PARESTHESIAS ASSOCIATED WITH GABAPENTIN: A PARADOX?

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Outline

- Patient story
- Paresthesias
- Compensatory vasodilation
- Gabapentin
- Why him
Patient story

• 38yo M h/o sacral chordoma
  – s/p partial sacrectomy and sacral root ligation
  – Discharged home on *Tramadol ER*, Norco

• Chronic pain clinic
  – Gabapentin started 6mo postop for BTP
    • 900mg daily
“Buzzing” in arm after “holding phone to my ears for a long time.”
  – Resolved when arm at rest
• GBP reduced to 300mg daily
  – Arm buzzing resolved
• How can that be?
Paresthesias

• Sensory fibers: 4 groups
  – Group IV: unmyelinated, slowest conduction
    • Noci /Mechano-receptors: skin and skeletal muscle
• Neuropathic: unstable firing of Aδ neurons
  – GBP classic action
• Post-ischemic
  – ↑extracell K+ w/ contraction, ↓perfusion/hypoxia
  – Inward K current→depolarization→buzzing

Al Luwimi et al, 2012
Kukkar et al, 2013
Mense, 2010
Compensatory vasodilation and SNS

- Mild exercise: blood flow ↑ by >300%
- In mild exercise, NE from post-ganglionic SN binds β2-AR → NO → vasodilation
  - ↑ muscle blood flow
- *Functional sympatholysis*
  - SNA blocked at post-junctional α1 and α2-AR
    - Local SNA reduced to pre-junction α2- and β2-AR

Bancroft et al, 1963
Joyner et al, 2014
Roatta et al, 2010
GBP and SNS

• α2-AR
  – Blocks presynaptic NE release
  – Multiple subtypes and locations
    • Skeletal muscle
• GBP is an α2-AR agonist
  – Descending noradrenergic pathways

Takasu et al, 2006
Tanabe et al, 2005
Hayashida et al, 2007
Eason et al, 1993
Trendelenburg, 2003
Proposed mechanism

- GBP at high doses binds presynaptic α2-AR
  - Mild exercise: less NE / E binding to β2-AR
  - Transient ischemia → K⁺ current → Buzzing
  - Intense exercise: less β2-AR action, other pathways

Joyner et al, 2014
Proposed mechanism

Gabapentin alpha-2 agonism inhibits vasodilation by reducing beta-2 stimulation that normally causes NO production.

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Why him?

- **Tramadol daily** $\rightarrow$ ↑NE and 5-HT levels
- GBP binds pre-junctional α2AR
  - NE withdrawal?
    - 5% of patients who abruptly stop Venlafaxine report “buzz” sensations
- Potential implication
  - Might need tighter GBP dose adjustment in patients on drugs that ↑NE

Campagne, 2005
Thanks

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References