Steroid Therapy and Stress Dose Steroids

Dan Roke, MD
Stress Dose Steroids

• Hydrocortisone
• 100 mg
• IV
Questions?
Steroid Therapy and Stress Dose Steroids

Dan Roke, MD
Disclosures

• No financial disclosures
• There will be graphic elements from a British documentary on the legend of King Arthur
It must be a good documentary – this guy is in it
What are we going to discuss?

• Steroid overview
• Perioperative Adrenal Insufficiency
• Cortisol
• Perioperative Stress Response
• Steroid Side Effects
• Recommendations
Steroids

• Adrenal cortex synthesizes two classes of steroids:
  – Corticosteroids
  – Androgens
Corticosteroids

- Corticosteroids divided into:
  - Glucocorticoids
  - Mineralocorticoids
Corticosteroids

• Glucocorticoid vs Mineralocorticoid based on:
  – Carbohydrate metabolism
  – Sodium retention
  – Inflammation
Corticosteroid Division

Some do all three

ONCE THE NUMBER THREE, BEING THE THIRD NUMBER, BE REACHED, THEN LOBBEST THOU THY HOLY HAND GRENADE OF ANTIQUH TOWARDS THY FOE.

WHO, BEING NAUGHTY IN MY SIGHT, SHALL SNUFF IT
Glucocorticoids

- Glucocorticoid effects:
  - Carbohydrate metabolism – INCREASE
  - Inflammation - DECREASE
Mineralocorticoids

• Mineralocorticoid effect:
  – Sodium retention - INCREASE
Adrenal Gland Physiology

- Adrenal glands are made up of:
  - Cortex
    - Glucocorticoids, mineralocorticoids, androgens
  - Medulla
    - Epinephrine, norepinephrine

- Adrenal glands are part of Hypothalamic-Pituitary-Adrenal Axis
  - HPA axis is critical to the stress response
Adrenal Gland Physiology

The Pituitary-Adrenal-Axis

- Hypothalamus
  - CRF (corticotropic releasing factor)
  - CRF inhibits further release of CRF

- Anterior pituitary
  - ACTH (adrenocorticotropic hormone)
  - ACTH stimulates adrenal cortex

- Adrenal cortex
  - Produces cortisol
  - Cortisol increases blood glucose, blood pressure, amino acids

- Cortisol feedback loop
  - Cortisol exerts a negative feedback effect on the hypothalamus that inhibits further release of CRF
Perioperative Adrenal Insufficiency

• 1949 – Cortisone developed – Adrenal insufficiency can be treated
Perioperative Adrenal Insufficiency

AND THERE WAS MUCH REJOICING
Perioperative Adrenal Insufficiency

• 1952 – 34 year old man being treated with cortisone for rheumatoid arthritis is anesthetized for a hip arthroplasty
  – Hemodynamic collapse immediately following the operation
  – Autopsy revealed bilateral adrenal atrophy
Perioperative Adrenal Insufficiency

• 1953 – 20 year old woman treated with cortisone is anesthetized for knee surgery
  – Hemodynamic collapse and death 5 hours postoperatively
  – Autopsy revealed adrenal atrophy
Perioperative Adrenal Insufficiency

• SUPRAPHYSIOLOGIC STEROID ADMINISTRATION RECOMMENDED PREOPERATIVELY
  – Up to 4 times the baseline dose
  – Baseline dose: 25 mg BID
  – Thus Hydrocortisone 100 mg
Perioperative Adrenal Insufficiency

– True incidence of perioperative adrenal insufficiency is unknown
  • Many studies identify adrenal insufficiency via signs and symptoms
    – Hypotension, Tachycardia, Fever, Lethargy, Arthralgias, Myalgias, Nausea, Emesis, Mental status changes
  • Few studies identify adrenal insufficiency via laboratory results
Cortisol

• A glucocorticoid

• Actions
  – Gluconeogenesis
  – Protein breakdown
  – Release of fatty acids
  – Anti-inflammatory
  – Has some mineralocorticoid effect

• Hydrocortisone is synthetic cortisol
But what about Dexamethasone?

• Also a glucocorticoid
• Much longer duration of action so doesn’t mimic the surge seen in the stress response
• No mineralocorticoid effect
Normal Cortisol Secretion

• Studies have cited cortisol secretory rates in children of:
  – 12 mg/m²/day
  – 6 mg/m²/day
• So, using the highly scientific method of averaging these we arrive at:
  – 9 mg/m²/day
And after some really complicated math requiring a great deal of mental acuity
Assuming cortisol secretion of 9 mg/m²/day

- Unstressed cortisol secretion per day (approximate) for the average male:
  - Birth: 3.6 kg, 50 cm, 0.22 m² = 2 mg
  - 6 month old: 7.8 kg, 67 cm, 0.38 m² = 3.5 mg
  - 1 year old: 10.4 kg, 76 cm, 0.46 m² = 4 mg
  - 2 year old: 13 kg, 87 cm, 0.56 m² = 5 mg
  - 5 year old: 18 kg, 109 cm, 0.74 m² = 7 mg
  - 10 year old: 32 kg, 139 cm, 1.1 m² = 10 mg
Perioperative Stress Response
Perioperative Stress Response

- HPA axis stimulated via:
  - Direct afferent signaling
  - Cytokine release from tissue at surgical site
  - Baroreceptor signaling as a result of hypovolemia
  - Psychological stress
So, What’s A Typical Stress Response?

• Taylor et al. 2013
  – 30 healthy patients, 5 months to 6 years of age
  – Elective urologic procedures
  – Blood sampled at 5 time points
    • IV placement, intubation, 50% of surgery completed, anesthesia reversal, 1 hour postoperatively
  – No significant differences between cortisol levels at any of the time points
  • Peak cortisol noted 1 hour postoperatively
So, What’s A Typical Stress Response?

• Hsu et al. 2012
  – 110 patients between 1 month to 17 years of age
  – Routine sedated procedures
  – Salivary cortisol measured at baseline, every 30 minutes during procedure, at completion, and in recovery
So, What’s A Typical Stress Response?

- Hsu et al. 2012 continued
  - All patients had a 3 times elevation in cortisol
  - 25% of patients had a 4 times elevation in cortisol
  - No differences in cortisol based on type of sedation or procedure
  - Highest cortisol levels in recovery
But If A Little Is Good...

- Steroids – They help you handle stress – like a little white rabbit...
Then How Can More Be Bad?
“That’s no ordinary rabbit. That’s the most foul, cruel, and bad tempered rodent you ever set eyes on.”
Steroid Side Effects

• Acute, supraphysiologic dosing of steroids can cause:
  – Hyperglycemia
  – Hypertension
  – Fluid retention
  – Increased risk of infection
Steroid Side Effects

- Chronic dosing of steroids can lead to HPA axis suppression
Steroid Side Effects

• Chronic dosing of steroids can lead hypothalamic-pituitary-adrenal axis suppression
• Or does it?...
Chronic Steroid Dosing And HPA Suppression

• Multiple studies showing no apparent suppression with chronic steroid usage
• Can it happen? Yes
• Does it ALWAYS happen? No
Chronic Steroid Dosing And HPA Suppression

• Likelihood of suppression increases with:
  – Dose
  – Duration
  – Decreasing time between cessation and anesthetic

• Laboratory testing can be expensive, slow, and unreliable
Recommendations

• Per Smith 8th edition (2011)
  – Brief and/or minimally invasive procedures
    • Hydrocortisone 50 mg/m² (5.5 times normal daily production)
    • As a single dose
  – Prolonged and/or significantly invasive procedures
    • Hydrocortisone 100 mg/m² (11 times normal daily production)
    • As continuous infusion or split into 4 doses per day
    • Taper may be needed
Recommendations

• Per Cote 5\textsuperscript{th} Edition (2013)
  - For fever, illness, or minor procedures
    • Replacement dosing of 3-5 times oral maintenance dose
  - For critical illness or major procedures
    • Replacement dosing of 5-10 times oral maintenance dose
Recommendations

• Taking what we’ve covered:
  – Minor procedures – 4 times maintenance dose
  – Major procedures – 6 times maintenance dose with 1-2 day taper

• Consider dosing after surgery and prior to recovery

• But there’s work to do before this issue is definitively settled
References

- de Lange D, Kars M. Perioperative Glucocorticoid Supplementation is Not Supported by Evidence. European Journal of Internal Medicine. 2008;19:461-7
- Smith 8th 2011
- Cote 5th 2013
- And for further reading if you are really interested in swallow airspeed velocity: http://style.org/unladenswallow/
Copy of slides

• DROKE@UAMS.EDU
RUN AWAY!

RUN AWAY!!
Steroid Equivalents

From Smith 8th ed (2011)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Glucocorticoid Effect (= 100 mg Cortisol)</th>
<th>Sodium Retention Effect (= 0.1 mg Fludrocortisone [Florinef])</th>
<th>Duration of Action</th>
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</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>Hydrocortisone Solu-Cortef</td>
<td>100</td>
<td>20</td>
<td>S</td>
</tr>
<tr>
<td>Cortisone</td>
<td>Cortone</td>
<td>125</td>
<td>20</td>
<td>S</td>
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<td>Prednisolone</td>
<td>Delta-Cortef</td>
<td>20</td>
<td>50</td>
<td>I</td>
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<tr>
<td>Prednisone</td>
<td>Deltasone Meticorten</td>
<td>25</td>
<td>50</td>
<td>I</td>
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<tr>
<td>Methylprednisolone</td>
<td>Medrol Solu-Medrol</td>
<td>15</td>
<td>No effect</td>
<td>I</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>Aristacort Kenacort</td>
<td>10</td>
<td>No effect</td>
<td>I</td>
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<tr>
<td>Dexamethasone</td>
<td>Decadron Hexadrol</td>
<td>1.5</td>
<td>No effect</td>
<td>L</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>Celestone</td>
<td>3</td>
<td>No effect or salt loss</td>
<td>L</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>NCA</td>
<td>300</td>
<td>0.1-0.04</td>
<td>—</td>
</tr>
<tr>
<td>9-Fluorocortisol</td>
<td>Florinef</td>
<td>6.5</td>
<td>0.1</td>
<td>I</td>
</tr>
<tr>
<td>Desoxycorticosterone</td>
<td>NCA</td>
<td>0</td>
<td>1 (IM)</td>
<td>I</td>
</tr>
</tbody>
</table>

S, Short (8-12 hr biological half-life); I, intermediate (12-36 hr biological half-life); L, long (36-72 hr biological half-life); IM, intramuscularly; NCA, not commercially available.