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# Treatment of uraemic anorexia with megestrol acetate

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## ABSTRACT

**Background:** Anorexia is a common disorder in patients treated with regular hemodialysis and a contributing factor of malnutrition. The aim of this study was to evaluate the effectiveness of megestrol acetate, an appetite stimulant used in cancer patients as a treatment for anorexia in dialysis patients. **Material and methods:** In 2009, 16 patients in our hemodialysis unit, three with diabetes mellitus were treated with megestrol (160 mg/day single dose) for anorexia defined as a Likert scale of Appetite. The pattern and dialysis dose were not changed during the study. **Results:** In the third month of treatment is aimed, in the total group, an increase of dry weight (60.8 vs. 58.9 kg, p <.01), concentration of albumin (4.02 vs 3.8 g/dl, p <.05), creatinine concentration (9.73 vs. 8.26 mg/dl, p <.01) and protein catabolic rate (1.24 vs. 0.97 g/kg/day, p <0001). Non significant variations in the concentration of hemoglobin, erythropoietin dose, and concentration of lipids were found. One patient with diabetes mellitus had to increase the dose of insulin and two other patients have had some mild hyperglycemia. Megestrol acetate did not suppress the secretion of pituitary sex hormones, but in 3 of 10 patients studied was found inhibition of ACTH secretion. The response was not homogeneous: a patient did not respond and reduced its dry in weight, 5 weight gain was quiet (less than 1 kg) and the remaining ten the response was good with an increase in dry weight ranged between 1.5 and 5.5 kg. **Conclusions:** Megestrol acetate can improve appetite and nutritional parameters in patients treated with periodic hemodialysis who report anorexia. Megestrol acetate can induce hyperglycemia and inhibit the secretion of ACTH in some patients. These side effects should be assessed when given this treatment.

**Key words:** Megestrol acetate. Anorexia. Malnutrition. Hemodialysis.

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## *Tratamiento de la anorexia urémica con acetato de megestrol*

## *RESUMEN*

***Introducción:*** *La anorexia es un trastorno frecuente en el enfermo tratado con hemodiálisis periódica, y factor contribuyente de la malnutrición. El objetivo del presente trabajo es comprobar la eficacia del acetato de megestrol, un estimulador del apetito utilizado en enfermos con cáncer, como tratamiento de la anorexia del enfermo sometido a diálisis.* ***Material y métodos:*** *En el año 2009, 16 enfermos de nuestra unidad de hemodiálisis, tres de ellos con diabetes mellitus, fueron tratados con acetato de megestrol (160 mg/día en dosis única), por anorexia definida según una escala Likert de apetito. La pauta y la dosis de diálisis no fueron modificadas durante el estudio.* ***Resultados:*** *Al tercer mes de tratamiento se objetivó, en el grupo total, un aumento del peso seco (60,8 frente a 58,9 kg; p <0,01), de la concentración de albúmina (4,02 frente a 3,8 g/dl; p <0,05), de la concentración de creatinina (9,73 frente a 8,26 mg/dl; p <0,01) y de la tasa de catabolismo proteico (1,24 frente a 0,97 g/kg/día; p <0,001). No hemos constatado variaciones significativas en la concentración de hemoglobina, dosis de eritropoyetina y concentración de lípidos. En un enfermo con diabetes mellitus hubo que aumentar la dosis de insulina y en otros 2 enfermos se detectó una hiperglucemia leve. El acetato de megestrol no suprimió la secreción de hormonas sexuales hipofisarias, pero en 3 de 10 enfermos estudiados se constató una inhibición de la secreción de corticotropina. La respuesta no fue homogénea: un enfermo no respondió y disminuyó su peso seco, en cinco el incremento de peso fue discreto (in-*

*ferior a 1 kg) y en los 10 restantes la respuesta fue buena, con un incremento de peso seco que osciló entre 1,5 y 5,5 kg.* ***Conclusiones:*** *El acetato de megestrol puede mejorar el apetito y los parámetros nutricionales en enfermos tratados con hemodiálisis periódica que refieran anorexia. El acetato de megestrol puede inducir hiperglucemia e inhibir la secreción de corticotropina en algunos pacientes. Estos efectos secundarios deben ser valorados cuando se administre este tratamiento.*

***Palabras clave:*** *Acetato de megestrol. Anorexia. Desnutrición. Hemodiálisis*

## INTRODUCTION

Anorexia, defined as a lack of desire to eat, is a frequent disorder among patients treated with periodic haemodialysis. A loss in appetite was noted by 33% of the patients in the HEMO[1] study, by 24% of those in the DOPPS[2] study, and in up to 38% in other series.[3]

Anorexia is one of the factors that contribute to malnutrition among patients undergoing dialysis.[4,5] Insufficient food intake is the main cause of type 1 uraemic malnutrition, which is characterised by weight and muscle mass loss with a modest impact on albumin concentrations, in contrast to type 2, which is more related to concurrent inflammatory processes.[6,7] Apart from its impact on nutrition, anorexia is itself an independent risk factor for morbidity and mortality.[1,2] Its pathogenesis is unknown. Inflammatory cytokines, deregulation of hormones and neuropeptides that control appetite, retention of medium molecular weight molecules, and alterations in amino acid concentrations seem involved.[4,8,9]

The control of anorexia is important for the prevention and treatment of malnutrition associated with renal failure; however, few studies have focused on appetite and specific measures to stimulate it. In the HEMO study, it was found that neither the administration of a greater dose of haemodialysis than that currently considered adequate nor the use of high-flux dialysers resulted in an improvement in appetite.[10] Appetite is lower on the day of haemodialysis,[11] but an increase has been reported as the number of sessions increases.[12]

Steroids, progestogens, and serotonin agonists have been used to stimulate appetite in various clinical situations.[13] Of all substances with orexigenic effects, the best known is megestrol acetate. It is a synthetic progestin that is used to increase appetite and weight in cancer patients or those infected with the HIV virus.[14,15] Two systematic reviews concluded that treatment with megestrol acetate is effective in those cases.[16,17] Its tolerance is considered to be good, with a rate of side effects no higher than those observed in placebo groups,[17] but adverse effects have been reported such as gastrointestinal intolerance, hyperglycaemia, and inhibition of secretion of pituitary hormones such as corticotropin (ACTH) and the gonadotropins.[14] The use of megestrol acetate in patients undergoing dialysis has limited experience; the doses used have varied, as have the results.[18-23]

In January 2009 we began a protocol of treatment of anorexia in dialysis patients with megestrol acetate. In this paper we describe our experience with the patients that began treatment during its first year of use.

## MATERIAL AND METHOD

For the definition of anorexia, we used the appetite questionnaire from the HEMO[11] and DOPPS[2] studies. It reflects the patient's current appetite as they see it on a Likert scale with five possibilities: very good, good, fair, poor, or very poor. Next the patients are asked if in the last four week their appetite has improved, stayed the same, or worsened. Anorexia is diagnosed when a patient reports that their current appetite is fair, poor, or very poor, and that in the last 4 weeks it has not changed or has worsened.

In 2009, 99 patients with chronic renal failure were cared for in our haemodialysis unit. During this year, 18 patients with anorexia gave their informed consent to receive treatment with megestrol acetate. One patient was excluded who stopped the treatment one month after starting, without obvious cause, and another was diagnosed with multiple myeloma and died from his illness two months later. The 16 remaining cases were treated with megestrol acetate for 3 months and make up the object of this study.

Age, gender, time on haemodialysis, and the possible cause of anorexia are shown in Table 1. Three patients had insulin-dependent diabetes mellitus (cases 1, 2 and 16). Eight patients (cases 3, 6, 7, 8, 11, 15, and 16) had resumed haemodialysis after a failed kidney transplant; none of them received immunosupression at the time of beginning treatment with megestrol acetate. In 7 patients, an intercurrent process triggered anorexia: initiation of treatment for hepatitis C with interferon (case 6); HIV infection treated with antiretroviral drugs (case 11), and admission to hospital for various complications (cases 2, 4, 7, 13 and 16). In the 9 remaining cases, the lack of appetite could not be attributed to a specific cause. All patients started treatment as outpatients. In the cases in which anorexia was brought on by intercurrent conditions that required hospital admission, the treatment with megestrol acetate started after the patients were discharged.

**Table 1.** Baseline data on patients and progress at three months of treatment with megestrol acetate

| | Age (years) | Months on HD | Cause of anorexia | Weight lost in the two months before treatment | Subjective improvement in appetite at month 3 | Weight gain at month 3 |
|---|---|---|---|---|---|---|
| **Case 1** | | | | | | |
| Male | 75 | 5 | None | 3 kg | Yes | 2 kg |
| **Case 2** | | | | | | |
| Female | 78 | 163 | Gastric ulcer with pyloric oedema | 4.5 kg | Yes | 5.5 kg |
| **Case 3** | | | | | | |
| Female | 44 | 9 | None | 2.5 kg | Yes | 1.5 |
| **Case 4** | | | | | | |
| Male | 72 | 4 | Heminephrectomy of a single kidney with post-surgical sepsis | 4 kg | Yes | 2.5 kg |
| **Case 5** | | | | | | |
| Female | 82 | 19 | None | 1 kg | Yes | 1.5 |
| **Case 6** | | | | | | |
| Female | 52 | 72 | Treatment with interferon | 2 kg | No | 0.5 kg |
| **Case 7** | | | | | | |
| Male | 59 | 10 | Graft intolerance transplantectomy | 0 | Yes | 2 kg |
| **Case 8** | | | | | | |
| Female | 72 | 7 | None | 1.5 kg | No | 0.5 kg |
| **Case 9** | | | | | | |
| Female | 79 | 1 | None | 0 | Yes | 4 kg |
| **Case 10** | | | | | | |
| Male | 78 | 43 | None | 2.5 kg | Yes | 0.5 kg |
| **Case 11** | | | | | | |
| Female | 53 | 45 | HIV infection | 5 kg | No | –1 kg |
| **Case 12** | | | | | | |
| Female | 71 | 62 | None | 1 kg | Yes | 0.5 |
| **Case 13** | | | | | | |
| Male | 41 | 34 | Surgery for cerebral haematoma | 9 kg | Yes | 5.5 kg |
| **Case 14** | | | | | | |
| Female | 40 | 6 | None | 0 | Yes | 2 |
| Case 15 | | | | | | |
| Male | 62 | 8 | None | 0.5 kg | Yes | 2 kg |
| **Case 16** | | | | | | |
| Female | 67 | 4 | Infection of arteriovenous fistula wound | 0.5 kg | Yes | 0.5 |

The starting dose of megestrol acetate was 160 mg daily in a single dose. No calorie or protein supplements were administered orally or intravenously during haemodialysis. After 3 months of treatment, response was assessed through a survey in which patients were asked whether their appetite had improved and the evolution of dry weight and laboratory parameters were analysed. The follow-up period ended 30 June 2010.

The patients had dialysis three times per week, 3.5-4 hours per session, with high-flux dialysis and ultra-pure dialysis liquid. The dialysis dose was calculated using standard urea

clearance (Kt/V) obtained using the simplified monocompartmental Daugirdas formula. The protein catabolic rate (PCR) was obtained using the Borah formula as modified by Sargent.[24] Dry weight was determined using clinical criteria. Twelve patients had residual diuresis less than 150 ml/day when treatment with megestrol acetate was indicated. Blood samples for the laboratory measurements were obtained immediately before the first haemodialysis session of the week, after the long interdialytic interval.

Data are expressed as mean (SD). For the statistical analysis we used the Student's t test for paired data. Values with $P<.05$ were considered statistically significant.

## RESULTS

The loss of dry weight in the two months prior to treatment with megestrol acetate, the subjective evaluation of appetite, and the evolution of dry weight at the three-month follow-up are shown in Table 1. Thirteen patients considered that their appetite had improved. Dry weight increased in 15 patients, although in five of them the increase was less than 1 kg.

The evolution of the parameters related to nutrition analysed after the third month of treatment is shown in Table 2. Overall, the group saw a significant increase in dry weight, in concentrations of albumin and creatinine, and in the rate of protein catabolism. The last two parameters were analysed only in the 12 patients without diuresis, in order to avoid the possible influence of variations in residual renal function.

The dialysis dose did not vary significantly: baseline spKtV 1.59 (0.37) and at 3 months: 1.63 (0.29). Statistically significant changes were not observed in the concentration of haemoglobin (baseline: 10.6 [1.2]; 3 months: 11.5 [1.4] g/dl). They were also not seen in the intravenous dose of recombinant human erythropoieitin (baseline dose: 19.062 [17.448]; 3 months: 15.906 [14.262] U/week).

The treatment with megestrol acetate did not have a statistically significant effect on total cholesterol (baseline: 152.3 [36]; 3 months: 145.4 [34.6] mg/dl), HDL cholesterol (baseline: 35.8 [14.6]; 3 months: 33.3 [8.2] mg/dl) and LDL cholesterol (baseline: 98.6 [37] mg/dl; 3 months: 86.2 [30.2] mg/dl).

The follow-up period from the start of treatment, the time of treatment with megestrol acetate, the cause of withdrawal and weight gain are shown in Table 3. Three patients died during the follow-up period. Cases 2 and 10, with severe vascular disease, died as a consequence of this disease, and case 3, due to tuberculosis pericarditis in a patient with AIDS. The 13 remaining patients were alive when the study ended. In 5 patients the dose of megestrol acetate was increased to 320 mg/day due to a lack of response to the initial dose (cases 6, 8, and 12) or due to a later decrease of appetite (cases 9 and 14), with good appetite evolution and weight in all cases. At the time the study ended, 3 patients continued taking megestrol acetate. In two of them, attempts to withdraw the treatment were associated with loss of appetite and the need to reintroduce the treatment (cases 1 and 7).

### Side effects

Of the three patients with insulin-dependent diabetes mellitus (cases 1, 2, and 6), two did not need their insulin dosage to be modified after administering megestrol acetate. In case 2, the dose of Lantus insulin needed to be increased from 15 to 18 U/day. An increase in glucose concentration was found in two of the 13 remaining patients. In one patient (case 13) who had dialysis in the afternoon, the postprandial blood glucose, which had been less than 125 mg/dl, increased starting the second month of treatment (maximum concentration 156 mg/dl) and returned to normal figures one month after the end of treatment. In case 6, baseline glucose increased with the administration of interferon up to a maximum of 153 mg/dl.

**Table 2.** Changes in dry weight, albumin and creatinine concentrations, lymphocyte count and protein catabolic rate (PCR) at the third month of treatment with megestrol acetate

| | Baseline | Three months | P |
|---|---|---|---|
| Weight (kg) | 58.9 (10.8) | 60.8 (10.8) | <.01 |
| Albumin (g/dl) | 3.8 (0.55) | 4.02 (0.41) | <.05 |
| Lymphocytes/µl | 1393 (762) | 1507 (831) | NS |
| Creatinine (mg/dl)[a] | 8.26 (1.90) | 9.73 (2.75) | <.01 |
| PCR (g/kg)[a] | 0.97 (0.26) | 1.24 (0.30) | <.001 |

[a] Analysed only for the 12 patients without residual renal function.

One patient (case 9), who received low doses of steroids for necrotising vasculitis with leukocyte cytoplasmic antibodies, had left deep femoral vein thrombophlebitis after the sixth month of treatment and needed anticoagulation for 3 months, with complete repermeabilisation of the femoral vein.

A study of the pituitary-adrenal axis was conducted in 10 patients during the treatment with megestrol acetate. We determined baseline ACTH, baseline cortisol, and at 30 and 60 minutes after stimulation with ACTH (0.25 mg of ACTH i.v.) (Table 4). Three patients had a basal cortisol level below the normal range, associated in 2 cases with concentrations of ACTH at the lower limits of normality. Concentrations of FSH and LH gonadotropins were measured in 8 patients, which were within the normal range in all of them (data not shown).

## DISCUSSION

We describe here our experience with the use of megestrol acetate in 16 patients treated with haemodialysis who reported anorexia. The diagnosis of anorexia was made using the HEMO and DOPPS questionnaire on subjective appraisal of appetite. The validity of the questionnaire was demonstrated in both studies by showing that the evaluation of appetite is a faithful reflection of the consumption of food,[1,11] has a good correlation with nutritional parameters and those of quality of life,[1,2] and is a predictor of morbidity and mortality.[1-3]

The initial dose of megestrol acetate was 160 mg/day. This is an intermediate dose among the wide range of doses used in patients on dialysis: 40 mg (18), 80 mg (22), 160 mg (21), 400 mg (20), and 800 mg daily.[19,23] At 3 months, 13 of the 16 patients believed their appetite had improved. Overall, the group saw an increase in dry weight, an improvement in nutritional parameters related to protein metabolism such as albumin concentration and protein catabolic rate (a reflection of the consumption of protein) and an increase in the concentration of creatinine (an indicator of muscular mass). The effect of megestrol acetate on albumin concentration has been observed in other studies with patients on dialysis.[18,20-22]

Treatment with megestrol acetate is usually temporary. In our series, 87% of the cases were treated for less than one year (4-11 months), stimulating appetite itself in clinically stable patients, or helping to recover from intercurrent conditions, which are frequent in patients on dialysis.

At the dose used, clinical tolerance was good and no patient reported symptoms such as headache, diarrhoea, confusion, or dizziness, which have been reported at doses of 800 mg per day.[19] However, we did observe other side effects attributable to the use of megestrol acetate. One diabetic patient needed an increase in her dose of insulin, and in 2

**Table 3.** Follow-up from the start of treatment until the end of the study (30 June 2010), time of treatment with megestrol acetate, cause of withdrawal and weight gain.

| Case | Months of follow-up | Months of treatment with megestrol | Reason for ending | Weight gain (kg)[a] |
|---|---|---|---|---|
| 1 | 17 | 17 | Continued | 1 |
| 2 | 7 | 7 | Death | 11.5 |
| 3 | 18 | 4 | No need | 2 |
| 4 | 18 | 7 | No need | 13 |
| 5 | 12 | 6 | No need | 2 |
| 6 | 18 | 11 | No need | 3 |
| 7 | 13 | 13 | Continued | 7 |
| 8 | 14 | 11 | No need | 10 |
| 9 | 11 | 9 | No need | 4.5 |
| 10 | 4 | 4 | Death | 0.5 |
| 11 | 4 | 4 | Death | ?1 |
| 12 | 10 | 8 | No need | 6 |
| 13 | 8 | 4 | No need | 6.5 |
| 14 | 12 | 7 | No need | 4.5 |
| 15 | 8 | 5 | No need | 4.5 |
| 16 | 6 | 6 | Continued | 0.5 |

[a] Until the end of treatment or the end of follow-up.

**Table 4.** Study of the pituitary-adrenal axis using the ACTH test (0.25 mg of ACTH i.v.)

| Case | Dose (mg/day) | Duration of treatment (months) | ACTH | Baseline Cortisol | Cortisol 30 min | Cortisol 60 min |
|---|---|---|---|---|---|---|
| 1 | 160 | 16 | 20.1 | 8.4 | 18.1 | 20.1 |
| 4 | 160 | 1 | 21 | 11 | 24.2 | 25.6 |
| 6 | 160 | 11 | 10.4 | 13.2 | 31.5 | 40.7 |
| 7 | 160 | 12 | 5 | 1 | 2.7 | 4.5 |
| 8 | 320 | 11 | 14.3 | 4.6 | 14.1 | 17.1 |
| 12 | 320 | 8 | 12.5 | 11.7 | 9.23 | 23.2 |
| 13 | 160 | 2 | 20.5 | 10.6 | 35.7 | 37.8 |
| 14 | 320 | 6 | 7 | 2.9 | 14.1 | 14.3 |
| 15 | 160 | 4 | 25.5 | 11.9 | 21.4 | 27.9 |
| 16 | 160 | 5 | 12.2 | 11.3 | 45.4 | 43.2 |

Normal range for ACTH: 5-46 pg/ml; normal range for baseline cortisol: 5-25 µg/dl.

patients an increase in plasma glucose concentration was detected. The inhibitory effect of megestrol acetate on the pituitary-adrenal axis was a more significant revelation. In 3 of 10 patients studied, a reduction in baseline cortisol was found, with low concentrations of corticotropin in two cases. These possible effects on the endocrine system have not been analysed in other studies on dialysis patients. One patient had thrombophlebitis. Relating this with megestrol acetate is hypothetical, since the patient was receiving steroids for necrotising vasculitis. We did not observe any effect of megestrol acetate on lipid profiles or on treatment for anaemia. No inhibition of FSH or LH concentrations was found in any of the patients studied.

We can conclude that megestrol acetate stimulates appetite in patients on haemodialysis who report anorexia. The increase in appetite is accompanied by an increase in weight and an improvement in other nutritional parameters related to protein metabolism. However, induced hyperglycaemia and inhibited secretion of ACTH are possible side effects that should be taken into account when administering this drug. The dose and duration of treatment should be established in future studies.

## REFERENCES

1. Burrowes JD, Larive B, Chertow GM, Cockram DB, Dwyer JT, Greene T, et al., for the HEMO Study Group: Self-reported appetite, hospitalization and death in haemodialysis patients: findings from the Hemodialysis (HEMO) Study. Nephrol Dial Transplant 2005;20:2765-74.
2. Lopes AA, Elder SJ, Ginsberg N, Andreucci VE, Cruz JM, Fukuhara S, et al. Lack of appetite in haemodialysis patients-associations with patients characteristics, indicators of nutritional status and outcomes in the international DOPPS. Nephrol Dial Transplant 2007;22:3538-46.
3. Kalantar-Zadeh K, Block G, McAllister CJ, Humphreys MH, Kopple JD. Appetite and inflammation, nutrition, anemia, and clinical outcome in hemodialysis patients. Am J Clin Nutr 2004;80:299-307.
4. Bossola M, Tazza L, Giungi S, Luciani G. Anorexia in hemodialysis patients: An update. Kidney Int 2006;70:417-22.
5. Heng AE, Cano NJM. Nutritional problems in adult patients with stage 5 chronic kidney disease on dialysis (both haemodialysis and peritoneal dialysis). NDT Plus 2010;3:109-17.
6. Stenvinkel P, Heimbürger O, Lindholm B, Kaysen GA, Bergström J. Are there two types of malnutrition in chronic renal failure? Evidence for relationships between malnutrition, inflammation and atherosclerosis (MIA syndrome). Nephrol Dial Transplant 2000;15:953-60.
7. Locatelli F, Fouque D, Heimburger O, Drücke TB, Cannata-Andía JB, Hörl WH, et al. Nutritional status in dialysis patients: a European consensus. Nephrol Dial Transplant 2002;17:563-72.
8. Aguilera A, Selgas R, Díez JJ, Bajo MA, Codoceo R, Álvarez V. Anorexia in end-stage renal disease: pathophysiology and treatment. Expert Opin Pharmacother 2001;2:1825-38.
9. Carrero JJ, Aguilera A, Stenvinkel P, Gil F, Selgas R, Lindholm B. Appetite disorders in uremia. J Ren Nutr 2008;18:107-13.
10. Rocco MV, Dwyer JT, Larive B, Greene T, Cockram DB, Chumlea WC, et al., for the HEMO Study Group: The effect of dialysis dose and membrane flux on nutritional parameters in hemodialysis patients: Results of the HEMO Study. Kidney Int 2004;65:2321-34.
11. Burrowes JD, Larive B, Cockram DB, Dwyer J, Kusek JW, McLeroy S, et al. Effects of dietary intake, appetite, and eating habits on dialysis and non-dialysis treatment days in hemodialysis patients: cross-sectional results from the HEMO study. J Ren Nutr 2003;13:191-8.
12. Galland R, Traeger J, Arkouche W, Cleaud C, Delawari E, Fouque D. Short daily hemodialysis rapidily improves nutritional status in hemodialysis patients. Kidney Int 2001;60:1555-60.

13. Loprinzi CL, Hesketh PJ, Savarese DMF, Jatoi A. Pharmacologic management of cancer anorexia/cachexia. 2010 UpToDate. www Uptodate.com
14. Corcoran C, Grinspoon S. Treatments for wasting in patients with the acquired immunodeficiency syndrome. N Engl J Med 1999;340:1740-50.
15. López AP, Fíguls MR, Cuchi GU, Berenstein EG, Pasies BA, Alegre MB, et al. Systematic review of megestrol acetate in the treatment of anorexia-cachexia syndrome. Pain Symptom Manage 2004;27:360-9.
16. Ruiz-García V, Juan O, Pérez Hoyos S, Peiró R, Ramón N, Rosero MA. Acetato de megestrol: una revisión sistemática de su utilidad clínica para la ganancia de peso en los enfermos con neoplasia y caquexia. Med Clin (Barc) 2002;119:166-70.
17. Berenstein EG, Ortiz Z. Megestrol acetate for the treatment of anorexia-caquexia syndrome. Cochrane Database Syst Rev 2005:CD004310.
18. Lien YH, Ruffenach SJ. Low dose megestrol increases serum albumin in malnourished dialysis patients. Int J Artif Organs 1996;19:147-50.
19. Boccanfuso JA, Hutton M, McAllister B. The effects of megestrol acetate on nutritional parameters in a dialysis population. J Ren Nutr 2000;10:36-43.
20. Rammohan M, Kalantar-Zadeh K, Liang A, Ghossein C. Megestrol acetate in a moderate dose for the treatment of malnutrition-inflammation complex in maintenance dialysis patients. J Ren Nutr 2005;15:345-55.
21. Golebiewska J, Lichodziejewska-Niemierko M, Aleksandrowicz E, Majkowicz M, Lysiak-Szydlowska W, Rutkowski E. Influence of megestrol acetate on nutrition and inflammation in dialysis patients-preliminary results. Acta Biochim Pol 2009;56:733-7.
22. Monfared A, Heidarzadeh A, Ghaffari M, Akbarpour M. Effect of megestrol acetate on serum albumin level in malnourished dialysis patients. J Ren Nutr 2009;19:167-71.
23. Yeh SS, Marandi M, Thode HC, Levine DM, Parker T, Dixon T, et al. Report of a pilot, doubleblind, placebo-controlled study of megestrol acetate in elderly dialysis patients with caquexia. J Ren Nutr 2010;20:52-62.
24. Sargent JA. Control of dialysis by a single-pool urea model: The National Cooperative Dialysis Study. Kidney Int 1983;23(Suppl 13):S19-S25.

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