

HYPERVITAMINOSIS AND ANTIHISTAMINES

Introduction

- VITAMIN is an essential substance, needed in tiny amounts to facilitate normal metabolism
- Not synthesized in the body....must be ingested in the diet
- Not provide energy.....BUT.....often act as **coenzyme** in **energy producing reactions** → هه ما بنشطوا او بعتوا energy الا ازا كانو ناقصين
- OTC
- large potential for misuse and toxicity.....believes that megadoses of vitamins prevent or ameliorate the effects of aging and cancer
- Only **rarely** is an **acute vitamins** toxicity reaction reported, → هاني جد باختر Vitamins عشان عشان ربحو فيحاول لينحرو فيالوقت مع الوقت most cases involved chronic utilization

في ناس
ازا حسوا
يتحسن عليهم
بهمير ياخذوهم
بكميات

كيرة
They say
that vitamins in
large quantities
are anti oxidants
→ against
aging
and cancer
which isn't
true

هاني
جد باختر
Vitamins
عشان عشان
ربحو لينحرو
فيالوقت مع الوقت

Introduction

قيد الواحد لازم ياخذ من الـ Vitamins كل يوم

- Recommended Daily Allowance (RDA).....vit deficiency / hypervitaminosis

- Megadosing: a dose that is 10 or more times the recommended daily allowance (RDA)

Vitamins

→ Soluble in water → excretion in urine → أمين أكثر
↳ Soluble in fats → يتخزن بالجسم
Lipophilic

- A, D, E, K
- Vitamin C
- Thiamine (B1)
- Riboflavin (B2)
- Niacin (B3)
- Pyridoxine (B6)
- Cyanocobalamin (B12)
- Folic acid (B9)
- Biotin (B7)
- Pantothenic acid (B5)

Vitamin A....Retinoids

❖ First vitamin recognized

❑ RDA: 3000IU

TOXICOKINETICS OF VITAMIN A

- ❑ More than 60,000 instances of vitamin toxicity are reported annually to US poison control centers
- ❑ fat-soluble vitamins have a higher potential for toxicity than do water-soluble vitamins (Owing to their ability to accumulate in the body).

↑ Toxicity ← fat-soluble vitamins

VITAMIN A TOXICITY

- Acute ingestion $>12,000$ IU/kg. Chronic ingestion $>25,000$ IU/d for 2–3 weeks. symptoms:
 - GI
 - Nausea, vomiting, gingivitis, mouth fissures, wt loss
 - CNS
 - Drowsiness, Headache, irritability, increased intracranial pressure, vision changes, dizziness
 - Skin
 - Dry, peeling skin, cheilosis, pruritis, alopecia
 - Muscles and joints
 - Myalgia, arthralgia
 - Other:
 - Hepatic enlargement, ascites, hepatocellular injury, elevated hepatic enzymes, hypercalcemia, bony changes

VITAMIN A TOXICITY

- Teratogenicity:
 - The risk of infant malformations in the first trimester approaches 25-30%....."retinoic acid dysmorphic syndrome":.....
 - CNS defects, ^{بالعين}optic atrophy, cleft palate small or absent ears, thymic and congenital heart defects
- outer part of the ear ←

TREATMENT OF VITAMIN A TOXICITY

- Immediate discontinuation, most S&S will disappear within several weeks
- If very huge dose was taken.....GI decontamination (administration of activated charcoal)
- High intracranial pressure treated with mannitol, hyperventilation → صدر

VITAMIN D TOXICITY

- Vit D acts to maintain serum **calcium** and **phosphate** concentration.....increase Ca levels by acting on its absorption, excretion and bone resorption → بزرگ absorption
→ Ca لہ وال
phosph وال
- Manifestations of **vit D toxicity** are related to the effects of hypercalcemia → ال Ca بروج تیز ہے
Tissues ہاں
Heart and lung ہاں
- Hypervitaminosis D & hypercalcemia in pregnant women may suppress PTH function in the newborn.....leading to hypocalcemia, tetany and seizures → in the new born
بہتر
بہتر

VITAMIN D TOXICITY

متى نرى
السمية
Toxicity

- 4-5 times the RDA can cause toxicity (conc. $>200\text{pg/ml}$)
- Symptoms
 - Hypercalcemia.....(polydipsia, polyuria, weakness, fatigue, anorexia, headache)
 - Altered mental status
 - GI upset
 - Renal tubular injury
 - Occasionally arrhythmias
 - Calcification of soft tissues (heart and lungs)

TREATMENT OF VITAMIN D TOXICITY

- Immediate discontinuation
- Reducing Ca intake by diet
- If cardiotoxicity due hypercalcemia.....fluids and diuretics
- Administration of glucocorticoids (prednisolone 20-40 mg), inhibit Ca absorption from the gut
- If Ca levels exceed 14mg/dlTx with calcitonin (i.m)

↳ reabsorption
of Ca through
the bones

ويخرج الـ Ca يطلع
من الأمعاء ويزيد
الخراج في البول
excretion الـ urine

VITAMIN C-ASCORBIC ACID

- Supplements are available in 100 to 500mg doses and found in high concentrations in green tea
- RDA for ascorbic acid is 60mg/day

VITAMIN C-TOXICITY

- WATER SOLUBLE VITAMIN....WHAT IS NOT UTILIZED WILL BE EXCRETED IN THE URINE.....toxicity is rare
- Toxicity is related to the osmotic effects in the intestine....
nausea and diarrhea
- Chronic excessive use can produce increased levels of the metabolite oxalic acid →
- Urinary acidification promotes calcium oxalate crystal formation..... nephrolithiasis and nephropathy

لها ناحه
يخزن فيه
المتابوليت
↓
oxalic acid
↓
والتي تعمل
حصوات
بالكلية

CLINICAL MANIFESTATIONS

- Toxic doses???.....
- Acute IV doses >1.5 g OR chronic ingestion >4 g/d have produced nephropathy
- Decrease abs of vit B12

* ما يصير عند كل الناس *

MANAGEMENT:

← ما يوقفه
في جأه

- Abrupt withdrawal not recommended....rebound deficiency (scurvy) following prolonged administration of megadose

- So.....gradual withdrawal

لما الواحد

يكون عنده deficiency of Vitamin C

يصير خشنان شديد بالشفائين والسكر والبشر
والتآكل ويقتب فلما يوقفه فجأة يصير
عنده scurvy نفسه symptoms of deficiency



THIAMINE (Vit B1)

- "Antiberiberi"Vit B1.....Thiamine
- Source: rice bran extracts, yeast extracts
- RDA of thiamine is 1.5mg/day.....Most exceed RDA in diet
- Deficiency results from poor dietary intake or more commonly from excess alcohol intake??!!
- Alcohol interfere with gastric absorption of vit B1 and its conversion to the active form

بكمي خاصة
من أكل

بسريره
Toxicity
إذا أكل
ما باكل
أومن
أركحول

THIAMINE (B1) TOXICITY

- Pain on injection and contact dermatitis → **التصلب بالحقن**
- Anaphylactic reaction after i.v administration
- Transient vasodilation
- Hypotension.....vascular collapse **vasodilation → كثير**
لما يوصل دم القلب بوقف القلب
- **MANAGEMENT:**
 - Administration of **epinephrine and antihistamines**
 - Pressor agent may be necessary in extreme cases

VITAMIN B₁₂ TOXICITY

- Vitamin B12 is non toxic unless very huge quantities are ingested
- Rare instances of allergic reactions.....pruritis, urticaria, anaphylaxis
- Contact dermatitis
- Management: discontinuation → **أقطعه**

Anti Histamine Classification

- H₁ antagonists are divided into 1st and 2nd generation;
- 1st generation has strong sedative effects (enter the CNS) and can block autonomic receptors
- 2nd generation: incomplete distribution to CNS → less sedation

H₁ Receptor Antagonists

- Competitive antagonists of H₁ receptor found in many OTC and prescription medication alone or in combined formulation

□ Major therapeutic uses:

1. motion sickness,
2. control of allergy-related itching,
3. cough and cold palliation
4. and used as sleep aids

موجودين
OTC كثير
لازهم موجود
بأدوية الرش
والأدوية التي يتساء
للهم قد يصير
Toxicity
غير مقصودة

Toxicity:

- H1 antagonists are rarely ingested for suicidal purposes and have a **high therapeutic/toxic ratio** → نادر ما حدث يستخدمة للإنتحار
- Wide spectrum of side effects
- Sedation, antimuscarinic action → most common undesirable actions

Toxicity:

- ^{1st gene} **Toxic dose.** The estimated fatal oral dose of diphenhydramine is 20–40 mg/kg Toxicity dose
- In general, toxicity occurs after ingestion of 3–5 times the usual daily dose → لتيكون اعلى من ال dose dialy ب 3-5 مرات
- ~~Children~~ **Children** are **more sensitive** to the toxic effects of antihistamines than are adults
- The non-sedating agents are associated with less toxicity

Toxicity:

- CNS: sedation (most common with 1st generation), coma, delirium, hallucinations, psychomotor agitation (myoclonic or choreoathetoid movements), or convulsions
- Anticholinergic effects: hyperpyrexia, tachycardia, HTN, urinary retention, dilated pupils, dry mouth
- Reports of cholinergic toxicity upon stopping taking the drug

لما نوقف الدواء بنشعر
بأنه يكون له
Cholinergic
Symptoms
↳ such as : ~~diarrhea~~ diarrhea - stomach
ache
مغص

Toxicity:

- CV effects: massive diphenhydramine overdose has been reported to cause myocardial depression and QRS widening....similar to TCAs overdose

هناك انسحاب
هناك بالاردن
لنسا فوجود
□ Overdosage of astemizole or terfenadine may induce cardiac arrhythmias through QT prolongation (removed from the US market)

Drug Interactions:

- **Arrhythmia** occur particularly when taken with P450 inhibitor (erythromycin, ketoconazole, grapefruit juice....)
 - ← مایه‌دگی دار دوز غای خاچه بال 2nd نیکون ال Arrhythmia اعلی
 - بتریزه Toxicity
 - بیمبر ال arrhythmia
 - لما یصیر inhibition ال P450
- Significant sedation when taken with alcohol, benzodiazepines → C/I while driving or operating machinery

Treatment

- Treatment **is supportive....** stabilization and reduce amount absorbable
 - 1. Maintain an open airway and assist ventilation if necessary
 - مافی antidote and Histamine واضح
 - بیس ممکن
 - نقطی antidote
 - لد
 - Cholinergic side effects
 - بنعطف Benzodiazepines
 - بیس ازا کان باخر مراحل
 - و مصاد رینا نسیطر علی ال Seizures
 - Usually Treatment بکون بیس Supportive
 - 2. Treat coma, seizures, hyperthermia, and atypical ventricular tachycardia if they occur
 - 3. Monitor the patient for at least 6-8 hours after ingestion.

Treatment

Decontamination:

Administer activated charcoal orally

Gastric lavage not necessary

N.B: GI decontamination helpful even in late-presenting patients because of slowed GI motility

Enhanced elimination

Hemodialysis, hemoperfusion, peritoneal dialysis, and repeat-dose activated charcoal are **not effective** in removing antihistamines

ممكن اعمله بس مؤخره

ممكن اعمله مؤخره
GI decontamination
Late-presenting
absorption
تأخره او
تأخره هو
تأخره

Treatment

There is no specific antidote for antihistamine overdose

Physostigmine used for the treatment of severe delirium or tachycardia

Not recommended routinely! may cause toxic effects as seizures, bronchoconstriction, bradycardia, asystole (may need to be reversed by atropine)

يعطيه
بسرعه
املا
Toxicity
تأخره
بحذر
ممكن
يعمل

بسرعه لما
anti cholinergic
effect
و يخلص
يخلص
حياة المريض