Minicorso 3

Terapia sostitutiva dell’iposurrenalismo primario e secondario

Terapia sostitutiva: fra efficacia e side-effects

Antonio Stigliano
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12° Congresso Nazionale AME
Associazione Medici Endocrinologi

6th Joint Meeting with AACE
American Association of Clinical Endocrinologists

Bari, 7-10 novembre 2013
A drawing from Addison’s original autopsy series showing pigmentation and co-existent vitiligo.
Asse HPA e ritmo circadiano
Il problema della terapia

5.7-10 mg/m² production rate

15–25 mg idrocortisone = 25–37.5 mg cortone acetato
Light activates the adrenal gland: Timing of gene expression and glucocorticoid release

Atsushi Ishida,1,5 Tatsushi Mutoh,1,5 Tomoko Ueyama,3 Hideki Bando,1,2 Satoru Masubuchi,1 Daiichiro Nakahara,3 Gozoh Tsujimoto,4 and Hitoshi Okamura1,*

CELL METABOLISM : NOVEMBER 2005 • VOL. 2

The magnitude of corticosterone response is dose dependently correlated with the light intensity. The light-induced clock-dependent secretion of glucocorticoids adjusts cellular metabolisms to the new light-on environment.
Ultradian hormone stimulation induces glucocorticoid receptor-mediated pulses of gene transcription

Diana A. Stavreva¹, Malgorzata Wiench¹, Sam John¹, Becky L. Conway-Campbell², Mervyn A. McKenna², John R. Pooley², Thomas A. Johnson³, Ty C. Voss⁴, Stafford L. Lightman² and Gordon L. Hager¹,³
Comorbidità
Comorbidità

- Addison non autoimmune
- Addison autoimmune isolato

- Sindromi polighiandolari autoimmune
  - Ipotiroidismo
  - Insufficienza ovarica
  - Diabete mellito tipo 1
  - Ipoparatiroidismo
  - Anemia perniciosa
  - et al........
Co-morbidities, management and clinical outcome of auto-immune Addison’s disease

Lalantha Leelarathna · Louise Breen · James K. Powrie · Stephen M. Thomas · Rustom Guzder · Barbara McGowan · Paul V. Carroll

Our data shows a high prevalence of both auto-immune and non-autoimmune co-morbidities in patients with AAD. In addition to common auto-immune diseases, patients should be screened for other cardiovascular risk factors. Further studies are needed to assess the cause of the observed increased prevalence of reduced BMD at the lumbar spine. There is a need for internationally agreed long-term management guidelines.
Problematiche della malattia isolata e delle comorbidità associate

0 Addison = malattia con side-effects

0 Addison + endocrinopatie = side-effects Addison + side-effects altre endocrinopatie

0 Terapia Addison: scelta degli steroidi, modalità di somministrazione

0 Terapia Addison + terapia endocrinopatie associate

0 La terapia induce side-effects?
  ✓ dosaggio?
  ✓ condizioni associate alla malattia?
  ✓ necessità di terapie associate alla terapia sostitutiva?
La terapia
Farmaci glucocorticoidi disponibili

- Glucocorticoidi short-acting
  
  ![Images of tablets](image1)
  
  - 619* 10 mg
  - 625* 20 mg
  
  *Hydrocortone*®
  (hydrocortisone)

  ![Image of tablet](image2)
  
  - 219* 25 mg
  
  *Cortone*®
  (cortisone acetate)

- Glucocorticoidi long-acting
  
  ![Images of tablets](image3)
  
  Prednisone

  ![Images of tablets](image4)
  
  - 20* 0.25 mg
  - 41* 0.5 mg
  - 63* 0.75 mg
  
  - 95* 1.5 mg
  - 97* 4 mg
  - 147* 6 mg

  *Decadron*®
  (dexamethasone)
Farmaci mineralcorticoidi e androgeni disponibili

Fludrocortisone Acetate Tablets USP 0.1 mg
100 TABLETS

0.05 – 0.20 mg/die

DHEA

12.5 – 50 mg/die
The Approach to the Adult with Newly Diagnosed Adrenal Insufficiency

Wiebke Adt  JCEM'09

Clinical Endocrinology (2012) 76, 21–25
doi: 10.1111/j.1365-2265.2011.04103.x

CLINICAL QUESTION

What is the best long-term management strategy for patients with primary adrenal insufficiency?

Marcus Quinkler* and Stefanie Hahner†

Endocrine (2013) 43:514–528
DOI 10.1007/s12020-012-9835-4

REVIEW

Therapy of adrenal insufficiency: an update

Alberto Falorni · Viviana Minarelli · Silvia Morelli
Current recommended daily starting dose for hydrocortisone and cortisone acetate are 20 and 25 mg, respectively, divided into two or preferably three doses. The mineralocorticoid depletion should be treated with fludrocortisone 0.05 – 0.2 mg/day. Replacement of dehydroepiandrosterone 20 – 50 mg has been advocated in adrenal failure, but the evidence for benefit is weak.
Requisiti e problematiche per l’ottimizzazione della terapia

- Mantenimento ritmo circadiano endogeno del cortisolo
- Minima variabilità interindividuale per prevedere la dose corretta
- Facile titolazione del dosaggio
- Monitoraggio terapia: marcatore biologico azione glucocorticoidi in vivo (percezione dello stato di benessere individuale ?, ACTH ?, CLU ?, cortisolo sierico ?, cortisolo salivare ?)
- Rischio minimo di overtreatment
- Consensus trattamento
Schemi terapeutici

- Dose unica giornaliera
- Dose doppia giornaliera
- Dose tripla giornaliera
- Dose relativa al peso o alla superficie corporea
REVIEW

Inadequacies of glucocorticoid replacement and improvements by physiological circadian therapy

Miguel Debono, Richard J Ross and John Newell-Price

Patients with adrenal insufficiency need lifelong glucocorticoid replacement, but many suffer from poor quality of life, and overall there is increased mortality. Moreover, it appears that use of glucocorticoids at the higher end of the replacement dose range is associated with increased risk for cardiovascular and metabolic bone disease. These data highlight some of the inadequacies of current regimes.
La terapia nella pratica

Carenza di studi che suggeriscano l’appropriatezza di uno schema terapeutico
Effetti a lungo termine della terapia: ipotesi discordanti

I. No effetti negativi per la natura sostitutiva della terapia

II. Effetti avversi dei glucocorticoidi
Problematiche della terapia

OVER-REPLACEMENT

- IGT
- adiposità centrale
- osteoporosi
- infezioni ricorrenti
- insonnia

UNDER-REPLACEMENT

- nausea
- disappetenza
- sonnolenza
- pigmentazione
- perdita di peso
- alterazione dello stato di benessere
Effetti a lungo termine della terapia

- Aumento della mortalità
- Rischio cardiovascolare
- Alterazione metabolismo osseo
Aumento mortalità

Premature Mortality in Patients with Addison’s Disease: A Population-Based Study

Ragnhildur Bergthorsdottir, Maria Leonsson-Zachrisson, Anders Odén, and Gudmundur Johannsson

<table>
<thead>
<tr>
<th>Obs. no.</th>
<th>Exp. no.</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular dis.</td>
<td>239</td>
<td>1.97 (CI 1.61-2.39)</td>
</tr>
<tr>
<td>men</td>
<td>103</td>
<td>2.31 (CI 1.94-2.74)</td>
</tr>
<tr>
<td>women</td>
<td>136</td>
<td>1.61 (CI 1.13-2.23)</td>
</tr>
<tr>
<td>Malignant dis.</td>
<td>73</td>
<td>1.47 (CI 1.03-2.02)</td>
</tr>
<tr>
<td>men</td>
<td>36</td>
<td>1.54 (CI 0.97-2.87)</td>
</tr>
<tr>
<td>women</td>
<td>37</td>
<td>3.74 (CI 2.52-5.34)</td>
</tr>
<tr>
<td>Respiratory dis.</td>
<td>45</td>
<td>6.57 (CI 2.56-15.17)</td>
</tr>
<tr>
<td>men</td>
<td>15</td>
<td>5.57 (CI 2.04-12.13)</td>
</tr>
<tr>
<td>women</td>
<td>30</td>
<td>8</td>
</tr>
<tr>
<td>Infectious dis.</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>men</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>women</td>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

Interpretation: Compared with the background population, we observed that the risk ratio for death was more than 2-fold higher in patients with Addison’s disease. Cardiovascular, malignant, and infectious diseases were responsible for the higher mortality rate. (J Clin Endocrinol Metab 91: 4849–4853, 2006)
CLINICAL STUDY

Normal overall mortality rate in Addison's disease, but young patients are at risk of premature death

Martina M Erichsen¹, Kristian Løvås¹,², Kristian J Fougner³, Johan Svartberg⁴,⁵, Erik R Hauge⁶, Jens Bollerslev⁷,⁸, Jens P Berg⁸,⁹,¹⁰, Bjarne Mella¹¹ and Eystein S Husebye¹,²

Conclusion: Addison’s disease is still a potentially lethal condition, with excess mortality in acute adrenal failure, infection, and sudden death in patients diagnosed at young age. Otherwise, the prognosis is excellent for patients with Addison’s disease.
Rischio cardiovascolare

Fasting and Postprandial Lipid Abnormalities in Hypopituitary Women Receiving Conventional Replacement Therapy

KAMAL A. S. AL-SHOUMEER, KATHARINE H. COX, CAROL L. HUGHES, WILLIAM RICHMOND, AND DESMOND G. JOHNSTON

<table>
<thead>
<tr>
<th>Triglycerides (mmol/L)</th>
<th>Patients</th>
<th>Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>154 ± 14</td>
<td>152 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>Males</td>
<td>129 ± 14</td>
<td>150 ± 15</td>
<td>NS</td>
</tr>
<tr>
<td>Females</td>
<td>179 ± 19</td>
<td>154 ± 13</td>
<td>NS</td>
</tr>
</tbody>
</table>

We conclude that hypopituitarism with conventional replacement therapy is associated with unfavorable fasting and postprandial lipid and lipoprotein concentrations, particularly in women. The changes may contribute to the observed increased vascular morbidity and mortality. (J Clin Endocrinol Metab 82: 2653–2659, 1997)
Metabolic and cardiovascular profile in patients with Addison’s disease under conventional glucocorticoid replacement

R. Giordano¹, S. Marzotti², M. Balbo³, S. Romagnoli², E. Marinazzo³, R. Berardelli³, G. Migliaretti⁴, A. Benso³, A. Falorni², E. Ghigo³, and E. Arvat³

Our study shows a higher prevalence of central adiposity, impaired glucose tolerance and dyslipidemia in AD patients.
BCII polymorphism of the glucocorticoid receptor gene is associated with increased obesity, impaired glucose metabolism and dyslipidaemia in patients with Addison’s disease

Roberta Giordano, Stefania Marzott, Rita Berardelli, Ioannis Karamouzitis, Annalisa Brozzetti, Valentina D'Angiò, Giulio Mengozzi, Giorgia Mandrile, Daniela Giachino, Giuseppe Migliaretti, Vittorio Bini, Alberto Falorni, Ezio Ghigo and Emanuela Avallone
Investigation of glucocorticoid receptor polymorphisms in relation to metabolic parameters in Addison's disease

I L Ross, N S Levitt, I Van der Merwe¹, D A Schatz², G Johannsson³, C Dandara⁴, T S Pillay⁵ and D J Blom⁶

La terapia convenzionale glucocorticoido è gravata da una alterazione del metabolismo glicidico e lipidico che peggiora con la presenza di polimorfismi predisponenti

Questi aspetti potrebbero contribuire all’aumento di mortalità osservata in alcuni studi

<table>
<thead>
<tr>
<th>Controllo</th>
<th>0 (0)</th>
<th>5 (1.00)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pazienti</td>
<td>2 (0.12)</td>
<td>15 (0.88)</td>
</tr>
<tr>
<td>Idrossicortisone (mg), mediana (IQR)</td>
<td>30.0 (25.0–30.0)</td>
<td>20.0 (20.0–30.0)</td>
</tr>
</tbody>
</table>
Long-term follow-up of bone mineral density in Addison’s disease

Esteban Jódar*, María Pilar Ruiz Valdepeñas*, Guillermo Martínez*, Antonino Jara† and Federico Hawkins*

CONCLUSIONS Patients on long-term therapy do not show accelerated bone loss at the lumbar spine. Nevertheless, a considerable proportion of patients, mainly those treated with prednisone, showed densitometric osteoporosis.
# Bone Mineral Density Is Not Significantly Reduced in Adult Patients on Low-Dose Glucocorticoid Replacement Therapy

K. R. Koetz, M. Ventz, S. Diederich, and M. Quinkler

<table>
<thead>
<tr>
<th>PAI</th>
<th>Women total</th>
<th>Premenopausal women</th>
<th>Postmenopausal women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Conclusions:** Adult PAI and CAH patients on low glucocorticoid doses showed normal BMD within the normal reference range. The use of longer acting prednisolone resulted in significantly lower BMD in PAI. In addition, DHEA treatment may have a beneficial effect on bone in Addison’s women. *(J Clin Endocrinol Metab 97: 85–92, 2012)*

<table>
<thead>
<tr>
<th></th>
<th>Women total</th>
<th>Premenopausal women</th>
<th>Postmenopausal women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported fractures after age of 30 y</td>
<td>13/48 (26.9%)</td>
<td>0/14 (0%)</td>
<td>13/33 (39.3%)</td>
<td>47/17 (44.8%)</td>
</tr>
<tr>
<td>Reported spontaneous spine fractures</td>
<td>4/58 (6.9%)</td>
<td>0/18 (0%)</td>
<td>4/40 (10%)</td>
<td>1/28 (3.6%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>4/58 (6.9%)</td>
<td>4/18 (22.2%)</td>
<td>0/40 (0%)</td>
<td>4/28 (14.3%)</td>
</tr>
</tbody>
</table>
CLINICAL STUDY

Glucocorticoid replacement therapy and pharmacogenetics in Addison’s disease: effects on bone

Kristian Lovás¹,², Clara G Gjesdal³,⁴, Monika Christensen⁵, Anette B Wolff¹,⁶, Bjorg Almås⁵, Johan Svartberg⁷,⁸, Kristian J Fougner⁹,¹⁰, Unni Syversen⁹,¹⁰, Jens Bollerslev¹¹,¹², Jan A Falch¹¹,¹³, Penelope J Hunt¹⁴, V Krishna K Chatterjee¹⁵ and Eystein S Husebye¹,²

The common rs1045642 polymorphism in the efflux transporter P-glycoprotein is associated with BMD in patients with Addison’s disease, and might be important for susceptibility to glucocorticoid induced osteoporosis. Glucocorticoid pharmacogenomics is likely to explain some of the variation in the effects of glucocorticoids on bone, and genotyping of the ABCB1, FKBP5, HSD11B1 and GR genes might become part of future pharmacogenomic individual tailoring of both replacement and pharmacological therapy with glucocorticoids.
BclI polymorphism of the glucocorticoid receptor gene is associated with increased bone resorption in patients on glucocorticoid replacement therapy

Kathrin R. Koetz*, Elisabeth F. C. van Rossum†, Manfred Ventz*, Sven Diederich† and Marcus Quinkler*

La terapia con preparati short-acting a basse dosi non è associata ad osteoporosi al contrario della terapia con prednisone

Polimorfismi predisponenti ne condizionano la comparsa
Qualità della vita e percezione dello stato di benessere
CONCLUSIONS  Patients with Addison’s disease under replacement therapy with cortisone acetate and fludrocortisone have reduced general health perception and vitality, and increased fatigue.  

Thus, there might be potential for further refinement of replacement therapy.
Impaired Subjective Health Status in 256 Patients with Adrenal Insufficiency on Standard Therapy Based on Cross-Sectional Analysis

Stefanie Hahner, Melanie Loeffler, Martin Fassnacht, Dirk Weismann, Ann-Cathrin Koschker, Marcus Quinkler, Oliver Decker, Wiebke Arlt, and Bruno Allolio

In conclusion, patients with both primary and secondary AI suffer from significantly impaired health-related subjective health status despite current standard replacement therapy, with a high percentage of patients being out of work and receiving disablement pensions. Importantly, this impairment is largely independent of concomitant endocrine and nonendocrine disease. In this cross-sectional, noninterventional study, patients receiving DHEA or GH replacement did not have improved measures of health-related subjective health status. This may indicate that current replacement regimens in AI are not suitable for reestablishing a normal health-related subjective health status in AI patients.
Conclusions: Glucocorticoid replacement therapy with PR seems to be equivalent to hydrocortisone regarding SHS in patients with AI. However, SHS remains impaired in all patient groups suggesting a need for further improved glucocorticoid replacement strategies.
Current practice of glucocorticoid replacement therapy and patient-perceived health outcomes in adrenal insufficiency - a worldwide patient survey

M Forss¹, G Batcheller¹, S Skrtic² and G Johannsson³

Figure 1 Change in activities due to adrenal insufficiency. Responses to the question “What activities do you need to alter due to your adrenal insufficiency?” in an international patient survey. A total of 1001 subjects responded to this question.
Conclusions Health-related QoL was impaired in patients with primary and secondary AI. HC doses above 30 mg/day were associated with a worse health status. Thrice daily intake of HC was not superior to twice daily intake. Our data support the perception that current replacement strategies are still insufficient to fully restore well-being and daily performance.
In sintesi

- la qualità della vita risulta alterata sia nell’insufficienza surrenalica primitiva che secondaria (anche con la supplementazione di DHEA e GH)
- no differenze tra prednisone e idrocortisone nella qualità della vita
- peggiore qualità della vita lavorativa, sociale, e fisica nell’insufficienza secondaria
- la triplice somministrazione della terapia peggiora la qualità della vita
- necessità di un nuovo schema terapeutico
Development of a Disease-Specific Quality of Life Questionnaire in Addison’s Disease

Kristian Løvås, Suzanne Curran, Marianne Øksnes, Eystein S. Husebye, Felicia A. Huppert, and V. Krishna K. Chatterjee

Conclusions: We envisage AddiQoL having utility in trials of hormone replacement and management of patients with Addison’s disease, analogous to similar questionnaires in GH deficiency (AGHDA) and acromegaly (AcroQoL). (J Clin Endocrinol Metab 95: 545–551, 2010)
Quality of Life in European Patients with Addison’s Disease: Validity of the Disease-Specific Questionnaire AddiQoL


Conclusion: The validation process resulted in a revised 30-item AddiQoL questionnaire and an eight-item AddiQoL short version with good psychometric properties and high reliability. (J Clin Endocrinol Metab 97: 568–576, 2012)
Limiti della terapia
Profilo tipo di un pz sottoposto a terapia sostitutiva con glucocorticoidi

Picchi sovrafisiologici 90-120’ dopo la terapia

Livelli di cortisolo ridotti o indosabili prima del risveglio e delle altre somministrazioni
Criticità

- mancato rispetto del ritmo circadiano responsabile della mancata compliance del pz

- probabile sovrastima della terapia sostitutiva come causa degli effetti collaterali indotti a lungo termine
Prospettive future
Novel strategies for hydrocortisone replacement

M. Debono, MRCP, Academic Clinical Fellow Endocrinology, J. Newell Price, MA, PhD, FRCP, Senior Lecturer in Endocrinology and Honorary Consultant Physician, Richard J. Ross, MD, FRCP, Head of Section Endocrinology and Reproduction, and Professor of Endocrinology
Circadian hydrocortisone infusions in patients with adrenal insufficiency and congenital adrenal hyperplasia

Z Merza, A Rostami-Hodjegan, A Memmott, A Doane, V Ibbotson, J Newell-Price, GT Tucker, RJ Ross

Clin Endocrinol 65 (16) ’06
Continuous subcutaneous hydrocortisone infusion in Addison's disease

Kristian Lavås¹,² and Eystein S Husebye¹,²

Indicazioni:

✓ pz con difficile controllo malattia con terapia orale

Limiti:

✓ presidi sperimentali che necessitano di ulteriori validazioni
Efficacia:

✓ Buona riproduzione del ritmo circadiano

Limiti:

✓ Lieve esposizione a maggiori livelli di cortisolo durante la notte
### CLINICAL STUDY

**Sleep disturbances in patients with Addison’s disease**

Kristian Lovás, Eystein S Husebye, Fred Holsten and Bjørn Bjorvatn

<table>
<thead>
<tr>
<th>Gender</th>
<th>Difficulties falling asleep</th>
<th>Repeated awakenings</th>
<th>Early morning awakenings</th>
<th>Tired or sleepy during daily activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (n = 34)</td>
<td>6</td>
<td>16</td>
<td>23</td>
<td>48</td>
</tr>
<tr>
<td>Men (n = 26)</td>
<td>23</td>
<td>12</td>
<td>17</td>
<td>31</td>
</tr>
<tr>
<td>P-value¹</td>
<td>0.08</td>
<td>&gt; 0.20</td>
<td>&gt; 0.20</td>
<td>&gt; 0.20</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt; 34 years (n = 15)</td>
<td>27</td>
<td>13</td>
<td>7</td>
<td>40</td>
</tr>
<tr>
<td>Age 35–50 years (n = 23)</td>
<td>8</td>
<td>9</td>
<td>14</td>
<td>35</td>
</tr>
<tr>
<td>Age &gt; 50 years (n = 22)</td>
<td>14</td>
<td>18</td>
<td>39</td>
<td>47</td>
</tr>
<tr>
<td>P-value²</td>
<td>0.15</td>
<td>&gt; 0.20</td>
<td>&gt; 0.20</td>
<td>&gt; 0.20</td>
</tr>
<tr>
<td>Disease category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Addison's disease (n = 26)</td>
<td>12</td>
<td>13</td>
<td>17</td>
<td>46</td>
</tr>
<tr>
<td>APS I (n = 7)</td>
<td>29</td>
<td>0</td>
<td>29</td>
<td>43</td>
</tr>
<tr>
<td>APS II (n = 27)</td>
<td>11</td>
<td>11</td>
<td>22</td>
<td>35</td>
</tr>
<tr>
<td>P-value³</td>
<td>0.20</td>
<td>&gt; 0.20</td>
<td>&gt; 0.20</td>
<td>&gt; 0.20</td>
</tr>
</tbody>
</table>

**Doseage of cortisone acetate**

| Last dose at 1800 h or before (n = 14) | 21 | 7   | 0   | 29 |
| Last dose after 1800 h (n = 11)       | 18 | 30  | 40  | 50 |
| P-value⁴                               | > 0.20 | 0.18 | > 0.20 | > 0.20 |

**All (n = 60)**

|               | 13 | 14 | 20 | 40 |
CLINICAL STUDY

Improving glucocorticoid replacement therapy using a novel modified-release hydrocortisone tablet: a pharmacokinetic study

Gudmundur Johannsson¹, Ragnhildur Berghorsdottir¹, Anna G Nilsson¹, Hans Lennernas³, Thomas Hedner² and Stanko Skrtic²

Conclusion: The dual release hydrocortisone tablet with once-daily administration produced a diurnal plasma cortisol profile mimicking the physiological serum cortisol profile.
Improved Cortisol Exposure-Time Profile and Outcome in Patients with Adrenal Insufficiency: A Prospective Randomized Trial of a Novel Hydrocortisone Dual-Release Formulation

Vantaggi:

✓ riproduzione ritmo circadiano
✓ miglioramento parametri metabolici
✓ unica somministrazione
The Approach to the Adult with Newly Diagnosed Adrenal Insufficiency

Riduzione della posologia nei pz ipertesi controllando i livelli elettrolitici

DOI 10.1007/s12020-012-9835-4

REVIEW

Therapy of adrenal insufficiency: an update

Alberto Falorni · Viviana Minarelli · Silvia Morelli
DHEA pro

- miglioramento benessere fisico e psicologico (anche nei bambini)
- miglioramento libido
- effetto antidepressivo (neurosteroidi)
- immunomodulatore
- miglioramento della densità minerale ossea
DHEA contro

- acne, seborrea spesso transitorie
- dati discordanti
- indisponibilità di preparazioni farmaceutiche controllate
Come dobbiamo trattare i pazienti?
Glucocorticodì replacement

O Riproduzione del ritmo circadiano del cortisolo

O Somministrazione glucocorticoidi ad azione short-acting

O Evitare over- e under-treatment

O Considerare terapia delle comorbidità

O Considerare interferenti
Mineralcorticoidi replacement

- Possibilità di riduzione della terapia nei pz ipertesi ma controllo elettrolitico costante
- Aumento della posologia nell’ultimo trimestre di gravidanza
Androgeni replacement

- Riservare terapia con DHEA a pazienti (prevalentemente donne) con riduzione della libido, cute ipoidratata e depressione