Substance P and NPY plasma levels in adults with chest pain due to coronary artery disease:
Potential implications for nursing assessment

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Pain in critical care

- Pain management is among the most complex problems in critical care, mainly due to limitations in pain assessment.

- Unrelieved pain may enhance pathophysiological phenomena of critical illness.

- In non-communicating patients, pain may be assessed through behavioral pain scales.

- The pain intensity in critical care patients is underestimated.
Background

• Coronary care unit patients are appropriate for the study of patient distress in critical care, since they are able to communicate and they experience a specific readily assessable stressor, coronary pain.

• Upon stress, stress neuropeptides are released into the systemic circulation

  Pert 1997

• Substance P (SP) is a neuropeptide involved in nociception and stress perception, along with neuropeptide Y (NPY)

  Pacak & Palkovits 2004
Substance P

• Substance P is the most abundant neurotransmitter in central and peripheral neuronal system
  (Ljuhgdahl et al 1979)

• It is a member of the tachykinin family and it is a peptide made of 11 amino-acids
  (Hokfelt et al 2001)

• It has a significant role in pain integration and transmission and the perception of nociception
  (Culman et al 1995)
Tachykinins and the heart

Preganglionic vagal neuron

ACh

Central nervous system

SP NKA

Sensory-motor neuron

myocardial ischemia

Axon reflex

Intracardiac ganglion

N

NK₃

SP NKA

ACh

M₂

contractility

Ventricular myocardium

M₂

conduction velocity

Conducting system

M₂ NK₂

heart rate

Sinoatrial node

NKA

SP

M₃

contraction relaxation

Coronary smooth muscle

NK₂

M₃

NO

Coronary endothelium
Neuropeptide Y

• The main function of NPY is vasoconstriction and, as result, is always increased in shock.

• It has an active role in blood pressure control and maintenance and in stress response.  
  Ruohonen et al 2009

• It may be involved in emotions’ perception.  
  Heinrichs et al 1992

• It performs important role in stress and depression.  
  Morales-Medina et al 2009
Purpose of the study

• We aimed to address the question of whether biochemical markers could be developed to assist nurses with the assessment of pain and distress experienced by critically ill individuals who are unable to communicate.
Aims of the study

This study aimed to explore:

a) alterations in plasma levels SP and NPY upon the experience and alleviation of coronary pain.

b) associations between stress neuropeptide levels and pain intensity, and

c) differences compared to a random sample of gender and age matched normal controls.
Study Design - Method

- The study employed a descriptive correlational repeated measures design with cross-sectional comparisons.
- A group of critically ill patients with cardiac pain (n=25), a group of 25 coronary patients free of pain and a control group (n=20) of healthy volunteers were studied.
- Plasma substance P and NPY levels were quantified by an immunosorbertent (ELISA) assay.
- Pain was assessed by behavioral pain scales (Payen’s 2001- Puntillo’s 1997 pain scale) and a numeric visual analogue scale (1-10).
# Pain Characteristics (coronary patients in pain)

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VAS-self report of pain</strong></td>
<td>4,00</td>
<td>10,00</td>
<td>7,63</td>
<td>1,88</td>
</tr>
<tr>
<td><strong>VAS-nurse’s report of pain</strong></td>
<td>4,00</td>
<td>10,00</td>
<td>6,92</td>
<td>1,97</td>
</tr>
<tr>
<td><strong>Puntillo Pain Scale</strong></td>
<td>17,00</td>
<td>24,00</td>
<td>20,87</td>
<td>2,049</td>
</tr>
<tr>
<td><strong>Payen Pain Scale</strong></td>
<td>3,00</td>
<td>8,00</td>
<td>5,95</td>
<td>1,45</td>
</tr>
<tr>
<td><strong>Multiorgan Failure Scoring System</strong></td>
<td>,00</td>
<td>3,00</td>
<td>1,1250</td>
<td>,9470</td>
</tr>
<tr>
<td><strong>Multiple organ Dysfuction Score</strong></td>
<td>,00</td>
<td>1,00</td>
<td>,2500</td>
<td>,4423</td>
</tr>
</tbody>
</table>
**Plasma Substance P and NPY Levels In Patients And Control Group**

<table>
<thead>
<tr>
<th>Substance P Levels</th>
<th>Coronary Patients During Pain</th>
<th>Coronary Patients Without Pain</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>195.3±181.1 pg/ml</td>
<td>128.6±109.0 pg/ml</td>
<td>113.5±76.32 pg/ml</td>
</tr>
<tr>
<td>NPY Levels</td>
<td>0.79±0.42 pg/ml</td>
<td>0.64±0.24 pg/ml</td>
<td>0.56±0.15 pg/ml</td>
</tr>
</tbody>
</table>
Plasma Substance P Levels In Patients And Control Group

Group A

SUBSTANCE P LEVELS

PATIENTS

CONTROLS
# Descriptive Statistics In All Diagnostic Categories

<table>
<thead>
<tr>
<th></th>
<th>AMI</th>
<th>ACS</th>
<th>PTCA</th>
<th>UNSTABLE ANGINA</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUBSTANCE P LEVELS IN PAIN</strong></td>
<td>313,49±187,42* (64,06-604,26)</td>
<td>81,19±112,64* (11,38-279,68)</td>
<td>9,913±11,43* (2,46-23,07)</td>
<td>185,99±125,17 (32,721-369,14)</td>
<td>113,51±76,32* (12,708-210,74)</td>
</tr>
<tr>
<td><strong>SUBSTANCE P LEVELS WITHOUT PAIN</strong></td>
<td>155,29±117,02* (11,41-361,25)</td>
<td>95,12±100,09* (18,04-208,24)</td>
<td>37,326-28,08* (5,10-56,59)</td>
<td>146,47±115,98 (17,079-311,16)</td>
<td></td>
</tr>
<tr>
<td><strong>PATIENTS’ SELF-REPORT OF PAIN</strong></td>
<td>8,7±2,058 (4-10)</td>
<td>6,40±1,140 (5-8)</td>
<td>7,00±1,732 (5-8)</td>
<td>7,17±1,602 (6-10)</td>
<td></td>
</tr>
<tr>
<td><strong>NURSES’ REPORT OF PAIN</strong></td>
<td>8,3±2,003 (4-10)</td>
<td>5,80±,837 (5-7)</td>
<td>5,67±1,528 (4-7)</td>
<td>6,17±1,472 (4-8)</td>
<td></td>
</tr>
<tr>
<td><strong>PAIN DURATION</strong></td>
<td>3,77±3,41 (0,30-12,0)</td>
<td>0,950±,7599 (10-2,00)</td>
<td>1,23±0,802 (0,40-2,00)</td>
<td>0,4417±,4363 (0,10-1,30)</td>
<td></td>
</tr>
</tbody>
</table>

SP levels during pain: ANOVA, df=3, F=4,615, p=0,013.
Plasma Substance P Levels In Coronary Patients With And Without Pain

*, p=0.006
*, p=0.001
Significant differences in NPY levels were detected in all coronary patients compared to controls (p<0.04).

The association of NPY levels with the pain experienced persisted even after the alleviation of coronary pain (p=0.03).
# Neuropeptides’ Levels and Pain Intensity

<table>
<thead>
<tr>
<th>Substance P Levels</th>
<th>VAS</th>
<th>Puntillo Pain Scale</th>
<th>Payen Pain Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r=0.744,\ p=0.02$</td>
<td>$r=0.474,\ p=0.010$</td>
<td>$r=0.562,\ p&lt;0.0001$</td>
</tr>
<tr>
<td>NPY Levels</td>
<td>$r=0.565,\ p=0.002$</td>
<td>$r=0.563,\ p=0.010$</td>
<td>$r=0.737,\ p&lt;0.0001$</td>
</tr>
</tbody>
</table>
Conclusions

• The observation of elevated SP and NPY plasma levels in coronary critical care patients and of associations with subjective pain perception and pain scale scores may have important clinical implications.

• Further studies are necessary to elucidate the effectiveness and feasibility of plasma SP and NPY levels as reliable markers of the level of coronary pain and the degree of distress.

Thank you for your attention!