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SBÜ Beyhekim Eğitim ve Araştırma Hastanesi Acil Tıp Kliniği

IV.Uluslararası Onkolojik Aciller Kongresi
17-20 Ekim 2024, Konya Şehir Hastanesi

Onkolojik Hastalarda Hiperkalsemi



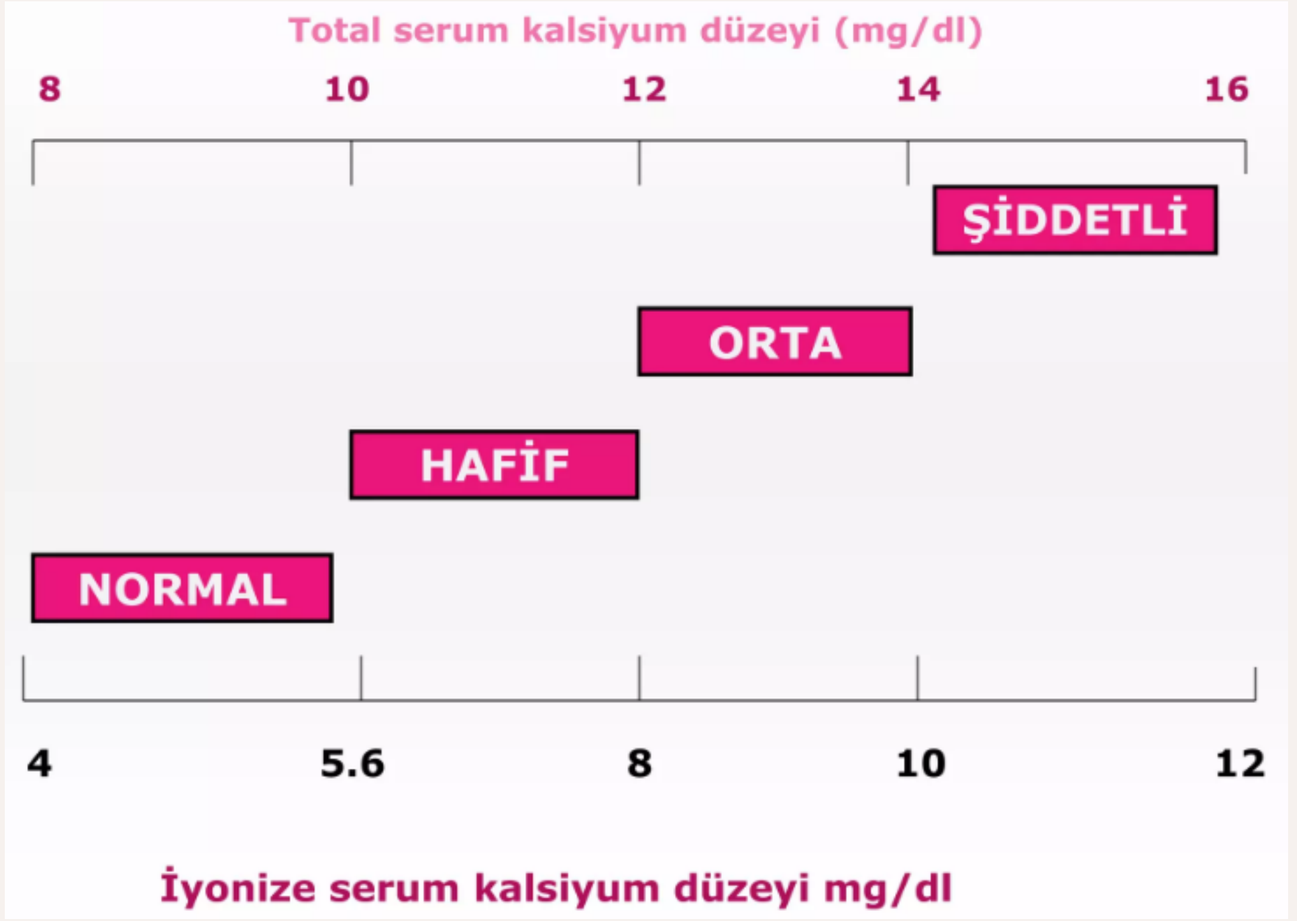
Hiperkalsemi

Serum Kalsiyum



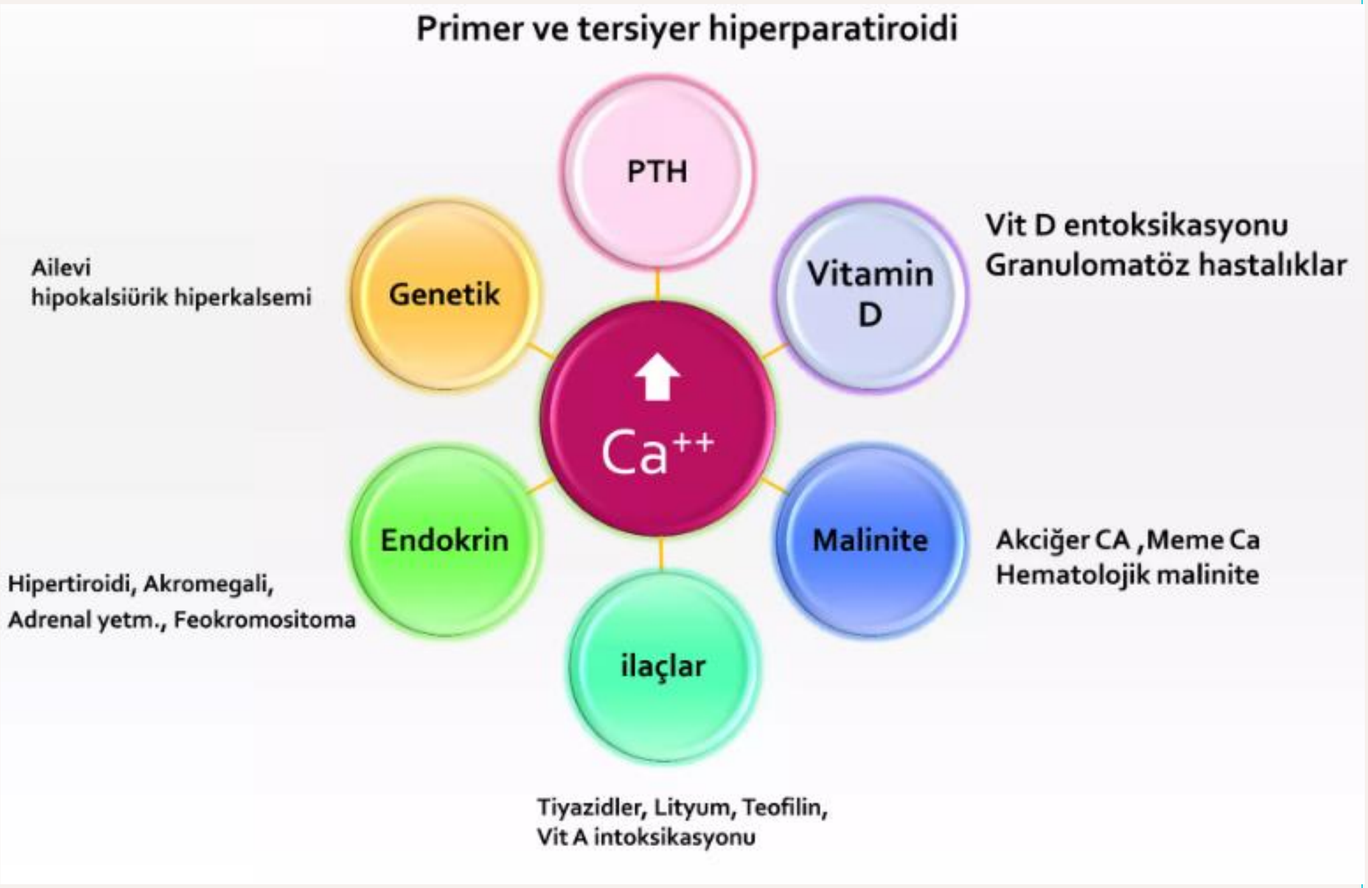
Düzeltilmiş kalsiyum = Ölçülen kalsiyum + [0,8 x (40-Albümin)]

Hiperkalsemi



Hiperkalsemi

- Toplumda sıklığı %0,5-1
- Primer hiperparatiroidizm ve malignite vakaların %90'ı



Hiperkalsemi



- Nörolojik
  - Baş ağrısı
  - Kas güçsüzlüğü
  - Letarji
  - Konfüzyon
  - Koma, stupor
  - Konsantrasyon bozukluğu
  - Halüsinasyon
  - Kişilik bozukluğu
  - Deliryum
- Gastrointestinal
  - Bulantı-kusma
  - İştahsızlık
  - Karın ağrısı
  - Kilo kaybı
  - Kabızlık
  - Peptik ülser
  - Pankreatit
- Üriner
  - Poliüri
  - Polidipsi
  - Noktüri
  - Dehidratasyon
  - Glikozüri
  - Nefrolitiazis
  - Nefrokalsinozis
- Kemik
  - Ağrı
  - Osteoporoz
  - Artrit
  - Deformite
  - Fraktür
- Kardiyovaksüler
  - Hipertansiyon
  - Aritmiler
  - EKG: Kısa QT
  - Vasküler kalsifikasyonlar

Hafif hiperkalsemi Orta hiperkalsemi Şiddetli hiperkalsemi

Onkolojik hastalarda hiperkalsemi

- Malignite şüphesini artırır
  - Sistemik semptomlar (ateş, kilo kaybı, iştah azalması, kötüleşen halsizlik)
  - Tipik olarak çok yüksek serum kalsiyum seviyeleri
  - Hızlı başlayan hiperkalsemi

Onkolojik hastalarda hiperkalsemi

- Onkolojik hastalarda %2-30 (en sık metabolik komplikasyon)
  - Meme kanseri
  - Akciğer kanseri
  - Böbrek kanseri
  - Multiple myelom
  - Paratiroid karsinomu
  - Lenfoma

- Hastanede kalış süresi medyan 4 gün

- Hastane içi mortalite %6,8

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Clinical Practice Guideline

Treatment of Hypercalcemia of Malignancy in Adults: An Endocrine Society Clinical Practice Guideline

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Abstract

Background: Hypercalcemia of malignancy (HCM) is the most common metabolic complication of malignancies, but its incidence may be declining due to potent chemotherapeutic agents. The high mortality associated with HCM has declined markedly due to the introduction of increasingly effective chemotherapeutic drugs. Despite the widespread availability of efficacious medications to treat HCM, evidence-based recommendations to manage this debilitating condition are lacking.

Objective: To develop guidelines for the treatment of adults with HCM.

Methods: A multidisciplinary panel of clinical experts, together with experts in systematic literature review, identified and prioritized 8 clinical questions related to the treatment of HCM in adult patients. The systematic reviews (SRs) queried electronic databases for studies relevant to the selected questions. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to assess the certainty of evidence and make recommendations. An independent SR was conducted in parallel to assess patients' and physicians' values and preferences, costs, resources needed, acceptability, feasibility, equity, and other domains relevant to the Evidence-to-Decision framework as well as to enable judgements and recommendations.

Results: The panel recommends (strong recommendation) in adults with HCM treatment with denosumab (Dmab) or an intravenous (IV) bisphosphonate (BP). The following recommendations were based on low certainty of the evidence. The panel suggests (conditional recommendation) (1) in adults with HCM, the use of Dmab rather than an IV BP; (2) in adults with severe HCM, a combination of calcitonin and an IV BP or Dmab therapy as initial treatment; and (3) in adults with refractory/recurrent HCM despite treatment with BP, the use of Dmab. The panel suggests (conditional recommendation) the addition of an IV BP or Dmab in adult patients with hypercalcemia due to tumors associated with high calcitriol levels who are already receiving glucocorticoid therapy but continue to have severe or symptomatic HCM. The panel suggests (conditional recommendation) in adult patients with hypercalcemia due to parathyroid carcinoma, treatment with either a calcimimetic or an antiresorptive (IV BP or Dmab). The panel judges the treatments as probably accessible and feasible for most recommendations but noted variability in costs, resources required, and their impact on equity.

Conclusions: The panel's recommendations are based on currently available evidence considering the most important outcomes in HCM to patients and key stakeholders. Treatment of the primary malignancy is instrumental for controlling hypercalcemia and preventing its recurrence. The recommendations provide a framework for the medical management of adults with HCM and incorporate important decisional and contextual factors. The guidelines underscore current knowledge gaps that can be used to establish future research agendas.

Tedavi-Hafif hiperkalsemi (Ca<12)

- Acilde tedavi gerektirmez
- Tiazid diüretiklerden kaçınılmalıdır
- Nefrolitiazis! - Hasta susuz kalmamalıdır (günde en az 8 bardak)
- Hasta uzun süreler hareketsiz kalmamalıdır
- Ca sınırlaması (<1000 mg/gün)
- Ek tedaviler hiperkalseminin tedavisine göre belirlenir

Tedavi:Orta derecede hiperkalsemi (Ca:12-14)

- Kalsiyum yükselişi kronik olan
  - Asemptomatik hastalar
  - Hafif semptomları olan hastalar

Acilde tedavi gerektirmez
Hafif hiperkalsemi gibi davranılmalıdır

- Kalsiyum yükselişi akut olan hastalar
- Kalsiyum yükselişi kronik olan semptomatik hastalar

Agresif tedavi gerektirir
Şiddetli hiperkalsemi gibi davranılmalıdır

Tedavi:Şiddetli hiperkalsemi (Ca>14)

- Hipovoleminin düzeltilmesi
  - IV izotonik salin

- Renal kalsiyum atılımının artırılması
  - IV izotonik salin
  - Loop diüretikler
  - Kalsitonin

- Kalsiyum rezorpsiyonunun azaltılması
  - Bifosfanatlar (zoledronik asit, pamidronat) (kemik)
  - Denosumab (kemik)
  - Kalsitonin (kemik)
  - Glukokortikoidler (barsak)
  - Kalsimimetikler (böbrek)

Table 1. Treatment regimens for hypercalcemia of malignancy

Intervention/dose frequency	Mode of action	Onset of action	Median duration of action/ effect/proportion of subjects achieving normocalcemia	Adverse events/comments
Isotonic saline hydration/ Bolus of 1 to 2 L then 200 to 500 mL/hour to maintain urine output at 100 to 150 mL/hour.	Restores depleted intravascular volume. Enhances urinary calcium excretion.	Immediate	During infusion. Lowers calcium by 1 to 1.5 mg/dL (0.25 to 0.375 mmol/L) over first 24 hours.	Carefully assess for volume overload.
Loop diuretics*/ Furosemide 160 mg/d to 100 mg/h intravenously, or 40 to 60 mg/d orally only to be administered after volume repletion.	Increase urinary calcium excretion by inhibiting renal calcium reabsorption in the thick ascending loop of Henle, and proximal and distal renal tubules. Interferes with the chloride cotransport system.	Within 3 to 60 minutes	2 hours if bolus. During therapy if IV drip. Lowers calcium by 0.5 to 1.0 mg/dL (0.125 to 0.25 mmol/L) after resolution of volume depletion.	Volume depletion, and worsening HCM. May be useful in patients at risk for volume overload/congestive heart failure.
Salmon Calcitonin/CT 4 to 8 units/kg Intramuscular or SQ every 6 to 12 hours for 48 to 72 hours.	Inhibits bone resorption by interfering with osteoclast function. Promotes urinary calcium excretion, as well as that of magnesium, sodium, potassium and phosphate.	4 to 6 hours	6 to 8 hours. Rapidly lowers calcium by 1 to 2 mg/dL (0.25 to 0.50 mmol/L).	Tachyphylaxis may occur after 48 to 72 hours.

Bisphosphonates/BPs	Pamidronate and zoledronic acid are nitrogen-containing BPs that inhibit bone resorption by inhibiting farnesyl pyrophosphate synthase (FPPS) within osteoclasts to cause osteoclast apoptosis. They also interfere with osteoclast recruitment and function.			
Pamidronate/APD 60 to 90 mg IV over 2 to 24 hours. Can be repeated every 2 to 3 weeks.		48 to 72 hours	7 to 14 days; may last 2 to 4 weeks. Normalizes calcium in 60% to 70% of patients.	May cause kidney damage especially if glomerular filtration rate <30 to 35 mL/minute. Acute-phase response relatively common; hypocalcemia; renal insufficiency possible if decreased glomerular filtration rate; Atypical femoral fractures are rare and ONJ occurs infrequently.
Zoledronic acid/ZLN 3 to 4 mg IV over 15 to 30 minutes. Can be repeated in 7 days, if desirable calcium level not achieved, and every 3 to 4 weeks thereafter.		48 to 72 hours	4 to 6 weeks. Normalizes calcium in 80% to 90% of patients.	May cause kidney damage especially if glomerular filtration rate <30 to 35 mL/minute. Dose adjustment required if glomerular filtration rate <60 mL/min, and administer over 30 to 60 minutes.

Glucocorticoids 200 to 400 mg hydrocortisone IV/day for 3 to 5 days. 60 mg/day of prednisone for 10 days, or 10 to 20 mg/day for 7 days.	Decrease intestinal calcium absorption. Inhibits 1α-hydroxylase and limits 1,25-dihydroxyvitamin D production by mononuclear cells in patients with granulomatous diseases or lymphoma.	2 to 5 days	As long as on therapy.	Hyperglycemia, altered mental status, and hypertension.
Denosumab/Dmab 120 mg SQ. Repeat 1, 2 and 4 weeks later, then monthly thereafter.	Inhibits bone resorption via inhibition of RANKL. Dmab is an antibody to RANKL. Upon binding to RANKL, Dmab blocks the interaction between RANKL and RANK (receptor on osteoclast surfaces) and prevents osteoclast formation and thus bone resorption.	3 to 10 days	Time to complete response 23 days. Median duration of effect 104 days. Normalizes calcium in at least 70% of patients.	Acute-phase response rare; Atypical femoral fractures are rare and ONJ occurs infrequently. Rebound osteoclastogenesis may occur with discontinuation. Patients with GFR < 30 mL/min have a higher risk of hypocalcemia, and a lower dose should be considered.
Calcimimetics Oral: Initial: 30 mg twice daily; increase dose incrementally every 2 to 4 weeks (to 60 mg twice daily, 90 mg twice daily, and 90 mg 3 to 4 times daily) as necessary to normalize SCa levels.	Calcium-sensing receptor agonist, reduces parathyroid hormone secretion, and may decrease renal calcium reabsorption.	2 to 3 days	During therapy. Reduces calcium by at least 1 mg/dL (0.25 mmol/L) in approximately 60% of patients.	Nausea, vomiting, headache, and fractures. Case reports indicate reduction of calcium levels in patients with refractory HCM related to non–small-cell lung, neuroendocrine, breast, or renal cancer.

Recommendation 1

In adults with hypercalcemia of malignancy (HCM), we recommend treatment with an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab) compared with management without an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab). (1⊕OOO)

Recommendation 2

In adults with hypercalcemia of malignancy (HCM), we suggest treatment with denosumab (Dmab) over an intravenous (IV) bisphosphonate (BP). (2⊕OOO)

Recommendation 3

In adults with severe hypercalcemia of malignancy (HCM) (serum calcium [SCa] > 14 mg/dL [3.5 mmol/L]), we suggest a combination of calcitonin and an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab) as initial treatment compared with only intravenous (IV) bisphosphonate (BP) or denosumab (Dmab). (2⊕OOO)

Recommendation 4

In adults with refractory/recurrent hypercalcemia of malignancy (HCM) on an intravenous (IV) bisphosphonate (BP), we suggest the use of denosumab (Dmab) compared with management without (denosumab) Dmab. (2⊕OOO)

Refractory/recurrent HCM on BP → Adequate IV saline hydration and suggest Dmab *(Recommendation 4, [⊕○○○])*

Remark

Calcitonin treatment should be limited to 48 to 72 hours due to tachyphylaxis.

Recommendation 5

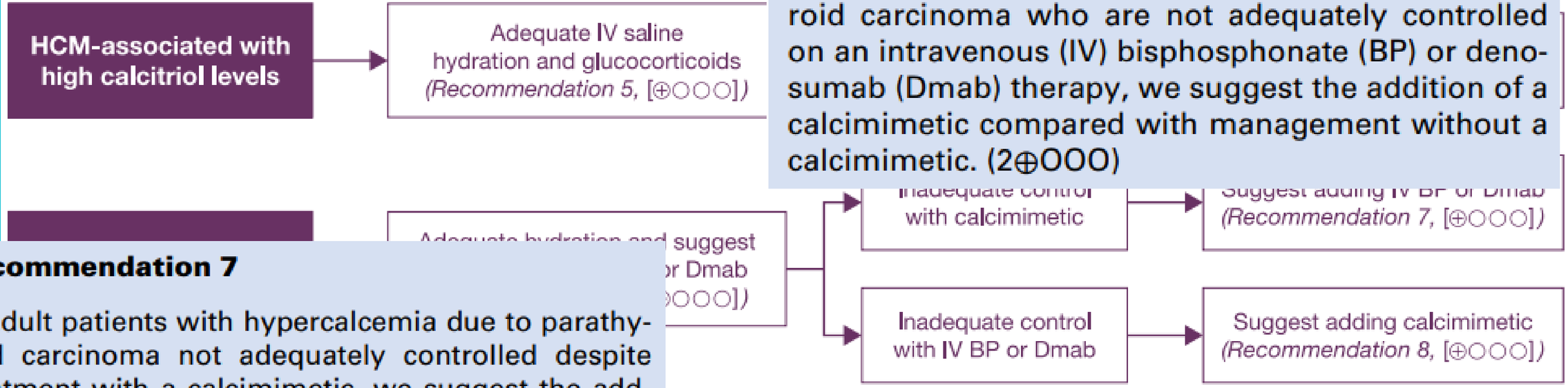
In adults with hypercalcemia of malignancy (HCM) from tumors associated with high calcitriol levels, such as lymphomas, who are already receiving glucocorticoid therapy but who continue to have severe or symptomatic hypercalcemia, we suggest the addition of an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab) compared with management without an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab). (2⊕OOO)

Recommendation 6

In adult patients with hypercalcemia due to parathyroid carcinoma, we suggest treatment with either a calcimimetic or an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab). (2⊕OOO)

Recommendation 8

In adult patients with hypercalcemia due to parathyroid carcinoma who are not adequately controlled on an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab) therapy, we suggest the addition of a calcimimetic compared with management without a calcimimetic. (2⊕OOO)



Recommendation 7

In adult patients with hypercalcemia due to parathyroid carcinoma not adequately controlled despite treatment with a calcimimetic, we suggest the addition of an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab) compared with management without an intravenous (IV) bisphosphonate (BP) or denosumab (Dmab). (2⊕OOO)

Tedavi:Hemodiyaliz

- Medikal tedavilerle düzeltilemeyen hiperkalsemi
- Böbrek yetmezliği
- Serum kalsiyumu 18-20 mg/dl ve daha yüksek olan hastalar



Başlık: Ophelia
Oluşturan: Sör John Everett Millais
Yaratıcının Ölüm Yeri: Londra, Birleşik Krallık
Yaratıcının Doğum Yeri: Southampton, Birleşik Krallık
Oluşturulma Tarihi: 1851 civarında
Fiziksel Boyutlar: en1118xy762 mm
Kaynak: Sir Henry Tate tarafından sunulmuştur 1894
Orijinal Başlık: Ophelia
Malzeme: Tuval üzerine Yağlıboya

TEŞEKKÜRLER