Exercise Associated Muscle Cramping (EAMC) – Risk, Causes, Diagnosis and Management

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Prof Martin Schwellnus
Acknowledgments

- My colleagues that I have had the privilege to work with over many years
- My students that have contributed to the work in this field
- All the athletes that have participated in many research studies
Outline

• Definition
• Classification of EAMC
• Epidemiology
• Etiology and risk factors
• Clinical approach
  – Diagnostic approach
  – Prevention
  – Acute treatment
• Summary
Definition:
Exercise Associated Skeletal Muscle Cramp (EAMC)

Painful, spasmodic, involuntary contractions of skeletal muscle that occur during, immediately after, or within 24 (6) hours after muscular exercise

Definition vs. Diagnosis

Exercise Associated Skeletal Muscle Cramp (EAMC)

- EAMC - collection of symptoms and clinical signs
- EAMC - is a syndrome and not a diagnosis
Causes of Skeletal Muscle Cramps

**Idiopathic**
- Autosomal cramping disease, familial nocturnal cramps, Continuous muscle fibers activity syndrome
- Continuous muscle fibers activity syndrome, Syndrome of progressive muscle spasm, alopecia and diarrhea (Satayashi’s syndrome), nocturnal cramps, generalized myokymia, myokymia-hyperhidrosis syndrome

**Symptomatic**
- Motor neuron disease
  - Motoneuron disease, occupational dystonias, Parkinson's disease, Tetanus, multiple sclerosis, radiculopathies, plexopathies, peripheral neuropathies, others
- CNS disease
  - Metabolic myopathies, mitochondrial myopathy, endocrine myopathy, dystrophinopathies, myotonia, inflammatory myopathies, others
- Muscular disease
  - Venous disease, arterial disease, heart disease, hypertension
- CVS disease
  - Thyroid disease, parathyroid disease, cirrhosis, isolated ACTH deficiency, Conn's, Addison's, Uremia and dialysis
- Endocrine-metabolic
  - Generalized dehydration (diarrhea, vomiting), sodium, potassium, magnesium, "heat"
- Hydro-electrolyte
  - Drugs, pesticides, black widow bite, malignant hyperthermia
- Toxic/pharmacological
  - Occasional cramps
- Psychiatric
  - Pregnancy
  - Sporting activity

**Paraphysiological**

Lecture dedicated to Joost Van Der Westhuizen

Joost van der Westhuizen dies

SOUTH AFRICA  Monday 6 February 2017 - 2:15pm
Lecture dedicated to Joost Van Der Westhuizen

- Died Monday 6 February from Motor Neuron Disease at the age of 45 years
- South African Rugby Player
- 89 Test matches
- Prolific tri-scorer
- Member of the 2005 Rugby World Cup winning team
# Causes of Skeletal Muscle Cramps

<table>
<thead>
<tr>
<th>Idiopathic</th>
<th>Familial</th>
<th>Autosomal cramping disease, familial nocturnal cramps, Continuous muscle fibers activity syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sporadic</td>
<td>Continuous muscle fibers activity syndrome, Syndrome of progressive muscle spasm, alopecia and diarrhea (Satayashi’s syndrome), nocturnal cramps, generalized myokymia, myokymia-hyperhidrosis syndrome</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>Muscle cramps in cancer patients</td>
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<tr>
<td>Symptomatic</td>
<td>CNS disease</td>
<td>Motorneuron disease, occupational dystonias, Parkinson's disease, Tetanus, multiple sclerosis, radiculopathies, plexopathies, peripheral neuropathies, others</td>
</tr>
<tr>
<td></td>
<td>Muscular disease</td>
<td>Metabolic myopathies, mitochondrial myopathy, endocrine myopathy, dystrophinopathies, myotonia, inflammatory myopathies, others</td>
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<td></td>
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<td></td>
<td>Sporting activity</td>
<td></td>
</tr>
</tbody>
</table>

**Exercise Associated Muscle Cramps (EAMC)**

Diagnostic Classification of EAMC

1. **Primary (Exercise as only apparent cause or precipitant)**
   - Intensity related, training related, fatigue, non-recurrent
   - Episodic (often isolated, single or irregular episode)

2. **Secondary (Exercise “unmasking” secondary factor/s)**
   - Cramping during exercise as a result of injury
   - Cramping during exercise “unmasking” underlying other chronic systemic disease
   - Drug associated (skeletal muscle or neurological)
   - Recurrent cramping
   - Other
Severity Classification of EAMC

1. Cramp “prone state” / “Near cramping”
   • Onset of heightened neuromuscular excitability ("cramp prone state") preceding EAMC (increased EMG activity, muscle fasciculation)

2. Less severe ("benign") EAMC
   • Localized
   • Self limiting if activity stops
   • No systemic or CNS symptoms

3. Severe EAMC
   • Localized EAMC together with associated systemic symptoms / signs:
     ♦ Confusion
     ♦ Dizziness
     ♦ Collapse
     ♦ Nausea/vomiting
     ♦ Dark urine
   • Diffuse (generalized) cramping (with or without associated systemic symptoms / signs)

Schwellnus M, BJSM, 2009;43;401-408
Schwabe, K, Schwellnus M; et al: BJSM 2014
Hoffman, MD, Stuempfle KJ: Sports Medicine Open 2: 8; 2016
1. Lifetime prevalence:

- 21km distance runners: 14%
- 42km marathon runners: 39%
- 56km ultra-marathon runners: 30%
- Tri-athletes: 78%
- Cyclists: 60%
- Elite football players: 46%

2. Incidence

- Marathon runners (42km): 18% of runners in a marathon (1 in 4 runners)
  - Cramping (14%), Near cramping (27%) (1 in 3 runners)
- 161-km running race: Serious EAMC (1 in 4000)
- 21km running race: Serious EAMC (1 in 526)
- 56km running race: Serious EAMC (1 in 526)
- Club Rugby (seasonal): 52%

3. Prevalence (% admissions) after an event:

- Marathon: 10-22% of admissions
- Ultra-marathon: 29% of admissions
- Ironman: 55% of admissions

Etiology and risk factors - EAMC
Debate over the past 20 years

Physical exercise

Abnormal sweating response (increased sodium and increased fluid loss)

Abnormal neuromuscular control

Skeletal muscle cramping

Schwellnus M, BJSM, 2009;43;401-408
Edouard P; Sci & Sport, 2014; 29: 299-305
Electrolyte deficit / dehydration hypothesis

- Physical exercise with resultant sweating
  - Abnormally high sodium sweat concentrations (20-80 meq/L)
  - Sodium loss from plasma and has been suggested to cause hypotonic hyponatremia (tends to decrease osmolality)
  - Fluid movement from the intravascular space to the interstitial space
- Certain motor neuron axon terminals become hyperexcitable by, 1) mechanical deformation, 2) exposure to increased levels of excitatory extracellular constituents such as acetylcholine, electrolytes, and exercise-related metabolites in the surrounding extracellular space
- Contracting (decreasing) plasma (intravascular) volume (tends to increase plasma osmolality)
  - Fluid moves from interstitial space into the intravascular space
  - Decreased interstitial fluid compartment volume
- Restoration of plasma volume
  - Fluid moves from interstitial space into the intravascular space
- "Certain" nerve terminals are at greater risk of spontaneously discharging
  - Starts as localized muscle cramping
  - Generalized muscle cramping
  - Abnormally high sweat volume (sweat is hypotonic)
  - Abnormally high sodium sweat concentrations (20-80 meq/L)

Schwellnus M, BJSM, 2009;43;401-408

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Schwellnus M, BJSM, 2009;43;401-408
Dehydration hypothesis

**Starts as localized muscle cramping**

- Abnormally high sodium sweat concentrations (20-80 meq/L)
- Sodium loss from plasma and has been suggested to cause hypotonic hyponatremia (tends to decrease osmolality)
- Favors fluid movement from the intravascular space to the interstitial space to

**Abnormally high sweat volume (sweat is hypotonic)**

- Contracting (decreasing) plasma (intravascular) volume (tends to increase plasma osmolality)
- Fluid moves from interstitial space into the intravascular space
- Decreased interstitial fluid compartment volume

- "Certain" motor neuron axon terminals become hyperexcitable by, 1) mechanical deformation, 2) exposure to increased levels of excitatory extracellular constituents such as acetylcholine, electrolytes, and exercise-related metabolites in the surrounding extracellular space

- "Certain" nerve terminals are at greater risk of spontaneously discharging

**Treatment by fluid intake**

- 500ml bolus of oral fluid

**Restoration of plasma volume**

- Fluid moves from interstitial space into the intravascular space

**Generalized muscle cramping**

Schwellnus M, BJSM, 2009;43;401-408
Evidence that athletes suffering from EAMC are more dehydrated compared with controls

Ultra-marathon runners (n=43)

Ironman Tri-athletes (n=18)


Evidence that athletes suffering from EAMC are more dehydrated compared with controls: 2016 study

160-km Ultra-marathon runners (n=181)

Hoffman, MD, Stuempfle KJ: Sports Medicine Open 2: 8; 2016
Is more serious dehydration (4.7% BW loss) associated with EAMC susceptibility?

- 10 euhydrated, unacclimated males exercised with their non-dominant limb on a cycle ergometer every 15 min at a moderate intensity until 5% body mass loss or volitional exhaustion
- Dominant limb flexor hallucis brevis cramp threshold frequency, cramp EMG amplitude and cramp intensity were measured
- Cramp variables were reassessed pre- and post-hypo-hydration (11% PV reduction)

Electrolyte deficit hypothesis

Starts as localized muscle cramping

“Certain” motor neuron axon terminals become hyper excitable by, 1) mechanical deformation, 2) exposure to increased levels of excitatory extracellular constituents such as acetylcholine, electrolytes, and exercise-related metabolites in the surrounding extracellular space

Abnormally high sodium sweat concentrations (20-80 meq/L)

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Treatment by fluid intake

Schwellnus M, BJSM, 2009;43;401-408
## Evidence for serum electrolyte abnormalities associated with EAMC in athletes

**Marathon runners (n=43)**

<table>
<thead>
<tr>
<th></th>
<th>Crampers (n=21)</th>
<th>Controls (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ (mmol/L)</td>
<td>140 (3)</td>
<td>142 (2)</td>
</tr>
<tr>
<td>K⁺ (mmol/L)</td>
<td>4.9 (0.6)</td>
<td>4.7 (0.5)</td>
</tr>
<tr>
<td>Ca²⁺ (mmol/L)</td>
<td>2.3 (0.2)</td>
<td>2.2 (0.1)</td>
</tr>
<tr>
<td>Mg²⁺ (mmol/L)</td>
<td>0.7 (0.1)</td>
<td>0.7 (0.1)</td>
</tr>
<tr>
<td>Osmolality (mosmol/L)</td>
<td>280 (16)</td>
<td>284 (10)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>6.8 (1.9)</td>
<td>6.5 (2.0)</td>
</tr>
</tbody>
</table>

**Ironman triathletes (n=18)**

<table>
<thead>
<tr>
<th></th>
<th>Crampers (n=9)</th>
<th>Controls (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ (mmol/L)</td>
<td>140 (2)</td>
<td>143 (3)</td>
</tr>
<tr>
<td>K⁺ (mmol/L)</td>
<td>4.4 (0.6)</td>
<td>4.2 (0.5)</td>
</tr>
<tr>
<td>Mg²⁺ (mmol/L)</td>
<td>0.9 (0.2)</td>
<td>0.8 (0.1)</td>
</tr>
<tr>
<td>Chloride (mmol/L)</td>
<td>101 (3)</td>
<td>104 (4)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>6.8 (1.9)</td>
<td>6.5 (2.0)</td>
</tr>
</tbody>
</table>

**Ironman triathletes (n=209)**

<table>
<thead>
<tr>
<th></th>
<th>Crampers (n=43)</th>
<th>Controls (n=166)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-race Na⁺ (mmol/L)</td>
<td>139.8 (1.8)</td>
<td>139.8 (1.5)</td>
</tr>
<tr>
<td>Post-race Na⁺ (mmol/L)</td>
<td>140.2 (3.4)</td>
<td>139.6 (2.5)</td>
</tr>
<tr>
<td>Pre-race K⁺ (mmol/L)</td>
<td>4.17 (0.31)</td>
<td>4.12 (0.21)</td>
</tr>
<tr>
<td>Post-race K⁺ (mmol/L)</td>
<td>4.29 (0.46)</td>
<td>4.20 (0.37)</td>
</tr>
<tr>
<td>Pre-race Cl⁻ (mmol/L)</td>
<td>101.7 (1.7)</td>
<td>101.6 (1.9)</td>
</tr>
<tr>
<td>Post-race Cl⁻ (mmol/L)</td>
<td>100.7 (2.5)</td>
<td>100.5 (2.1)</td>
</tr>
</tbody>
</table>

Post-race serum sodium concentration is not associated with EAMC in runners

Ultra-marathon runners
181 runners completing a 161km ultra-marathon race

- Control
- Cramping
- Near Cramping
- Near Cramping and Cramping

Hoffman, MD, Stuempfle KJ: Sports Medicine Open: 2(8); 2016
Laboratory study evidence:
Does oral ingestion of a high Na+ and electrolyte solution (“pickle juice”) alter cramp duration and EMG activity?

Five reviews (2009, 2013, 2014, 2016 X2) all conclude that evidence supporting the “serum electrolytes and dehydration” hypothesis for EAMC is poor.
Novel finding from Laboratory study:
Does oral ingestion of a high Na+ and electrolyte solution ("pickle juice") alter cramp duration and EMG activity?

Rapid inhibition of the electrically induced cramps reflects a neurally mediated reflex that originates in the oropharyngeal region and acts to inhibit the firing of alpha motor neurons of the cramping muscle.

Introducing TRP (Transient Receptor Potential) channels

- Membrane receptors contributing to the transduction of noxious signals on free nerve ending
- Sub-populations (TRPV1, TRPA1, and TRPM8) are primary extrinsic afferent nerves in the GIT (mouth, esophagus, stomach, intestine, and colon)
- Act as afferent nociceptors for thermal and chemical stimuli (pungent irritants from mustard, onion and garlic, as well as volatile environmental toxins)
TRP channels and possible role EAMC – novel mechanism?

- Transient receptor potential (TRP) agonists (e.g. chemical compounds in “pickle juice”) may have a role in the treatment of acute EAMC
- Stimulation of oral/esophageal TRP ion channels may the the mechanism for the observed reduction in laboratory induced muscle cramps (electrical stimulation) by “pickle juice”
- Clinical trials of TRP agonists in the management of prevention of EAMC are under way
- Beware of treating the symptoms and not the cause!
Alternate hypothesis for the etiology and pathophysiology of EAMC: 1997

“Exercise associated muscle cramping occurs as a result of an imbalance between the excitatory and inhibitory input to the alpha motor neuron”

Hypothesis that EAMC is related to abnormal neuromuscular control

1997

Hypothesis that EAMC is caused by sustained abnormal spinal reflex activity, which appears to be secondary to muscle fatigue.
Evidence for the “altered neuromuscular control” hypothesis (1997 - 2017)

1. Historical data
2. Animal studies
3. Neurological literature (muscle stimulation)
4. EAMC in athletes - laboratory studies:
   • EMG activity during fatiguing exercise in runners
   • Repetitive muscle contraction causes cramping
5. EAMC in athletes - field studies: EMG activity in runners with acute EAMC
6. EAMC in athletes – Risk factors (epidemiological studies)
Localized repetitive muscle exercise

- Increased exercise intensity
- Increased exercise duration
- Decreased muscle energy stores

- Hot and/or humid environmental conditions
- Contraction of a muscle in a shortened position (inner range)

- Inadequate conditioning

- Increased excitatory afferent activity (e.g. muscle spindle)
- Decreased inhibitory afferent activity (e.g. Golgi tendon organ)

- Development of localized muscle fatigue

- Increased excitatory afferent activity (e.g. muscle spindle)
- Decreased inhibitory afferent activity (e.g. Golgi tendon organ)

- Altered neuromuscular control (spinal)

- Increased alpha motor neuron activity (spinal)
- Increased muscle cell membrane activity

- Altered Central Nervous System function

- Reflex inhibition

- Treatment by passive stretching

- ? Agonist of TRP ion channels in GIT

- Localized muscle cramping

- ? Muscle injury/damage
- ? Reflex contraction

- ? Genetic predisposition
- ? Chronic disease

- IOC Research Centre
Risk factors for EAMC during exercise – risk model

Inherent risk profile (Intrinsic risk factors)

Predisposed individual

Exposure (Extrinsic risk factors)

Inciting event/s

Susceptible Individual

EAMC
Factors associated with a history of EAMC in Ironman triathletes were:

a. Exercising at a higher intensity
b. Positive family history
c. History of a soft tissue injury
Risk factors for EAMC
Prospective cohort study in ultra-distance runners

Increased running speed and pre-race muscle damage as risk factors for exercise-associated muscle cramps in a 56 km ultra-marathon: a prospective cohort study

Martin P Schwellnus, Siddieg Allie, Wayne Derman, Malcolm Collins

Risk factors associated with EAMC in ultra-distance runners:

a. Exercising at a higher intensity (increased speed)
b. Pre-race muscle damage

Schwellnus M, Allie S, Collins M, Derman W, BJSM, June 2011
Independent Risk Factors for EAMC in Ironman triathletes
Prospective cohort study

Increased running speed and previous cramps rather than dehydration or serum sodium changes predict exercise-associated muscle cramping: a prospective cohort study in 210 Ironman triathletes

Martin P Schwellnus,¹ ² Nichola Drew,¹ Malcolm Collins¹ ³

Two independent risk factors for the development of self-reported EAMC in Ironman triathletes were:

a. past history of muscle cramping (in particular the number of EAMC reported in the last 10 races)
b. overall faster race time during the Ironman triathlon

Risk Factors for EAMC in Rugby League Players
Prospective cohort study over one season

Predictors of EAMC (logistic regression modeling)

- Competition level
- Age
- Ethnicity
- Playing position
- History of cramping
- Pre-cramping
- Low back pain
- Foot orthotic usage,
- Foot posture
- Foot strike
- Muscle flexibility
- Calf girth
- Hydration status
- Number of games played

Odds Ratio of EAMC

- Control
- History of cramping
- Low back pain (missed min)
- Lower level of competition

Prior history of EAMC is associated with the development of EAMC

Ultra-marathon runners
181 runners completing a 161km ultra-marathon race

- Control
- Cramping
- Near Cramping
- Near Cramping and Cramping

% runners with past history of EAMC

- Control: 52.1%
- Near Cramping: 82.7%
- Near Cramping and Cramping: 81.7%
- Cramping: 80%

P<0.0001

Hoffman, MD, Stuempfle KJ: Sports Medicine Open: 2(8); 2016
Genetic Risk Factors for History of Exercise Associated Muscle Cramping (EAMC) in triathletes

1. The COL5A1 gene is a potential marker for the development of EAMC
2. COL5A1 BstUI RFLP is associated with history of EAMC
3. The CC genotype may be “protective” against a history of developing EAMC
4. These effects may be mediated through the effects that type V collagen exerts on collagen fiber diameter and strength in the endo- and perimysium

K O'Connell, M Posthumus, M Schwellnus, M Collins; CJSM 2012 (in review)
Risk factors associated with a serious EAMC in recreational 56km distance runners
Prospective cohort study in 26354 runners presenting with serious EAMC

Two independent risk factors

<table>
<thead>
<tr>
<th>Age group</th>
<th>Incidence (per 1000 starters)</th>
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<tbody>
<tr>
<td>&lt;30 yrs</td>
<td>1.96</td>
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<tr>
<td>31-40 yrs</td>
<td>2.07</td>
</tr>
<tr>
<td>41-50 yrs</td>
<td>0.87</td>
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<tr>
<td>&gt;50 yrs</td>
<td>3.72</td>
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<table>
<thead>
<tr>
<th>Running pace</th>
<th>Incidence (per 1000 starters)</th>
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<tbody>
<tr>
<td>&lt;6 min/km (Faster)</td>
<td>2.89</td>
</tr>
<tr>
<td>6-7 min/km</td>
<td>1.12</td>
</tr>
<tr>
<td>&gt;7 min/km (Slower)</td>
<td>1.51</td>
</tr>
</tbody>
</table>

Past history of a running injury as a risk factor for EAMC in recreational distance runners
Cross sectional study in 15 778 runners with history of EAMC

Prevalence Risk Ratio of history of EAMC

Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)
Medication use as a risk factor for EAMC in recreational distance runners
Cross sectional study in 15 778 runners with history of EAMC

Prevalence Risk Ratio of history of EAMC

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk Ratio</th>
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<tbody>
<tr>
<td>Control</td>
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<tr>
<td>Use of regular medication</td>
<td>1.67</td>
</tr>
<tr>
<td>Medication use during racing</td>
<td>1.55</td>
</tr>
</tbody>
</table>

Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)
Cardiovascular disease as a risk factor for EAMC in recreational distance runners
Cross sectional study in 15 778 runners with history of EAMC

Prevalence Risk Ratio of history of EAMC

Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)
Other chronic disease as a risk factor for EAMC in recreational distance runners
Cross sectional study in 15 778 runners with history of EAMC

Prevalence Risk Ratio of history of EAMC

Control
Any GIT disease
Any kidney / bladder disease
Allergies

1 1.39 1.21 1.2

Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)
Summary - Risk factors for EAMC during exercise

Inherent risk profile (Intrinsic risk factors)
- Male
- Older age
- Past history of EAMC
- Past history of injury (muscle, lower back)
- Pre-race muscle damage
- Past history of chronic disease (CVD, risk factors for CVD, symptoms of CVD, kidney disease, GIT disease, allergies)
- Use of medication (regular use, during races)
- Positive family history
- Genetic: CC genotype of COL5A1 (protective)(past history of EAMC)

Predisposed individual

Exposure (Extrinsic risk factors)
- Exercise
  - Longer duration
  - Higher intensity (pace)
- Poor race preparation

Inciting event/s
- Fatiguing exercise
- Hot, humid environmental conditions
- Injury (? Muscle damage)
- Acute medication (or supplement) intake
- Other …..

Susceptible Individual
Whilst it is clear that further evidence to support the “altered neuromuscular control” hypothesis is also required, research data are accumulating that support this as the principal pathophysiological mechanism for the aetiology of EAMC.
Recent experimental findings have proved unambiguously the relevance of spinal mechanisms in the generation and development of muscle cramps. These findings are important for identifying the most effective and safe medications for managing (preventing or reducing the occurrence of) cramps.
Review of evidence that EAMC is related to abnormal neuromuscular control

2014

The “Altered neuromuscular control theory” seems to be the most scientifically acceptable theory, and suggests that EAMC are caused by an imbalance between increased afferent activity (e.g. muscle spindle, Ia) and decreased inhibitory afferent activity (e.g. Golgi tendon organs, Ib) which leads to increased alpha-motor neuron activity and muscle cramping, especially with muscle contraction in a shortened position.

Review of evidence that EAMC is related to abnormal neuromuscular control

EAMC is multifactorial in nature and stems from an imbalance between excitatory drive from muscle spindles and inhibitory drive from Golgi tendon organs to the alpha motor neurons rather than dehydration or electrolyte deficits. This imbalance is believed to stem from neuromuscular overload and fatigue.

INVITED REVIEW

A NARRATIVE REVIEW OF EXERCISE-ASSOCIATED MUSCLE CRAMPS: FACTORS THAT CONTRIBUTE TO NEUROMUSCULAR FATIGUE AND MANAGEMENT IMPLICATIONS

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Localized repetitive muscle exercise

- Increased exercise intensity
- Increased exercise duration
- Decreased muscle energy stores

? Muscle injury/damage

- Increased excitatory afferent activity (e.g. muscle spindle)
- Decreased inhibitory afferent activity (e.g. Golgi tendon organ)

Development of localized muscle fatigue

- Hot and/or humid environmental conditions
- Inadequate conditioning
- Contraction of a muscle in a shortened position (inner range)

Altered neuromuscular control (spinal)

- ? Genetic predisposition
- ? Chronic disease

- Increased alpha motor neuron activity (spinal)
- Increased muscle cell membrane activity

Reflex inhibition

? Reflex contraction

- Treatment by passive stretching

Localized muscle cramping

- Altered Central Nervous System function

? Agonist of TRP ion channels in GIT

IOC Research Centre
Clinical investigation of the athlete with EAMC

• EAMC is not a diagnosis (it is a clinical syndrome)
• Not every athlete with EAMC has 1\textdegree{} or “benign” EAMC
Clinical investigation of the athlete with EAMC

Who should be investigated for secondary causes?

- Recurrent cramping
- Cramping associated with collapse, confusion, coma
- Cramping associated with “dark” urine (? myoglobinuria or hematuria)
- History of cramping/spasms at rest
- History of cramping in “non-exercising” muscles
- Cramping associated with other muscle symptoms (fatigue, weakness, swelling, pain)
- Cramping associated with other neurologic or systemic symptoms
- History of generalized (systemic) cramping
- Strong family history of cramping
Clinical investigation of the exercising individual with EAMC

**Medical history**
- Cramping (onset, duration, muscles, relation to exercise, precipitants)
- Neurological history (motor, sensory, co-ordination)
- Injury history
- Systematic medical history
- Drugs and medication
- Family history

**Clinical examination**
- General medical examination
- Neurological examination
- Musculoskeletal examination (muscle pain, stiffness, swelling, weakness)
- Systematic comprehensive examination

**Special investigations**
- CBC
- Activity markers
- Renal function
- Thyroid function
- Muscle strength / fatigue
- Muscle damage (resting and post-exercise CK)
- Skeletal muscle biopsy
- Others as indicated
Management of 1° acute EAMC

Non-pharmacologic treatment

1. Reduce intensity (running speed) – “cramp prone” state
2. Stop activity
3. Passive stretching
4. Drinking ad libitum

Other proposed non-pharmacologic treatment methods

1. Hyperventilation / re-breathing
2. Ice / ice massage
3. Walking

Management of 1º acute EAMC

Proposed pharmacologic treatment

1. Stimulation of the TRP ion channels (also known as the wasabi receptor) in the oral and esophageal mucosa
   - Clinical trials under way
   - ? Use in 1º and 2º EAMC
   - ? Not treating the cause

Other proposed pharmacological interventions (poor evidence)

1. Sodium
2. Magnesium
3. Quinine

Clinical approach
Prevention of 1º (‘benign’) EAMC

- Identify the possible secondary cause and treat it
- Prevent premature fatigue
  - Training
  - Racing at appropriate exercise intensity
  - Nutrition (? carbohydrate)
  - Other methods
- Prevent muscle damage
  - Tapering
  - Appropriate conditioning
- Prevent injury (muscle)
- Stretching regularly
- Fluid intake (? avoid too much)
- Avoid use of drugs
- ? Thermoregulation
EAMC prevention intervention:

1. Be well trained for the race
2. Avoid running too fast (faster than your normal training pace) particularly in the earlier parts (first half) of the race
3. Make sure you have recovered fully from injuries (including muscle rehabilitation)
4. Regular stretching of muscles in which you previously experienced cramping may help
5. Enquire about increased risk of cramping when your doctor prescribed any new medication
6. Slow down at the first sign of any twitching in muscles
7. Stop and stretch muscles as they start twitching and then start walking/jogging slowly if the twitching stops
8. Do not try to run through muscle cramping
Pre- vs. post EAMC educational intervention

Incidence of serious EAMC

- Pre intervention (2008-2011)
- Post intervention (2012-2015)

Incidence per 1000 runners

- All races: 0.91 (Pre) vs. 0.42 (Post) - 54% reduction
- 56 Km race: 1.9 (Pre) vs. 0.58 (Post) - 69% reduction
- 21km race: 0.25 (Pre) vs. 0.32 (Post)

Summary

1. EAMC is common – still under researched
2. Etiology and pathophysiology – multifactorial
3. Accumulating and strong evidence that final common pathway in pathophysiology of EAMC is a neuromuscular control abnormality
4. EAMC is a syndrome – not a diagnosis (many 2o causes)
5. Investigation of recurrent cramping requires careful and comprehensive medical assessment for secondary causes
6. Acute treatment – diagnosis, rest and stretching (? role of TRP ion channel agonists)
7. Prevention – ? Different for primary and secondary, role of education is important
Thank you for your attention

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