CLINICAL RESEARCH

C Reactive protein concentrations during long distance running

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Abstract

Long distance runners competing in events ranging from 15 to 88 km showed a distance related acute phase response as indicated by significantly raised serum C reactive protein concentrations. In trained athletes only a small rise in C reactive protein concentrations was seen after races of less than 21 km. After an 88 km ultramarathon concentrations comparable to those found in patients with small myocardial infarctions were detected. Indomethacin did not affect the increases in C reactive protein after the ultramarathon.

This study has established serial C reactive protein concentrations for given race distances. These data may help in diagnosing myocardial infarction during long distance running. The acute phase response should be measured in untrained people running shorter distances to provide comparative data for the physically untrained population.

Introduction

C Reactive protein is the classical acute phase protein in man, concentrations rising up to 1000-fold in infection, neoplasia, or tissue necrosis.[1 2] In myocardial infarction serum C reactive protein concentrations correlate well with serum activity of creatine kinase MB isoenzyme and thus with the extent of myocardial necrosis[3] (Kendall rank correlation coefficient: $\tau = 0{\cdot}441$; $p < 0{\cdot}001$).

Muscle necrosis occurs during long distance running,[4 5] resulting in the release of muscle enzymes, especially creatine kinase,[6] including the MB fraction.[7 8] This may lead to difficulty in confirming the diagnosis of myocardial infarction during or after long distance running.[1 8]

We have carried out serial measurements of C reactive protein concentrations in trained long distance runners competing in events ranging from 15 to 88 km to determine the extent and duration of the acute phase response as an index of tissue necrosis in these athletes.

Materials and methods

Serial blood samples were obtained from 38 volunteer runners in five different long distance races. Six runners were studied in each of the 15 and 21 km races, where samples were obtained before and 24 hours after the race. In the 56 km race six runners were sampled immediately before and after the race and every 24 hours for five days thereafter. Twelve runners were studied during and after the 88 km Comrades marathon; samples were obtained immediately before, immediately after, and every 24 hours for 10 days after the race. Three of the runners in the Comrades marathon took 100 mg indomethacin as a suppository (MSD, South Africa) eight hours before the race and 25 mg every eight hours after the race for four days.

During the 42 km marathon eight runners were sampled every third day for a week preceding the race, covering the training to prerace rest period. Samples were also taken immediately before, after, and at 12 hour intervals for the first two days after the event, and daily for a further two days. As part of a comprehensive metabolic study rectal temperatures were also taken immediately the athletes finished the race, and percutaneous muscle biopsies were performed by the technique of Bergström[9] as modified by Evans *et al*[10] for analysis of glycogen concentration.[11] (Glycogen concentrations were expressed in mmol/kg wet muscle; 1 mmol = 180 mg.)

Blood samples were kept at 4°C and separated within two hours after races. Serum was frozen at −70°C, thawed, and run in batches for assaying. Concentrations of C reactive protein were measured by a magnetisable cellulose solid phase immunoradiometric assay standardised to pure isolated human C reactive protein.[12] Creatine kinase activity was measured in serial samples using a creatine kinase-*N*-acetyl-L-cysteine kit (Boehringer Mannheim).[7]

Correlations between peak C reactive protein and peak creatine kinase values in individuals and between peak C reactive protein and

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peak creatine kinase values and postrace rectal temperatures and muscle glycogen concentrations were tested by linear regression analysis.

Results

Figures 1 and 2 show the C reactive protein concentrations (median and range) before and after the five races. There was a distance related increase in the peak C reactive protein concentration, reaching a median of 27 mg/l after the 88 km race. The time course of the increase was the same in all races, peaking 24 hours after the event. Races of 15 and 21 km produced only a minute increase in C reactive protein concentrations. In the immediate postrace samples concentrations were raised only after the 88 km ultramarathon, which took the athletes between seven and 11 hours to complete. Concentrations were not raised in the immediate postrace samples of the other events, including the 56 km race, which the athletes completed in four to five hours. Individual C reactive protein concentrations of the athletes who took indomethacin during the 88 km race are shown in figure 2. Indomethacin did not affect the increase in concentrations. C Reactive protein concentrations had returned to normal 10 and five days after the 88 and 56 km races respectively.

Muscle glycogen concentrations fell from a prerace mean of 230·4 mmol/kg wet muscle (range 83·4-363·1 mmol/kg) to a mean of 43·1 mmol/kg wet muscle (range 18·0-128·0 mmol/kg) after the 42 km marathon, and rectal temperatures rose to a mean of 38·7°C (range 37·7-39·5°C). Neither of these postrace values showed any correlation with either peak postrace C reactive protein concentrations or peak postrace creatine kinase activities.

The runners showed the expected major responses in serum creatine kinase activity (table), which followed the same time course except that values were already raised in the postrace samples after the 42, 56, and 88 km events. Individual creatine kinase responses did not correlate with C reactive protein concentrations, and peak activities were highest after the 56 km marathon.

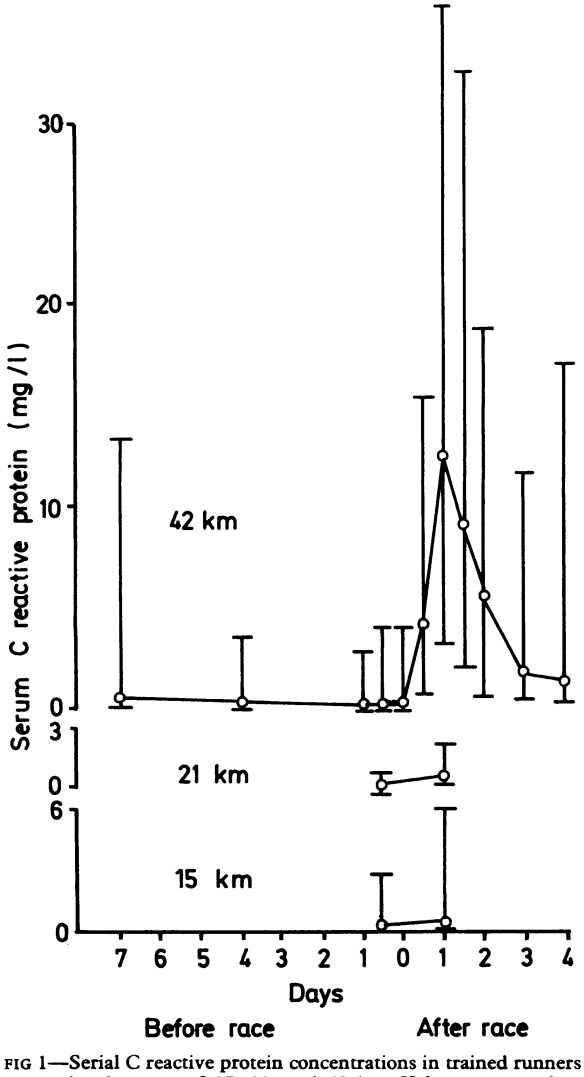

FIG 1—Serial C reactive protein concentrations in trained runners competing in races of 15, 21, and 42 km. Values expressed as median and range.

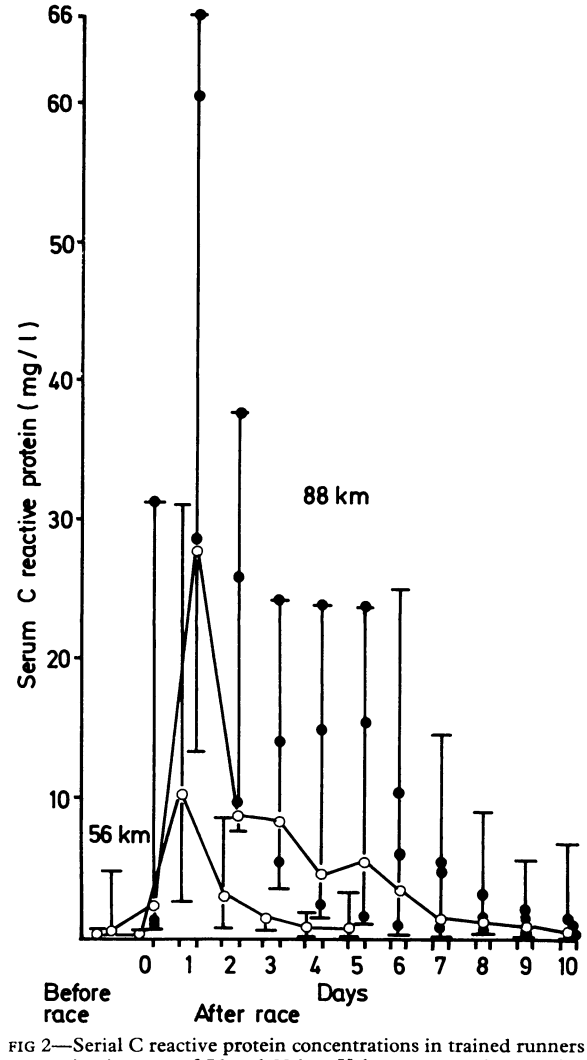

FIG 2—Serial C reactive protein concentrations in trained runners competing in races of 56 and 88 km. Values expressed as median and range. ●=Individual values for three runners who took indomethacin before and after 88 km race.

Peak serum creatine kinase activity measured 24 hours after long distance races of varying lengths

Distance (km)	Creatine kinase activity (U/l)		No of samples
	Median peak	Range	
15	70	48-106	5
21	87	65-127	6
42	491	210-820	7
56	2633	441-5360	6
88	1878	926-3708	6

Discussion

Our finding of a distance related acute phase response to long distance running provides additional evidence for significant tissue necrosis associated with this severe form of exercise.[4,5] The serum concentrations of C reactive protein after the 88 km ultramarathon were comparable to those measured in patients with small myocardial infarctions,[3] and concentrations significantly exceeding those in our subjects for the different racing distances might therefore indicate myocardial

infarction. Peak concentrations occurred 24 hours after exercise, which is earlier than in myocardial infarction. It has been suggested that the duration of the period of accelerated synthesis of C reactive protein is related to the extent of tissue injury.[13 14] Our finding, however, may be suggestive of differing kinetics of induction of the acute phase response resulting from differences in the duration of the necrotising process. That C reactive protein concentrations were raised in the immediate postrace sample only after the 88 km ultramarathon lasting seven to 11 hours is compatible with the expected half life of the protein.[2 3 11]

The acute phase response is probably induced by endotoxin and prostaglandins acting on macrophages and causing release of interleukin 1, which then affects hepatic protein synthesis. Infusion of prostaglandin E_1 in man may cause major increases in concentrations of C reactive and other acute phase proteins.[15] Indomethacin administered in dosages sufficient to block prostaglandin synthesis, however, did not affect the response of C reactive protein to intramuscular injection of turpentine in rabbits.[16] In our study indomethacin had no effect on the acute phase response. This suggests that prostaglandins themselves are not essential for the induction of this response.

The fall in C reactive protein concentrations during the premarathon rest period indicates a continuing minor acute phase response during running training. Although these fit athletes showed only small increases in concentrations after races of 21 km or less, possibly less trained individuals would show a more significant rise at shorter running distances.

In myocardial infarction there is an excellent correlation between peak C reactive protein concentration and creatine kinase MB activity.[3] By contrast, no such correlation could be shown between peak creatine kinase activities and C reactive protein concentrations in individual athletes after distance running. Postrace serum creatine kinase activity in these athletes probably reflects a combination of transmembrane leakage and muscle necrosis. The rise in C reactive protein concentration may prove to be a more accurate index of necrosis.

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Pathways to complement activation during cardiopulmonary bypass

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Abstract

Complement activation was assessed in 34 patients undergoing cardiopulmonary bypass. Arterial concentrations of complement fragments Ba and C3d rose in all patients, the increase in Ba preceding that of C3d. At the same time as complement fragments were being generated the arterial neutrophil count fell. These findings suggest (a) that complement activation is initiated by the alternative pathway during cardiopulmonary bypass and (b) that complement activation mediates loss of neutrophils during bypass.

Complement mediated loss of neutrophils during the analogous setting of haemodialysis is the result of leucosequestration in the pulmonary vasculature. During cardiopulmonary bypass the lungs are out of circuit, so that activated leucocytes may sequester in other target organs. This may be an aetiological factor in the multiorgan failure occasionally seen after uneventful cardiopulmonary bypass.

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Introduction

The activation of complement during cardiopulmonary bypass is a subject of controversy. A reduction of complement haemo-