Medical Hypotheses 73 (2009) 479–484

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Exercise-induced reduction in systemic vascular resistance: A covert killer and an unrecognised resuscitation challenge?

Tom S. Hogan *

Department of Anaesthesia, Connolly Hospital, Dublin 15, Ireland

ARTICLE INFO

Article history:
Received 6 June 2009
Accepted 11 June 2009

SUMMARY

Background: Systemic vascular resistance falls in exercise as a consequence of metabolically-linked vasodilatation in active skeletal muscles. This exercise-induced vasodilatation is closely linked with reduced muscle tissue oxygen tension in and is characterised by reduced response to adrenergic vasoconstrictor mechanisms which is often referred to as *functional sympatholysis*.

Systemic arterial blood pressure in exercise is maintained at normal or, more commonly, at elevated levels by increase in cardiac output and increased sympathetic vasomotor tone.

Recovery of normal resting skeletal muscle tissue oxygen tension and skeletal muscle vascular tone after exercise depends on the post-exercise recovery process. This process requires ongoing elevated skeletal muscle perfusion and can therefore be predicted to be impaired in shock and cardiopulmonary resuscitation scenarios.

Comprehensive consideration of this exercise physiology and its extrapolation into shock, cardiac arrest and resuscitation scenarios supports the proposal that exercise-induced sympatholytic vasodilatation in skeletal muscle may be of considerable unrecognised significance for resuscitation medicine.

Main hypothesis: Reduced systemic vascular resistance due to pre-existing exercise-induced sympatholytic vasodilatation in skeletal muscle can significantly exacerbate systemic arterial hypotension in acute shock states and resuscitation scenarios.

Sub-hypotheses: 1. Onset of syncope, clinical shock states and pulseless electrical activity can occur at significantly higher cardiac output levels in subjects who were engaged in immediate pre-morbid exercise as compared to resting subjects.

2. The efficacy of external chest compression in generating coronary and cerebral perfusion in cardiopulmonary resuscitation can be significantly impaired when cardiac arrest has occurred during exercise.

3. The efficacy of adrenergic vasopressor agents in resuscitation scenarios can be significantly impaired in subjects who were engaged in immediate pre-morbid exercise.

Current evidence: The limited available evidence is compatible with the hypothesis being true but does not provide direct confirmation. There is no evidence available directly supporting or refuting the hypothesis.

Implications: Significant potential clinical implications are outlined relating to the management of cardiopulmonary and trauma resuscitation for patients who were involved in immediate pre-morbid exercise, particularly, but not exclusively, at higher exercise intensities.

There are also significant potential prognostic implications.

Conclusion: Reduction in systemic vascular resistance due to exercise-induced sympatholytic vasodilatation in skeletal muscle may largely explain the reported poor success rate for cardiopulmonary resuscitation with prompt defibrillation for sudden cardiac arrest in young previously healthy athletes.

Investigation of this unexplored area of pathophysiology poses major difficulties but could lead to significant improvements in the outcomes of resuscitation for patients who were involved in immediate pre-morbid exercise.

Introduction

Systemic vascular resistance (SVR) falls in exercise due to vasodilatation in active skeletal muscles [1]. Blood pressure is maintained at normal or elevated levels during exercise by increasing cardiac output (CO) and increasing sympathetic vasomotor tone

Abbreviations: CO, cardiac output; CPR, cardiopulmonary resuscitation; CVP, central venous pressure; ECC, external chest compression; EPOC, excess post-exercise oxygen consumption; LOC, loss of consciousness; MAP, mean systemic arterial pressure; MET, metabolic equivalent unit; PEA, pulseless electrical activity; SCA, sudden cardiac arrest; SVR, systemic vascular resistance.

* Tel.: +353 87233493.
E-mail address: dr.tshogan@eircom.net

0306-9877/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.mehy.2009.06.021

as exercise intensity increases [1–3]. There appears to be no published research relating to the significance of exercise-induced reduction in SVR for cardiopulmonary or trauma resuscitation. Searches have also failed to find any theoretical paper on the subject.

Acute cardiovascular collapse associated with loss of SVR is well recognised in many scenarios such as anaphylaxis, acute high spinal cord injuries, accidental high spinal anaesthetic and vasodilator overdose. It is therefore logical to consider whether pre-existing physiological exercise-induced reduction in SVR could significantly affect prognosis and the optimum management of resuscitation in the event of acute impairment of CO or sudden cardiac arrest (SCA) in exercising subjects.

Several papers have shown a poor level of success for cardiopulmonary resuscitation (CPR) in athletes [4–7]. Detailed analysis of nine cases of SCA in high school athletes in a retrospective outcome study lead the authors to conclude that survival was "less than expected" [7]. Editorial comment on this study in Heart *Rhythm* described the success rate for CPR as "dismal" in the context of witnessed SCA with prompt defibrillation in young previously healthy adults [8]. The editorial highlighted the problem of pulseless electrical activity (PEA) post defibrillation in athletes and concludes that "our efforts to resuscitate young athletes in circumstances of SCA and our understanding of why we are not successful are disappointing."

Could exercise-induced reduction in SVR provide at least part of the explanation and could it have wider therapeutic and prognostic implications?

In the absence of directly relevant research evidence this paper attempts a theoretical assessment of the potential significance of exercise-induced reduction in SVR for out-of hospital resuscitation. This will be done with a view to proposing clinically relevant hypothesis.

Evaluation of background evidence

SVR and systemic perfusion pressure

It is a basic physiological fact that systemic perfusion pressure [mean systemic arterial blood pressure (MAP) minus central venous pressure (CVP)] is a simple product of CO and SVR: **Systemic perfusion pressure = SVR·CO**. The systemic perfusion pressure resulting from acute onset of a restricted CO state in exercise, such as due to an acute cardiac arrhythmia, will be directly proportional to the subject's SVR. The systemic perfusion pressure generated by any given level of CO produced by external chest compression (ECC) in CPR will similarly be determined patient's SVR.

Metabolically linked vasodilatation in exercising muscle and functional sympatholysis

Vasodilatation in exercising muscle results from the effects of multiple mediators including nitric oxide, adenosine and prostaglandins on vascular smooth muscle [9–12]. Reduced skeletal muscle vascular resistance is closely related to reduction in muscle tissue oxygen tension [13].

Metabolically linked vasodilatation in exercising skeletal muscle is associated with reduced response to adrenergically mediated vasoconstrictor mechanisms [14–21]. This exercise-associated adrenergic resistance in skeletal muscle vasculature is often referred to as *functional sympatholysis.*

The mechanism of skeletal muscle vasodilatation in exercise has considerable similarities to the mechanism of vasodilatation in vasodilatory shock states which are associated clinically with adrenergic vasopressor resistance [22].

Increased sympathetic vasomotor tone in exercise

Sympathetic vasomotor tone increases during exercise [2,3]. The fact that SVR falls in spite of increased vasomotor tone is further evidence of the sympatholytic nature of the vasodilatation in exercising skeletal muscle. It also may be of considerable significance in acute shock and resuscitation scenarios in subjects who have been involved in immediate pre-morbid exercise; *prima facie,* if vasomotor tone is already elevated pre-morbidly, then this must limit the potential for compensatory post-morbid increase in vasomotor tone in the event of an acute fall in systemic arterial blood pressure.

Exercise related syncope

Exercise related syncope due to hypotension and cerebral hypoperfusion in patients who have restricted ability to increase their CO in exercise is a well recognised clinical entity. This syndrome provides clinical evidence which appears to support the experimental evidence of the sympatholytic nature of exercise-induced vasodilatation in skeletal muscles. If the vasomotor system was capable of predominating over exercise-induced vasodilatation in skeletal muscles then blood pressure should be better maintained by sympathetic response to falling carotid sinus blood pressure at the expense of skeletal muscle perfusion.

The post-exercise recovery process

Normalisation of cardiovascular and respiratory parameters after exercise depends on the post-exercise recovery process. The recovery process requires continued elevation of skeletal muscle perfusion and oxygen delivery and uptake. Pathological reduction in CO below the elevated levels necessary for normal post-exercise recovery can therefore be predicted to slow the recovery process by delaying delivery of the oxygen required to meet the excess post-exercise oxygen consumption (EPOC). EPOC is necessary to allow normalisation of the muscle tissue oxygen tension and we have already seen that exercise-induced vasodilatation in skeletal muscle is closely related to reduced oxygen tension in exercising muscle.

In CPR oxygen delivery to the muscles is likely to fall to levels close to or bellow that required for basal muscle tissue oxygen consumption and it follows that the recovery process will effectively be blocked.

The scale of reduction of SVR in exercise

There is adequate published data on CO and blood pressure changes in exercise on which to base simple illustrative mathematical modelling of SVR and total systemic vascular conductance in exercise [1,23–25]. Details of modelling are given in the Appendix. Results of modelling of SVR for a defined exercise scenario are presented in Fig. 1. The model inputs are compatible with a scenario of dynamic lower limb exercise in a broad range of 30–40 year old men who partake in regular vigorous exercise such as competitive amateur sports or military assault course training. The calculations are based on simple established physiological relationships.

Maximum exercise level in the model is 16 metabolic equivalent units (MET). At this level of exertion SVR is only 26% of normal resting SVR in the model. 16 MET equates approximately to running 400 m in 90 s (equivalent to 6 min/mile pace or 16 kph (10 mph). In an athletic context this is a moderate running pace.

The basic inverse nature of the relationship between SVR and increasing CO as exercise intensity increases is clearly illustrated