	0.5303472	0.0000	0.6243052	0.0465	1.237477	0.0000	0.5000416	0.0000
ALP	134.0033	0.0000	3.602703	0.0000	2.349961	0.0000	0.7205412	0.0000	3.701187	0.0000
AST	1.149264	0.0391	0.9347365	0.0000	0.6695775	0.0000	0.7631082	0.0000	0.8224656	0.0000
Mean	13.678620	0.0249	2.854616	0.0000	2.827506	0.0026	1.0829736	0.0128	3.3053484	0.0000

Endpoint / Variable	1h	p-value	1.5h	p-value	2h	p-value	Reperfusion time	p-value	interaction	p-value
Mean corpuscular hemoglobin concentrations	-0.2774225	0.0000	-0.5504722	0.0000	-0.8522433	0.0000	+3.044774	0.0000	-0.7793243	0.0000
Plateletcrit	-0.2312044	0.0000	-0.6719365	0.0000	-1.330756	0.0886	+5.620077	0.0000	-0.9771515	0.0000
ALT	+0.5955473	0.0000	-1.157335	0.0000	+7.967324	0.0000	+0.4734427	0.0000	-0.6208232	0.0000
γGT	1	1.0000	+0.5367033	0.0000	-0.9428571	0.8982	+2.146813	0.0000	-0.2683513	0.0000
Mean	-0.4757810	0.0250	-0.9450332	0.0000	-0.6052695	0.2467	+2.0421598	0.0000	-0.5968125	0.0000

Conclusion

The anti-oxidant agent U-74389G was proved having 4.09626-fold [4.092989 - 4.099534] more hyperkinasemic effect than Epo whether all variables have been considered (p-value=0.0000); a trend attenuated along the short term time frame of the experiment in rats. A biochemical investigation remains about how U-74389G mediates in these actions.

References

1. C. Tsompos, C. Panoulis, K. Toutouzas, G. Zografos, A. Papalois. The Effect of the Antioxidant Drug "U-74389G" on Creatine Phosphokinase Levels during Ischemia Reperfusion Injury in Rats. Erciyes Med J 2015; 37(3): 91-7.

2. C. Tsompos, C. Panoulis, K. Toutouzas, G. Zografos, A. Papalois. The effect of erythropoietin on creatine phosphokinase levels during ischemia reperfusion injury in rats. Rev Cubana Med Mil. 2014; 43(3): 277-284.

3. Quan W, Wu B, Bai Y, Zhang X, Yin J, Xi M, Guan Y, Shao Q, Chen Y, Wu Q, Wen A. Magnesium lithospermate B improves myocardial function and prevents simulated ischemia/reperfusion injury-induced H9c2 cardiomyocytes apoptosis through Akt-dependent pathway. JEthnopharmacol. 2014; 151(1): 714-21.

4. YoshinoT, NagoshiT, AnzawaR, KashiwagiY, ItoK, KatohD, FujisakiM, KayamaY, DateT, HongoK, YoshimuraM. Preconditioning actions of aldosterone through p38 signaling modulation in isolated rat hearts. J Endocrinol. 2014 Aug; 222(2): 289-99.

5. Takhtfooladi H, Takhtfooladi MA, Karimi P, Asl HA, Mobarakeh SZ.Influence of tramadol on ischemia-reperfusion injury of rats' skeletal muscle. Int J Surg. 2014; 12(9): 963-8.

6. Dianat M, Hamzavi GR, Badavi M, Samarbafzadeh A.Effects of losartan and vanillic Acid co-administration on ischemia-reperfusion-induced oxidative stress in isolated rat heart. Iran Red Crescent Med J. 2014 Jul; 16(7): e16664.

7. Liao Z, Liu D, Tang L, Yin D, Yin S, Lai S, Yao J, He M.Long-term oral resveratrol intake provides nutritional preconditioning against myocardial ischemia/reperfusion injury: involvement of VDAC1 downregulation. MolNutr Food Res. 2015 Mar; 59(3): 454-64.

8. Zhang N, Lei J, Liu Q, Huang W, Xiao H, Lei H. The effectiveness of preoperative trimetazidine on myocardial preservation in coronary artery bypass graft patients: a systematic review and meta-analysis. Cardiology. 2015; 131(2): 86-96.

9. Lemarié J, Boufenzer A, Popovic B, Tran N, Groubatch F, Derive M, Labroca P, Barraud D, Gibot S. Pharmacological inhibition of the triggering receptor expressed on myeloid cells-1 limits reperfusion injury in a porcine model of myocardial infarction. ESCHeartFail. 2015 Jun; 2(2): 90-99.

10. KashiwagiY, NagoshiT, YoshinoT, TanakaTD, ItoK, HaradaT, TakahashiH, IkegamiM, AnzawaR, YoshimuraM. Expression of SGLT1 in Human Hearts and Impairment of Cardiac Glucose Uptake by Phlorizin during Ischemia-Reperfusion Injury in Mice. PLoS One. 2015 Jun 29; 10(6): e0130605.

11. Li CM, Shen SW, Wang T, Zhang XH. Myocardial ischemic post-conditioning attenuates ischemia reperfusion injury via PTEN/Akt signal pathway.Int J ClinExp Med. 2015 Sep 15; 8(9): 15801-7.

12. Luo SY, Chen S, Qin YD, Chen ZW.Urotensin-Receptor Antagonist SB-710411 Protects Rat Heart against Ischemia-Reperfusion Injury via RhoA/ROCK Pathway. PLoS One. 2016 Jan 15; 11(1): e0146094.

13. Qiu LY, Chen HP, Yan YF, Li YY, Wang H, Liao ZP, Huang QR. Sasanquasaponin promotes cellular chloride efflux and elicits cardioprotection via the PKCε pathway. Mol Med Rep. 2016 Apr; 13(4): 3597-603.

14. Takhtfooladi HA, Asghari A, Amirkamali S, Hoseinzadeh HA, Takhtfooladi MA. Evaluation of low-level laser therapy on skeletal muscle ischemia-reperfusion in streptozotocin-induced diabetic rats by assaying biochemical markers and histological changes. Lasers Med Sci. 2016 Aug; 31(6): 1211-7.

15. Claroni C, Torregiani G, Covotta M, Sofra M, Scotto Di Uccio A, Marcelli ME, Naccarato A, Forastiere E. Protective effect of sevoflurane preconditioning on ischemia-reperfusion injury in patients undergoing reconstructive plastic surgery with microsurgical flap, a randomized controlled trial. BMCAnesthesiol. 2016 Aug 22; 16(1): 66.

16. FujisakiN, KohamaK, NishimuraT, YamashitaH, IshikawaM, KanematsuA, YamadaT, LeeS, YumotoT, TsukaharaK, KotaniJ, NakaoA. Donor pretreatment with carbon monoxide prevents ischemia/reperfusion injury following heart transplantation in rats. Med Gas Res. 2016 Oct 14; 6(3): 122-129.

17. Kundra TS, Thimmarayappa A, Dhananjaya M, Manjunatha N. Dexmedetomidine for prevention of skeletal muscle ischaemia-reperfusion injury in patients with chronic limb ischaemia undergoing aortobifemoral

bypass surgery: A prospective double-blind randomized controlled study. Ann Card Anaesth. 2018 Jan-Mar; 21(1): 22-25.

18. Zeng G, Liu H, Wang H. Amelioration of myocardial ischemia-reperfusion injury by SIRT4 involves mitochondrial protection and reduced apoptosis. BiochemBiophys Res Commun. 2018 Jul 7; 502(1): 15-21.

19. Yin TC, Wu RW, Sheu JJ, Sung PH, Chen KH, Chiang JY, Hsueh SK, Chung WJ, Lin PY, Hsu SL, Chen CC, Chen CY, Shao PL, Yip HK. Combined Therapy with Extracorporeal Shock Wave and Adipose-Derived Mesenchymal Stem Cells Remarkably Improved Acute Ischemia-Reperfusion Injury of Quadriceps Muscle. Oxid Med Cell Longev. 2018 Apr 2; 2018: 6012636.

20. Tsompos C, Panoulis C, Toutouzas K, Triantafyllou A, Zografos GC, Tsarea K, Karamperi M, Papalois A. Comparison of the Hypertransferasemic Effects of Erythropoietin and U-74389G on Aspartate Aminotransferase Levels. Clin Res Hematol 2018; 1(2): 1-7.

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