Lamotrigine Case 2: Drug-Drug Interactions 2-02-16

Jose de Leon, MD

2. Lamotrigine Case 2

Bipolar Disorders 9:310-313, 2007

http://www.ncbi.nlm.nih.gov/pubmed/17430308

Lamotrigine Case 2

2.1. Pharmacology of Lamotrigine

2.2. Lamotrigine Case 2

Lamotrigine Case 2

2.1. Pharmacology of Lamotrigine

- 1.1.1. Pharmacokinetics
- 1.1.2. Pharmacodynamics

2.2. Lamotrigine Case 2

- 2.1.1. Case Description
- 2.1.2. Medications
- 2.1.3. Outcome
- 2.1.4. Diagnosis
- 2.1.5. Interpretation

Educational Objectives

At the conclusion of this presentation, the participant should be able to:

1. Think about pharmacological principles in the context of polypharmacy
2. Appreciate that for understanding lamotrigine safety, one must consider
   - 2.1. Pharmacodynamics and pharmacokinetics
   - 2.2. Personal, environmental and genetic factors
3. Recognize the relevance of lamotrigine drug-drug interactions and their contribution to the risk for Stevens-Johnson Syndrome.

Abbreviations

- ADR: adverse drug reaction
- AED: anti-epileptic drug
- DDI: drug-drug interaction
- ER: extended release
- RCT: randomized controlled trial
- UGT: uridine 5’-diphosphate glucuronosyltransferase

2.0. Lamotrigine Pharmacology

http://www.ncbi.nlm.nih.gov/pubmed/25745819 Focus on inducers (free pdf)

http://www.ncbi.nlm.nih.gov/pubmed/25196459 Focus on DDI

2.0. Lamotrigine: Pharmacology

What do you know about lamotrigine's pharmacological mechanisms?

2.0. Lamotrigine Pharmacology

2.0.1. Pharmacokinetics
2.0.2. Pharmacodynamics

2.0.1. Lamotrigine Pharmacokinetics

2.0.1. Lamotrigine Case 1: Pharmacokinetics

What do you know about lamotrigine's pharmacokinetics?

2.0.1. Lamotrigine Pharmacokinetics

2.0.1.1. Metabolism
2.0.1.2. Lamotrigine Effects on Other Drugs
2.0.1.3. Genetic, Personal & Environmental Factors
2.0.1.4. Dosing

2.0.1.1. Lamotrigine Metabolism

2.0.1.1. Lamotrigine Case 1: Metabolism

- Glucuronidation: 65-90%
  - UGT1A4: major enzyme
  - UGT2B7: may or may not be relevant, depending on the articles.
- Urine excretion: small contribution
  - lamotrigine and its metabolites
- Mild auto-induction:
  - within the first 2 weeks
  - not seen in patients on potent inducers

2.0.1.2. Lamotrigine Effects on Other Drugs

2.0.1.2. Lamotrigine Case: Effects on Other Drugs

- Mild inducer:
  - UGTs
  - possibly of quetiapine
- Mild inhibitor:
  - possibly of olanzapine, but only in smokers http://www.ncbi.nlm.nih.gov/pubmed/18555573

In summary, in most patients, lamotrigine is not likely to produce a clinically-relevant DDI with other psychiatric drugs.

2.0.1.3. Genetic, Personal & Environmental Factors

2.0.1.3. Lamotrigine Case 1: Genetic, Personal & Environmental Factors

- Genetics: currently unknown
  - UGT1A4 genetic variations:
    - not well understood
    - not ready for clinical use
- Personal:
  - Pregnancy: important in ↑ metabolism
    Estrogens are inducers.
  - Tobacco smoking: mild inducer
  - Mild ↓ in elimination when ↓ in renal function:
    - geriatric age, or
    - renal impairment

2.0.1.3. Lamotrigine Case 1: Genetic, Personal & Environmental Factors

- Environmental factors:
  <u>DDIs with lamotrigine are important:</u>
  - Inducers:
    - adding: ↓ serum lamotrigine concentration (it may contribute to ↓ efficacy)
    - discontinuing: ↑ serum lamotrigine concentration (it may contribute to ADRs)
  - Inhibitors:
    - adding: ↑ serum lamotrigine concentration (it may contribute to ADRs)
    - discontinuing: ↓ serum lamotrigine concentration (it may contribute to ↓ efficacy)

2.0.1.3. Lamotrigine Case 1: Genetic, Personal & Environmental Factors

- Lamotrigine inducers:
  - AEDs:
    - carbamazepine,
    - phenytoin,
    - phenobarbital (and primidone)

    (The prescribing information recommends the same 2 x dose correction factor for all AED potent inducers, but 1.5 x may be better for carbamazepine.)
  - Rifampin
  - Lopinavir/ritonavir
  - Estrogens (oral contraceptives)
  - Acetaminophen may also be a inducer.

http://www.ncbi.nlm.nih.gov/pubmed/2225696

2.0.1.3. Lamotrigine Case 1: Genetic, Personal & Environmental Factors

- Valproate is the most important lamotrigine inhibitor:
  - Adding valproate requires decreasing the dose (0.5 x dose).
  - Its inhibitory effects may:
    - happen across all therapeutic doses
    - be similar (or stronger) than phenytoin or carbamazepine inductive effects.

http://www.ncbi.nlm.nih.gov/pubmed/16157751

    - ↓ estrogen inductive effects on lamotrigene.
- Ginseng may also be an inhibitor: avoid it. If patient refuse to stop it, warn him/her of the risks and use slower titration for lamotrigine, similar to that for valproate. http://www.ncbi.nlm.nih.gov/pubmed/25756365

2.0.1.3. Lamotrigine Case 1: Genetic, Personal & Environmental Factors

If you forget that **valproate is an inhibitor of lamotrigine metabolism,** you might kill your patients.

2.0.1.4. Lamotrigine Dosing

2.0.1.3. Lamotrigine Dosing

2.0.1.3.1. Half-Life
2.0.1.3.2. Bipolar Disorder
2.0.1.3.3. Epilepsy
2.0.1.3.4. Other Correction Factors

2.0.1.3.1. Lamotrigine Half-Life

(If you do not remember the concept of half-life, please review the presentation "Clozapine Case 6: Half-Life")

2.0.1.3.1. Lamotrigine Case 1: Lamotrigine Half-Life

Do lamotrigine and lamotrigine and lamotrigine ER have different half-lives?

2.0.1.3.1. Lamotrigine Case 1: Lamotrigine Half-Life

Do lamotrigine and lamotrigine and lamotrigine ER have different half-lives?

Yes;

not only different half-lives but

different bioavailability.

2.0.1.3.1. Lamotrigine Case 1: Lamotrigine Half-Life

Another concept that you cannot forget is that **lamotrigine has different bioavailability (and dosing) than lamotrigine ER.**

2.0.1.3.1. Lamotrigine Case 1: Lamotrigine Half-Life

Moreover, you also need to remember that **valproate has different bioavailability (and dosing) than valproate ER formulations.**

2.0.1.3.1. Lamotrigine Case 1: Lamotrigine Half-Life

- Lamotrigine and lamotrigine ER:
  - have different half-lives
    and this is relevant for TDM.
  - have different bioavailablity
    and this is relevant for dosing.
- Similarly, valproate and valproate ER formulations:
  - have different half-lives
    and this is relevant for TDM.
  - have different bioavailablity
    and this is relevant for dosing.

See presentation “Valproate Case 3 Formulation”

2.0.1.3.1. Lamotrigine Case 1: Lamotrigine Half-Life

- Normal formulation: administered twice a day.
- Lamotrigine half-life in adults (prescribing information): http://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=LAMOTRIGINE

Co-medication	Lamotrigine Half-Life Mean (range)[1]
Inducers	12.6 (7.5-23.1) hours
No other meds	25.4 (11.6-61.6) hours
Inducers + valproate	27.2[2](11.2-51.6) hours
Valproate	70.3 (41.9-113.5) hours

[1]Notice that the ranges are pretty wide; therefore, using the mean for a specific patient is a rough approximation.

[2]Notice that adding valproate at least compensates for the effect of potent inducers, due to its potent inhibitory effects.

2.0.1.3.1. Lamotrigine Case 1: Lamotrigine Half-Life

- Lamotrigine extended-release (ER) tablets:
  - are administered once a day.
    http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=32611&CFID=23862226&CFTOKEN=c27600d6f001498c-2E8A6594-CF03-8B9C-CC79F8CFAF92C929&jsessionid=ca308e763e412cb1e542
  - require higher doses than the normal formulation: 1.2 to 1.5 x higher.
    ER tablets have lower bioavailability than the normal formulation.

2.0.1.3.2. Lamotrigine Dosing: Bipolar Disorder

2.0.1.3.2. Lamotrigine Case 2: Bipolar Dosing

	Dose (mg/day)		
	VPA	No Inducers	
Weeks 1 & 2	25 every 2 days	25	50
Weeks 3 & 4	25	50	100
Week 5	50	100	200
Week 6	100	200	300
Week 7	100	200	400
Target	100	200	400

Package insert: http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=32038

No description of ER dosing is provided.

2.0.1.3.3. Lamotrigine Dosing: Epilepsy

2.0.1.3.3. Lamotrigine Case 2: Epilepsy

	Dose (mg/day)		
	VPA	No	Inducers
Weeks 1 & 2	25 every 2 days	25	50
Weeks 3 & 4	25	50	100
↑ every 1–2 weeks	25–50	50	100
Target	100-200	225-375	300-500
ER	200-250	300-400	400-600

Package insert: http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=32038

ER package insert:
http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=32611&CFID=23862226&CFTOKEN=c27600d6f001498c-2E8A6594-CF03-8B9C-CC79F8CFAF92C929&jsessionid=ca308e763e412cb1e542

2.0.1.3.4. Other Correction Factors

2.0.1.3.4. Lamotrigine Case 2: Other Correction Factors

- Personal characteristics:
  - Hepatic impairment: mild effects
    no dose adjustment
  - Renal impairment (not well studied):
    lower doses are probably needed.
  - Elderly: the same dose is recommended.
    (but it provides 35% ↑ in concentration)

http://www.ncbi.nlm.nih.gov/pubmed/18296554

  - Smoking: ↑ metabolism by 1.2.

http://www.ncbi.nlm.nih.gov/pubmed/18583161

  - Pregnancy: ↑ metabolism in 2nd & 3rd trimesters;
    (Use TDM to individualize dosing;
    as an approximation it requires 2 x dose).

http://www.ncbi.nlm.nih.gov/pubmed/17144777

2.0.1.3.4. Lamotrigine Case 2: Other Correction Factors

- Dr. de Leon's plan for the 2016 course includes a case describing lamotrigine TDM.
- There is no doubt that pregnancy requires lamotrigine TDM:
  - A fertile woman stabilized on lamotrigine and considering pregnancy should receive several TDMs as a baseline.
  - A woman recently found to be pregnant should receive a few TDMs as a baseline before the major ↑ of sexual hormones (in 2nd trimester).
  - A ↑ lamotrigine dose may be needed during the 2nd and 3rd trimesters. If you have no access to lamotrigine TDM, consider 2 x dose (this is the best approximation based in available limited literature).

2.0.2. Lamotrigine Pharmacodynamics

2.0.2. Lamotrigine Pharmacodynamics

What do you know about lamotrigine's pharmacodynamics?

2.0.2. Lamotrigine Pharmacodynamics

- AED:
  - ↓ activity of voltage-gated sodium channels
  - ↓ activity of voltage-gated calcium channels

- As a mood stabilizer:
  - not well understood

2.1. Lamotrigine Case 2

2.1. Lamotrigine Case 2

2.1.1. Case Description
2.1.2. Medications
2.1.3. Outcome
2.1.4. Diagnosis
2.1.5. Interpretation

2.1.1. Case Description

2.1.1. Lamotrigine Case 2: Description

http://www.ncbi.nlm.nih.gov/pubmed/17430308

- 36 yo Caucasian ♂ with bipolar II disorder:
  - He was treated for hypertension and GERD.
  - His most recent episode was severe depression without psychotic features.
  - After a sequence of several hospitalizations and recurrent suicide attempts, he tried to hang himself on an inpatient psychiatric unit.
  - He suffered mild brain anoxia (intensive care unit for <24 hours).
    Phenytoin was added for seizure prophylaxis.

2.1.2. Case Medications

2.1.2. Lamotrigine Case 2: Medications

- At the time of admission to a psychiatric hospital:
  - oxcarbazepine (600 mg/day),
  - phenytoin (300 mg/day),
  - lithium carbonate (900 mg/day),
  - venlafaxine slow-release (225 mg/day),
  - mirtazapine (45 mg/day),
  - metoprolol xl (50 mg/day), and
  - famotidine (40 mg/day).

2.1.2. Lamotrigine Case 2: Medications

- During a 3-week hospitalization:
  - Lithium was discontinued.
  - Phenytoin was discontinued on day 4.
  - Lamotrigine (50 mg/day) was added on day 11.
    It was increased to 100 mg/day on day 14; this titration was too rapid.

2.1.2. Lamotrigine Case 2: Medications

- At the time of discharge (day 21):
  - lamotrigine (100 mg/day),
  - oxcarbazepine (1200 mg/day),
  - venlafaxine slow-release (225 mg/day),
  - mirtazapine (60 mg/day),
  - metoprolol xl (50 mg/day),
  - propranolol (60 mg/day), and
  - famotidine (40 mg/day).

- No signs of toxicity were seen after 10 days on lamotrigine in spite of rapid titration.

2.1.3. Case Outcome

2.1.3. Lamotrigine Case 2: Outcome

- The patient's oxcarbazepine dosage was reduced to 600 mg/day after leaving the hospital.
- He was doing well.

2.1.3. Lamotrigine Case 2: Outcome

- On day 44 (after the first day of admission):
  - after 30 days on lamotrigine 100 mg/day and
  - 22 days after decreasing oxcarbazepine.
- The patient developed painful mouth sores on:
  - lips,
  - gums and
  - tongue.
- The ulcers appeared to be similar to the common aphthous ulcers; however, the significant number of ulcers was unusual.
- The ulcers were so painful, it was difficult for the patient to swallow or eat.

2.1.3. Lamotrigine Case 2: Outcome

- On day 50, the outpatient psychiatrist
  - became very concerned that oral lesions were an ADR, and
  - discontinued oxcarbazepine and lamotrigine.
- As soon as the medications were stopped, the mouth ulcers began to clear and soon were completely resolved.

2.1.4. Case Diagnosis

2.1.4. Lamotrigine Case 2: Diagnosis

Are oral ulcers compatible with initial Stevens-Johnson Syndrome?

2.1.4. Lamotrigine Case 2: Diagnosis

Are oral ulcers compatible with initial Stevens-Johnson Syndrome?

Absolutely.

2.1.4. Lamotrigine Case 2: Diagnosis

- The patient had no skin rash; oral ulcers cleared with medication discontinuation.
- See the presentation “Lamotrigine Case 1: Stevens-Johnson Syndrome” for:
  - pictures
  - a more thorough description of Stevens-Johnson Syndrome
- The next 4 slides taken from that presentation remind readers of the differential diagnosis between lamotrigine benign rash (around 5%) and Stevens-Johnson Syndrome (<1/1000).
  Clinicians are much more likely to face benign rash.

2.1.4. Lamotrigine Case 2: Diagnosis

- Benign Rash and Stevens-Johnson Syndrome can be distinguished by 3 characteristics:
  http://www.ncbi.nlm.nih.gov/pubmed/17430308
  - Time evolution:
    early in benign rash
  - Systemic involvement:
    absent in benign rash
  - Type of rash:
    more spotty and less confluent in benign rash

2.1.4. Lamotrigine Case 2: Diagnosis

- Time evolution:
  - Benign Rash: often occurs within 5-10 days of first exposure and improves within one to two weeks
  - Stevens-Johnsons Syndrome: often occurs much later, after the first 5 days and up to months after initiation

2.1.4. Lamotrigine Case 2: Diagnosis

- Systemic involvement :
  - Benign Rash:
    - no systemic involvement
    - normal blood counts
    - normal liver and kidney function tests
  - Stevens-Johnson Syndrome:
    - Ulcers in mucosal areas (eyes, lips or mouth) also often occur.
    - Systemic symptoms such as fever, malaise, anorexia, lymphadenopathy are often present.
    - Hematological, hepatic and kidney tests can be abnormal.

2.1.4. Lamotrigine Case 2: Diagnosis

- Type of rash:
  - Benign Rash:
    - spotty,
    - raised,
    - erythematous,
    - non-confluent and
    - non-tender
  - Stevens-Johnson Syndrome:
    - more likely confluent and widespread,
    - not raised,
    - purpuric and tender and
    - includes blistering with varying degrees of skin detachment

2.1.5. Case Interpretation

2.1.5. Lamotrigine Case 2: Interpretation

- Most physicians would probably agree that in this case:
  - the oral ulcers that cleared with medication discontinuation were very likely ADRs.
    (as a matter of fact, they are compatible with early Stevens-Johnson Syndrome).
  - It was a good idea not to wait for rash or other symptoms to make the full diagnosis.
- Assuming this was an early Stevens-Johnson Syndrome, there are 2 possible causes:
  - lamotrigine, or
  - oxcarbazepine.

2.1.5.1. Lamotrigine as the Cause

2.1.5.1. Lamotrigine Case 2: Lamotrigine as the Cause

- In this patient, 100 mg/day of lamotrigine was well tolerated for 30 days (in spite of fast titration).
- Based on Lamotrigine Case 1, we think:
  - ↓ oxcarbazepine from 1200 to 600 mg/day was crucial.
  - After 3 weeks and loss of induction: serum lamotrigine concentration ↑ and the patient developed oral ulcers.
- Phenytoin is a potent inducer of lamotrigine metabolism:
  - De-induction typically happens in 2-3 weeks.
  - It was discontinued after 40 days, and therefore, unlikely to have contributed.

2.1.5.2. Oxcarbazepine as the Cause

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

Can oxcarbazepine cause Stevens-Johnson Syndrome?

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

Can oxcarbazepine cause Stevens-Johnson Syndrome?

Yes.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

How do we know that oxcarbazepine can cause Stevens-Johnson Syndrome?

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

How do we know that oxcarbazepine can cause Stevens-Johnson Syndrome?

Search PubMed.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Go to PubMed.

http://www.ncbi.nlm.nih.gov/pubmed

- Type in the search box: "oxcarbazepine and Stevens-Johnson syndrome"
- 20 articles appear on the list. (This was on 1-26-16; later on you may find more).

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Start looking at abstracts, beginning with article 20. Only the most relevant are included in this presentation.
- Article 18: http://www.ncbi.nlm.nih.gov/pubmed/18331816

Dogan EA, Usta BE, Bilgen R, Senol Y, Aktekin B. Efficacy, tolerability, and side effects of oxcarbazepine monotherapy: a prospective study in adult and elderly patients with newly diagnosed partial epilepsy. Epilepsy Behav. 2008 Jul;13(1):156-61. doi: 10.1016/j.yebeh.2008.02.001. Epub 2008 Mar 10. PubMed PMID: 18331816

It is a Turkish study; the abstract says: "Side effects leading to discontinuation were: Stevens-Johnson syndrome (n=2,1.4%)…"

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Article 17: http://www.ncbi.nlm.nih.gov/pubmed/18785891

Chen YC, Chu CY, Hsiao CH. Oxcarbazepine-induced Stevens-Johnson syndrome in a patient with HLA-B*1502 genotype. J Eur Acad Dermatol Venereol. 2009 Jun;23(6):702-3. doi: 10.1111/j.1468-3083.2008.02988.x. Epub 2008 Sep 10. PubMed PMID: 18785891.

Notice that it has no abstract.

The pdf describes the patient:

- A Han Chinese from Taiwan
- HLA-B*15:02 genotype

  (This is associated with carbamazepine-induced Stevens-Johnson Syndrome. See the presentation “Pharmacogenetic Tests in Psychiatry”.)

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Article 15: http://www.ncbi.nlm.nih.gov/pubmed/19321411

Lin LC, Lai PC, Yang SF, Yang RC. Oxcarbazepine-induced Stevens-Johnson syndrome: a case report. Kaohsiung J Med Sci. 2009 Feb;25(2):82-6. doi: 10.1016/S1607-551X(09)70045-2. PubMed PMID: 19321411.

The article has an abstract and the pdf is available.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Article 12: http://www.ncbi.nlm.nih.gov/pubmed/21169036

Hu FY, Wu XT, An DM, Yan B, Stefan H, Zhou D. Pilot association study of oxcarbazepine-induced mild cutaneous adverse reactions with HLA-B*1502 allele in Chinese Han population. Seizure. 2011 Mar;20(2):160-2. doi: 10.1016/j.seizure.2010.11.014. Epub 2010 Dec 18. PubMed PMID: 21169036.

It is a Chinese study; the abstract says: "Our findings indicate that HLA-B*1502 allele may contribute to the genetic susceptibility to OXC-induced MPE".
MPE: mild maculopapular eruptions

Remember, in Chinese on carbamazepine , HLA-B*15:02 genotyping is associated with Stevens-Johnsons Syndrome (see the presentation on "Pharmacogenetic Testing in Psychiatry").

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Article 11: http://www.ncbi.nlm.nih.gov/pubmed/23130207

Sharma SR, Sharma N, Yeolekar ME. Oxcarbazepine-induced Stevens Johnson syndrome: A rare case report. Indian Dermatol Online J. 2011 Jan;2(1):13-5. doi: 10.4103/2229-5178.79861. PubMed PMID: 23130207; PubMed Central PMCID: PMC3481788.

This case report describes an Indian patient. A free pdf with pictures is available.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Article 10: http://www.ncbi.nlm.nih.gov/pubmed/22013310

Wal P, Wal A, Pandey U, Rai AK, Bhandari A. Genetic predisposition to oxcarbazepine induced Stevens-Johnson syndrome. Indian J Crit Care Med. 2011 Jul;15(3):173-5. doi: 10.4103/0972-5229.84904. PubMed PMID: 22013310; PubMed Central PMCID: PMC3190469.

Here is another case report on an Indian patient. A free pdf is available.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Article 1: http://www.ncbi.nlm.nih.gov/pubmed/26288485

Guleria VS, Sharda C, Rana T, Sood AK. Oxcarbazepine induced toxic epidermal necrolysis - a rare case report. Indian J Pharmacol. 2015 Jul-Aug;47(4):459-61. doi: 10.4103/0253-7613.161279. PubMed PMID: 26288485; PubMed Central PMCID: PMC4527075.

This case report is also about an Indian patient. A free pdf with pictures is available.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Summarizing the PubMed search:
  - oxcarbazepine can cause Stevens-Johnson Syndrome.
- Summarizing a textbook chapter:
  - Stevens-Johnson Syndrome is less frequent with oxcarbazepine than with carbamazepine.
  - About 75% of patients with carbamazepine rash tolerate oxcarbazepine.

http://www.amazon.com/American-Psychiatric-Publishing-Psychopharmacology-Schatzberg/dp/1585623091/ref=sr_1_1?ie=UTF8&s=books&qid=1278966588&sr=1-1
Chapter by Ketter et al.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

What are the arguments in favor of oxcarbazepine as the cause of Stevens-Johnson Syndrome in this case?

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- In favor of oxcarbazepine being the cause:
  - the discontinuation of 600 mg/day of oxcarbazepine was associated with the resolution of the oral ulcers.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

What are the arguments against oxcarbazepine as the cause of Stevens-Johnson Syndrome in this case?

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as the Cause

- Against oxcarbazepine being the cause:
  - The resolution of oral ulcers happened with the discontinuation of oxcarbazepine, but occurred at the same time as the lamotrigine discontinuation.
  - If oxcarbazepine was the cause of the oral ulcers, a dose of 1200 mg/day may be more likely to cause them.
  - The oral ulcers occurred 3 weeks after oxcarbazepine was ↓ from 1200 to 600 mg/day. Assuming that oxcarbazepine is a mild inducer, this is compatible with a slow ↑ of serum lamotrigine Cs.

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as Cause

In summary,
can we completely rule out that oxcarbazepine caused Stevens-Johnson Syndrome in this case?

2.1.5.2. Lamotrigine Case 2: Oxcarbazepine as Cause

In summary,
can we completely rule out that oxcarbazepine caused Stevens-Johnson Syndrome in this case?

No, but it is not likely.

Questions

- Please review the 10 questions on the pdf entitled “Questions on the Presentation Lamotrigine Case 2 Drug Drug Interaction”.
- You will find the answers on the last slide after the “Thank you” slide. No peeking until you have answered all the questions.
- If you do not answer all the questions correctly, please review the PowerPoint presentation again to reinforce the pharmacological concepts.

Thank you

Answers

1. A
2. D
3. C
4. B
5. D
6. B
7. D
8. D
9. A
10. A