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The Responses of Plasma Biochemical Parameters to a 56-km Race in Novice and Experienced Ultra-Marathon Runners

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Summary. A number of blood biochemical parameters, including the activities of the plasma enzymes creatine kinase (CK), aspartate aminotransferase (ASAT), lactate dehydrogenase and alkaline phosphatase, were measured in 23 athletes before, and immediately after a 56-km running race. Of the 23 athletes, 18 had previously completed standard 42-km marathon or longer (up to 90-km) ultra-marathon races, whereas not one of the other five athletes had previously run in a long-distance race. After the race, plasma CK and ASAT activities had both risen at least 280% more in the novice runners despite their much slower mean running speed (9.8 ± 0.4 vs. 13.8 ± 0.3 hm/h). There were no other inter-group differences in the absolute levels of the other measured biochemical parameters, although the rise in plasma calcium during the race was significantly greater in the experienced marathon runners.

This study shows that either higher levels of training, or previous ultra-marathon racing experience, or both, is associated with lower immediate post-exercise levels of plasma enzyme activity. This is compatible with the finding that physical training reduces post-exercise plasma enzyme levels.

Key words: Plasma enzymes – Creatine kinase – Aspartate aminotransferase – Ultra-marathon running

Introduction

Although the precise mechanism(s) causing serum enzyme activities to increase during exercise is not known, it is generally held that the extent of this rise is determined by the intensity and duration of the exercise, and is lower in physically-trained persons (Schmidt and Schmidt 1969). Recently Berg and

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Haralambie (1978) have shown that the exercise-induced rise in serum enzyme activity is also related to the type of exercise, and is highest in "impact type" sports like running-skating-walking, and lowest in bicycle-ergometer exercise. Furthermore, these authors found that the rise in serum creatine kinase (CK) activity during "impact type" sports is linearly related to exercise duration for up to $5^1/_2$ h, but thereafter the increment in CK activity is accelerated and no longer directly proportional to work duration. They therefore concluded that 5 h represents an exercise duration threshold, beyond which cellular energy production is no longer able to prevent an intracellular metabolic disturbance which causes intracellular enzymes to be released into the bloodstream.

In two previous studies (Kielblock et al. 1979; Noakes and Carter 1976) in which serum enzyme (activity) levels were measured after 160-km athletic events lasting between 12 and 24 h, large individual variations were found in the post-exercise serum CK and lactate dehydrogenase (LDH) activities (Fig. 1). This suggests that even in very prolonged exercise beyond the $5^1/_2$-h threshold identified by Berg and Haralambie, there exist variations in the resistance of individual athletes to those factors causing intracellular enzymes to enter the bloodstream.

In order to study this individual variability in serum enzyme levels after exercise, and to determine whether it could be related to the individual athlete's previous racing experience or to alterations in other blood parameters, a number of biochemical parameters, including the activity of the enzymes CK, LDH, alkaline phosphatase (AP), and aspartate aminotransferase (ASAT), were measured in 23 athletes the day before, and immediately after, they had completed a 56-km ultra-marathon running race.

Materials and Methods

Twenty-three competitors in the 56-km Argus Two Oceans Marathon, run annually in Cape Town, South Africa, consented to participate in this study. Of these athletes, 18 had competed in previous 42-km standard marathon and ultra-marathon races, 16 of them had completed the 90-km Comrades Marathon, run annually between Durban and Pietermaritzburg, South Africa, on at least one occasion. Of the remaining five athletes, three had only recently started long-distance running but had not previously completed marathon races, whilst two runners were medical students, active in other non-endurance-type sports and with essentially no previous long-distance running experience.

On the evening prior to the race, and again immediately after completion of the race, 20 ml of venous blood were drawn from each competitor. The plasma obtained from these specimens was analysed by the Technicon SMA 12/60 "Auto-analyser" for plasma total protein, albumin, globulin (by difference), calcium, inorganic phosphate, cholesterol, urea, uric acid, total bilirubin, CK, ASAT, LDH, and AP, as previously described (Noakes and Carter 1976).

Statistical Methods

The data were calculated on a Hewlett Packard 67 Calculator, using standard programms. The Student's *t*-test was used to determine differences between unpaired data. A p-value of < 0.05 was considered to be statistically significant.

Table 1. Mean age, running time, and speed of experienced and novice runners completing a 56-km running race

No. of runners	Age (years)	Running time	Speed ($km \cdot h^{-1}$)
Experienced runners			
18	28 ± 1	4 h, 11 min, 24 s ± 4 min, 48 s	13.8 ± 0.3
Novice runners			
5	25 ± 4	5 h, 51 min, 36 s ± 12 min, 36 s	9.8 ± 0.4

Results are expressed as mean ± SEM

Table 2. Comparison of plasma biochemical parameters in experienced and novice ultra-marathon runners before and after a 56-km running race

Parameter (units)	Experienced runners ($n = 18$)	Novice runners ($n = 5$)	p Value
Creatine kinase (units)	60 ± 8[a]	32 ± 9	n.s.
	337 ± 34[a]	956 ± 122	0.0001
	277 ± 33[a]	924 ± 177	0.0001
Aspartate aminotransferase (units)	13 ± 1	10 ± 1	n.s.
	22 ± 1	36 ± 4	0.0001
	9 ± 1	26 ± 4	0.0001
Calcium (mg/dl)	9.2 ± 0.1	9.8 ± 0.6	n.s.
	10.2 ± 0.2	10.0 ± 0.5	n.s.
	1.0 ± 0.2	0.2 ± 0.2	0.05

Values are expressed as mean ± SEM

[a] First line = pre-race values; second line = post-race value; third line = difference between post- and pre-race values

Results

The mean ages of the two groups of runners were similar (Table 1). The average running speed of the experienced runners (Numbers 1–18) was, however, considerably faster than that of the novice runners (Numbers 19–23): 13.8 vs. 9.8 km/h.

The major biochemical finding was the different response to the race of the plasma CK and ASAT activities in the experienced and novice runners (Table 2). Thus, the mean post-race plasma activities, and the mean rise of CK (ΔCK) and ASAT activities were significantly greater in the novice runners despite their much slower average running speeds. The only additional parameter that was significantly different between the groups was the race-induced rise in serum calcium, which was greater in the experienced

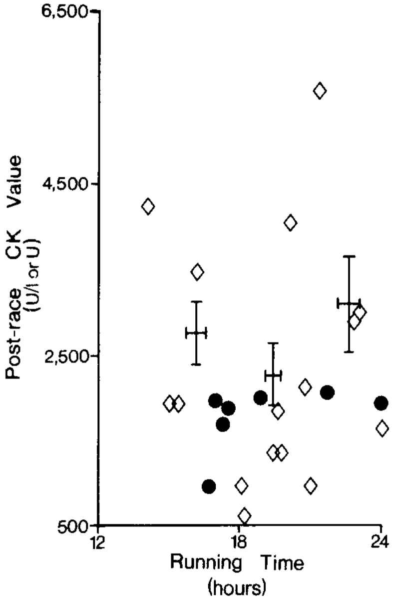

Fig. 1. Post-race plasma CK activity as a function of exercise duration in athletes completing 160-km athletic races. The data from two studies (Kielblock et al. 1979; Noakes and Carter 1976) are shown. Although the CK assay technique used in the two studies was not the same, the range of normal values for both assays is very similar; 30–128 U/l for assay used by Kielblock et al. (1979), 10–110 U for that used by Noakes and Carter (1976). It will be seen that there is considerable individual variation in post-race plasma CK activity. The same applies to post-race LDH activity. Key: ◇ Data of Kielblock et al. (1979); ● Data of Noakes and Carter (1976). Also shown are the mean ± SEM for three groups of runners; the fastest eight runners, the second fastest eight runners and the last seven runners. The mean values for these three groups are not different ($p > 0.05$)

runners. The insignificantly higher pre-race CK levels in the experienced runners could have been due to their having exercised in the days immediately preceding the race, thereby increasing plasma CK levels (Berg and Haralambie 1978; Sanders and Bloor 1975). There were no significant differences between experienced and novice runners in the plasma levels of any of the following parameters either before or after the race: LDH, AP, total protein, albumin, globulin, phosphate, cholesterol, urea, uric acid, or total bilirubin.

When compared to the same parameters measured in athletes completing a 160-km race (Noakes and Carter 1976), the following differences were noted: plasma CK, ASAT and, to a lesser extent, LDH activities were higher after the 160-km race, although the mean post-race LDH level of the novice runners in this study was the same as that measured in the 160-km runners (Noakes and Carter 1976). Urea and total bilirubin levels were also higher after the 160-km race. The post-race levels of AP, protein, albumin, globulin, calcium, and uric acid were essentially the same in both races, whereas phosphate and cholesterol levels, which were reduced in this study, were elevated following the 160-km race.

Figure 2 shows the relationship of these findings to those of other studies of changes in plasma CK activities after prolonged exercise (Berg and Haralambie 1978; Kielblock et al. 1979; Noakes et al. 1982; Olivier et al. 1978). The exercise-induced change in CK activity (ΔCK) in those studies of trained runners competing in long distance races (this study; Kielblock et al. 1979; Noakes and Carter 1976; Noakes et al. 1982; Olivier et al. 1978) lie slightly to the left of the curve of Berg and Haralambie (1978) but the curves would seem to meet after 1,000 min. Thus the general validity of Berg and Haralambie's curve is

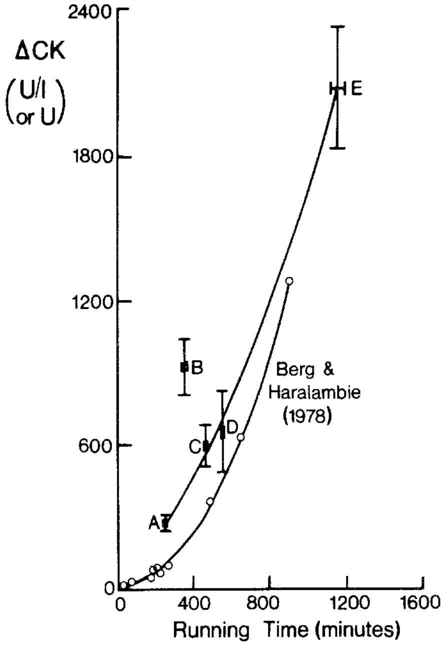

Fig. 2. Changes in plasma CK activity as a function of exercise duration in ultra-marathon runners. Values are plotted as mean ± SEM for data from the following studies: A = Experienced runners (this study $n = 18$); B = Novice runners (this study $n = 5$); C = 88-km Comrades Marathon Runners (Noakes et al. 1982 $n = 75$); D = 88-km Comrades Marathon runners (Olivier et al. 1978; $n = 22$. The running times of these athletes was not given, thus a mean time of 555 min was assumed as that study included only athletes older than 40 years); E = 160-km runners (combined data of Kielblock et al. 1979, and Noakes and Carter 1976). It will be seen that the two lines appear to be converging after 1,000 min, and that the mean ΔCK for the novice runners in this study (point B) is inappropriately high

confirmed. Figure 2 also shows that the mean ΔCK of the novice runners in this study does not fit the curve described for the trained runners, but is much greater than would have been predicted on the basis of these other studies.

Discussion

The principal finding in this study was the greater rise in plasma CK and ASAT activities measured in a group of novice runners after a 56-km ultra-marathon race. There are three possible reasons for this:

1. The $5^{1}/_{2}$ Hour Time Threshold Proposed by Berg and Haralambie (1978). Four of the five novice runners in this study exceeded the $5^{1}/_{2}$-h exercise duration threshold proposed by Berg and Haralambie (1978) and this could possibly explain why the enzyme levels in this group were so markedly elevated. However, extrapolation from Berg and Haralambie's paper (Fig. 2) indicates that the mean ΔCK of 932 units measured in the novice runners should only occur after about $12^{1}/_{2}$-h exercise, whereas in these novice runners it occurred after an average of only $5^{3}/_{4}$ h. It should be noted, however, that the two highest ΔCK values in Berg and Haralambie's curve come from studies of long-distance walkers and it is possible that very prolonged running may cause a greater CK elevation than predicted from Berg and Haralambie's graph. To exclude this possibility, the change in plasma CK activity as a function of time was calculated from other studies of South African ultra-marathon runners (Kielblock et al. 1979; Noakes and Carter 1976; Noakes et al. 1982; Olivier et al. 1978) (Fig. 2).

As these data fit a line not greatly different from that originally described by Berg and Haralambie (1978), it is clear that the ΔCK measured in the novice runners in this study is clearly inappropriate and cannot be explained simply because they had exercised for more than $5^1/_2$ h.

2. That the Novice Runners Ran at Higher Exercise Intensities Than Did the Experienced Runners. Exercise intensity is known to be an important factor determining the degree to which plasma enzyme activities rise after exercise (Fowler et al. 1968; Gardner et al. 1964; Schmidt and Schmidt 1969; Shapiro et al. 1973) with the greatest elevations occurring after the most intensive exercise. However, even if the maximum potential for aerobic exercise ($\dot{V}O_2$ max – Maximum oxygen consumption) was considerably lower in the novice runners, it would not have been possible for them to have run at greater relative intensities (% $\dot{V}O_2$ max) than the trained runners, because only trained runners have the ability to run at a high % $\dot{V}O_2$ max (Davies and Thompson 1979).

3. That it is Due to the Lower Fitness Level of the Novice Runners. This would seem to be the most likely explanation as it is in accord with most, but not all (Misner et al. 1973) studies which show either that the rise in serum enzyme activity after a standard work protocol is reduced by training (Gardner et al. 1964; Hunter and Critz 1971; Nuttal and Jones 1968) or that, in response to similar workloads, trained persons have lower post-exercise serum enzyme levels (Fowler et al. 1968; Gardner et al. 1964; La Porta et al. 1978; Olerud et al. 1975; Schmidt and Schmidt 1969; Shapiro et al. 1973). Exertional myoglobinaemia is also reduced by training (Ritter et al. 1979).

This interpretation is also in accord with other published data in which serum enzyme levels have been measured in well-trained and less-trained athletes competing in the same events. Thus Rutledge et al. (1978) reported that, whereas the mean ΔCK for six trained athletes completing a non-competitive 60-min run was only 40 units/litre (U/1), an untrained subject able to run for only 30 min had a ΔCK of 440 U/l. Similarly, Schnohr (1974) reported a ΔCK of 6,051 U/l in the least-trained of three physicians competing in a 100-km running race. The mean ΔCK for the other two physicians was only 1,174 U/l. It is also of interest that Berg and Haralambie found that the mean ΔCK of a group of trained athletes walking 100-km in $10^5/_6$ h was 590 U/l, whereas the mean ΔCK of a group of medical students who required more than 15 h to walk 85-km was twice as much: ΔCK = 1,281 U/l (Griffiths 1966).

These data are at variance with those of Siegel et al. (1980) who found that 42-km standard marathon runners who completed the course in between $2^3/_4$ and $3^1/_2$ h had very much higher CK levels that did those who took longer than $3^1/_2$ h to finish the race, and who were presumably less fit. It should be noted, however, that those workers measured serum CK levels 24 h after the race, by which time the levels are considerably higher than they are immediately after exercise (La Porta et al. 1978; Nuttal and Jones 1968; Refsum et al. 1971; Riley et al. 1975; Schiff et al. 1978; Siegel et al. 1980), the time when our studies were performed. The difference between Siegel et al.'s study (1980) and our own might, therefore, be explained if there was a different time course of intracellular enzyme release between experienced and novice runners. Thus, novice runners might reach peak plasma enzyme levels immediately post-race, whereas much higher enzyme values might be reached in experienced runners only 24 h after the race. This does not seem likely, however, particularly as the data of Nuttal and Jones (1968) show that not only is the peak post-exercise serum CK level reduced after training, but it occurs sooner, 8 h (trained state) versus 16 h (untrained state), after a standardized exercise session.

Alternatively, our group of experienced runners may have developed greater resistance to exercise-induced serum enzyme rises than Siegel et al.'s runners because, for example, these runners may have had greater experience in training and racing at distances longer than that at which they raced in this event (56-km).

This study shows that it is unwise for persons who have not trainer properly, to attempt ultra-marathon races. As there is a close correlation between post-exercise serum CK levels and the level of myoglobinaemia (Olerud et al. 1975; Schiff et al. 1978) and if myoglobinaemia is indeed a factor associated with exercise-induced acute renal failure (Schiff et al. 1978), our study would predict that novice marathon runners are more likely to develop this complication than those with more experience.

The scientific interest of this study relates to the postulate that training reduces the severity of muscle cell enzyme leakage by preventing total muscle glycogen depletion during exercise (Olerud et al. 1976; Siegel et al. 1980). If this is true, our study suggests that novice ultra-marathon runners either develop more severe glycogen depletion than do experienced runners or, alternatively that they become glycogen depleted earlier in the race, and must, therefore, run for longer periods in this depleted state. Further studies, in which post-exercise serum enzyme activities and muscle glycogen levels are measured simultaneously in experienced and novice distance runners, might provide further insights into the mechanisms explaining muscle enzyme leakage during exercise.

References

Berg A, Haralambie G (1978) Changes in serum creatine kinase and hexose phosphate isomerase activity with exercise duration. Eur J Appl Physiol 39: 191–201

Davies CTM, Thompson MW (1979) Aerobic performance of female marathon and male ultramarathon athletes. Eur J Appl Physiol 41: 233–245

Fowler WM, Gardner GW, Kazerunian HH, Lauvstad WA (1968) The effect of exercise on serum enzymes. Arch Phys Med Rehabil 49: 554–565

Gardner GW, Bratton R, Chowdhury SR, Fowler WM, Pearson CM (1964) Effect of exercise on serum enzyme levels in trained subjects. J Sports Med Phys Fitness 4: 103–110

Griffiths PD (1966) Serum levels of ATP: Creatine phospho-transferase (creatine kinase). The normal range and effect of muscular activity. Clin Chim Acta 13: 413–420

Hunter JB, Critz JB (1971) Effect of training on plasma enzyme levels in man. J Appl Physiol 31: 20–23

Kielblock AH, Manjoo M, Booysens J, Katzeff I (1979) Creatine phosphokinase and lactate dehydrogenase levels after ultra long-distance running. S Afr Med J 55: 1061–1064

La Porta MA, Linde HW, Bruce DL, Fitzsimons EJ (1978) Elevation of creatine phosphokinase in young men after recreational activity. JAMA 239: 2685–2686

Misner JE, Massey BH, Williams BT (1973) The effect of physical training on the response of serum enzymes to exercise stress. Med Sci Sports 5: 86–88

Noakes TD, Carter JW (1976) Biochemical parameters in athletes before and after having run 160 kilometers. S Afr Med J 50: 1562–1566

Noakes TD, Kotzenberg G, McArthur P, Dykman J (1982) Elevated serum creatine kinase MB- and BB-isoenzyme fractions after an 88-km running race (submitted)

Nuttal FQ, Jones B (1968) Creatine kinase and glutamatic oxalacetic transaminase activity in serum: Kinetics of change with exercise and effect of physical conditioning. J Lab Clin Med 71: 847–854

Olerud JE, Homer LD, Carrol HW (1975) Serum myoglobin levels predicted from serum enzyme values. N Engl J Med 293: 483–485

Olerud JE, Homer LD, Carrol HW (1976) Incidence of acute exertional rhabdomyolysis. Arch Intern Med 136: 692–697

Olivier LR, de Waal A, Retief FJ, Marx JD, Kriel JR, Human GP, Potgieter GM (1978) Electrocardiographic and biochemical studies on marathon runners. S Afr Med J 53: 783–787

Refsum HE, Strømme SB, Tveit B (1971) Changes in serum enzyme levels after 90 km cross-country skiing. Acta Physiol Scand 84: 16A–17A

Riley WJ, Pyke FS, Roberts AD, England JF (1975) The effect of long-distance running on some biochemical variables. Clin Chim Acta 65: 83–89

Ritter WS, Stone MJ, Willerson JT (1979) Reduction in exertional myoglobinaemia after physical conditioning. Arch Intern Med 139: 644–647

Rutledge J, Clayson KJ, Strandjord PE (1978) Effect of physical conditioning on serum creatine kinase after exercise. JAMA 240: 2633

Sanders TM, Bloor CM (1975) Effects of repeated endurance exercise on serum enzyme activities in well-conditioned males. Med Sci Sports 7: 44–47

Shapiro Y, Magazanik A, Sohar E, Reich CB (1973) Serum enzyme changes in untrained subjects following a prolonged march. Can J Physiol Pharmacol 51: 271–276

Schiff HB, MacSearraigh ETM, Kallmeyer JC (1978) Myoglobinuria, rhabdomyolysis and marathon running. Q J Med 47: 463–472

Schmidt E, Schmidt FW (1969) Enzyme modifications during exercise. In: Poortsman JR (ed) Biochemistry of exercise. Medicine and Sport, vol 3. Karger, Basel, pp 216–238

Schnohr P (1974) Enzyme concentrations in serum after prolonged physical exercise. Dan Med Bull 21: 68–71

Siegel AJ, Silverman LM, Lopez RE (1980) Creatine kinase elevations in marathon runners: Relationship to training and competition. Yale J Biol Med 53: 275–279

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