Psychopharmacology in The Elderly

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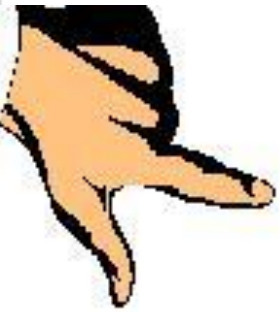
OUTLINE

- General principles
- Depression and ischemic heart disease as a case study

General Principles: Background



- There is more body fat
- Hepatic blood flow is less
- Renal functioning is poorer
- Neuropil is smaller

There is more Body Fat

- Implications for lipophilic drugs
  - Accumulate in fat compartments
  - Are released slowly from fat compartments
  - E.g. benzodiazepines

Hepatic Blood Flow is Less

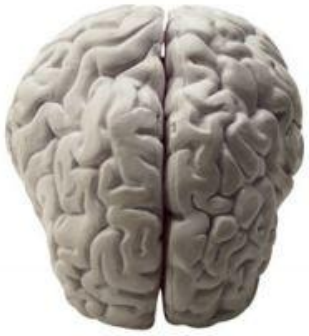
- So rate of hepatic metabolism of drugs decreases
- Implications for drugs metabolized by the liver
  - Most drugs

Renal Functioning is Poorer

- Implications for drugs eliminated by the kidneys
  - Lithium
  - Milnacipran, levomilnacipran, (tianeptine)
  - Paliperidone, amisulpride, sulpiride, levosulpiride
  - Gabapentin, pregabalin
  - Varenicline
  - Memantine
- Implications for metabolite accumulation

Neuropil is Smaller

- Cortical atrophy, ventricular dilatation
- Fewer neurons and glia
- Target tissue for drug action is smaller



Implications and Guidance

- Implications
  - Standard doses could lead to higher drug levels and more adverse effects
- Guidance
  - Start low, go slow
  - Monitor blood levels, if possible
  - Monitor for AEs

NOTE

- Polypharmacy is common in the elderly
  - Medications for DM, HT, IHD, other accumulated conditions
  - Record all medications
- Proactively consider drug-drug interactions
- Proactively consider drug-disease interactions
- Note that patients may get mixed up with drugs, doses, and timings

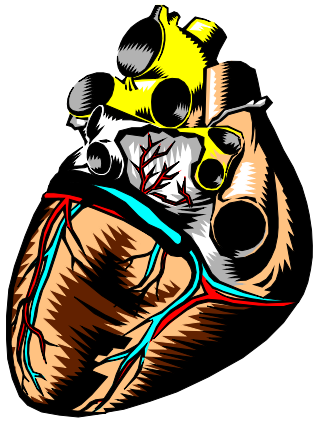
General Points

- Sedating drugs: Falls and fractures
- Anticholinergic drugs: Constipation, BPH symptoms, cognitive impairment, delirium
- Antidepressants: Hyponatremia
- Valproate: Thrombocytopenia
- SSRIs: Bleeding
- Antipsychotics: CVS events, mortality
- Benzodiazepines, anticholinergic drugs: MCI and dementia?

Depression and IHD: 1

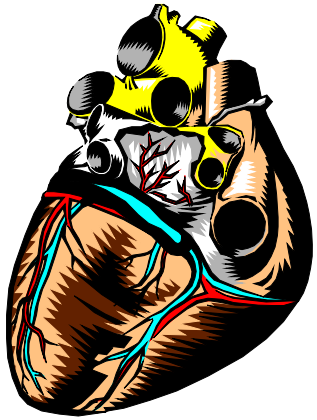
- Depression and IHD:
  - Each increase the risk of the other
  - Each worsen the course and outcome of the other
  - Reasons (audience)

Glassman and Shapiro, Am J Psychiatry 1998



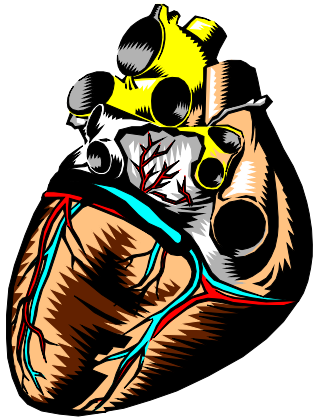
Depression and IHD: 2

- How IHD precipitates or worsens depression:
  - As a stressor
  - As a biological marker of small artery disease in the brain, which increases the risk of periventricular WMH, lacunar infarcts, and late-life depression.



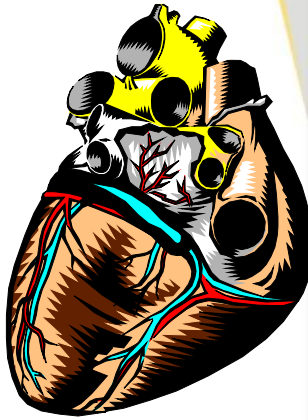
Depression and IHD: 3

- How depression precipitates or worsens IHD:
  - Through autonomic dysfunction
  - Through disregard of advice regarding diet and exercise
  - Through poor drug compliance with cardiological treatments



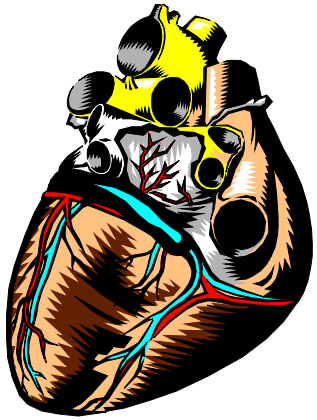
Depression and IHD: 4

- In a Danish twin study (n=6714), Wium-Andersen et al (Acta Psychiatr Scan 2019) found that
  - Higher depression scores were associated with higher incidence of IHD.
  - The twin with higher depression scores developed IHD more often or earlier than the twin with lower depression scores.
  - The findings were similar in a 2-year time lag analysis of depression symptomatology that protected against reverse causality.



Depression and IHD: 5

- Treatment implications (audience)
  - TCA?
  - SNRIs?
  - SSRIs?



Antidepressants for IHD: 1

- TCA increase the risk of IHD events

  (Cohen et al, Am J Med 2000; Rosenberg et al, Int J Cardiol 2010)

  - TCA may also increase arrhythmia risk.
  - TCA are poorly tolerated in the elderly, the population affected by IHD.
  - Anticholinergic effects (dry mouth, constipation, problems with near vision, urinary hesitancy) are a particular problem.

Antidepressants for IHD: 2

- Nortriptyline is not a safer TCA:
  - Relative to PAROX in IHD, NORT was associated a higher risk of drop out due to AEs (25% vs 5%; Nelson et al, AJP 1999) and with an increased risk of adverse cardiac events (18% vs 2%; Roose et al, JAMA 1998).
  - QT variability was higher with NORT than with PAROX in panic disorder (Yeragani et al, Depr Anx 2000).
  - Relative to PAROX in panic, NORT decreased chaos in heart rate variability (Yeragani and Rao, J Psychosom Res 2003).

Antidepressants for IHD: 3

- SNRIs (esp. venlafaxine) increase HR, BP.
  - The risk is dose-dependent
  - Whereas the increase is small (e.g. 2-3 BPM or 2-3 mm Hg), even small increases are important, especially at the population level.
- SSRIs have beneficial and adverse implications in IHD patients (Andrade, J Clin Psychiatry, 2012 & 2013; Andrade et al, Int Clin Psychopharmacol 2013)

Question

- How might SSRIs benefit patients with IHD?

SSRIs may reduce IHD events: 1
(Andrade et al, Int Clin Psychopharmacol 2013)

- When depression remits, patients may
  - Cope better with stress; so stress has a lower impact on HR, BP etc.
  - Eat less
  - Exercise more
  - Adhere better to CVS drugs

SSRIs may reduce IHD events: 1
(Andrade et al, Int Clin Psychopharmacol 2013)

- By inhibiting uptake of 5HT into platelets and thereby inhibiting platelet aggregation.
- By decreasing platelet/endothelial activation.
- By reducing levels of adhesion molecules, C reactive protein, interleukin 6.
- By inhibiting collagen-induced platelet aggregation and activation.
- Benefits are over and above those obtained with aspirin and clopidogrel.

Question

- Which is the best studied SSRI in IHD patients?
- Which SSRIs might you want to avoid in IHD?

SSRIs may reduce IHD events
(Andrade et al, Int Clin Psychopharmacol 2013)

- What does the evidence in IHD show?
  - There are favorable, neutral, inconclusive, as well as (very few) unfavorable studies.
  - The balance of evidence seems to suggest favorable outcomes.
  - A meta-analysis found that SSRIs reduced the risk of IHD readmissions and mortality (Pizzi et al, Am J Cardiol 2011).
  - Sertraline is the best studied drug (e.g. SADHART study).
- SSRIs have also been found safe in cardiac failure.

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Question

- What are the risks of using SSRIs in IHD patients?
- Hint: With what CVS medications may there be a drug interaction?

SSRIs and Bleeding Risks: 1
(Andrade et al, J Clin Psychiatry 2010)

- IHD patients usually receive aspirin and/or clopidogrel.
- SSRI increase GI bleeding risks with these drugs
  - By inhibiting platelet aggregation
  - By increasing gastric acidity
- Question: How high is the risk?

SSRIs and Bleeding Risks: 2
(Andrade et al, J Clin Psychiatry 2010)

- Risk with the SSRI + aspirin/clopidogrel combination is 1 in 65 to 1 in 200 per year.
  - Is this a big risk?
  - Elderly at higher risk of bleeds
- Risks is low with non-SSRIs (e.g. mirtazapine)
- Risk can be reduced by proton pump inhibitors
  - But what are potential concerns?

SSRIs and Bleeding Risks: 3
(Andrade et al, J Clin Psychiatry 2010)

- Clopidogrel is a prodrug, activated by CYP2C19
- This enzyme is
  - Potently inhibited by omeprazole, esomeprazole
  - Moderately inhibited by lansoprazole, deslansoprazole
  - Weakly inhibited by rabeprazole, pantoprazole
- 2C19 is also potently inhibited by fluoxetine and fluvoxamine
- FDA warning: Don't combine clopidogrel with potent 2C19 inhibitors

SSRIs and Bleeding Risks: 4
(Andrade et al, J Clin Psychiatry 2010)

- Ranitidine can be given instead of a proton pump inhibitor.
  - The evidence, however, only supports proton pump inhibitor benefits. There are no data for ranitidine (because it is an old drug?).
  - Ranitidine may need to be given twice daily.
  - Ranitidine inhibits CYP2D6 and may increase the activity of metoprolol and carvedilol.

SSRI Interactions with Beta Blockers

(Andrade, J Clin Psychiatry 2013)

- IHD patients commonly receive beta blockers
- Different SSRIs increase the blood levels and half-lives of different beta blockers.
- So what?

SSRI Interactions with Beta Blockers

(Andrade, J Clin Psychiatry 2013)

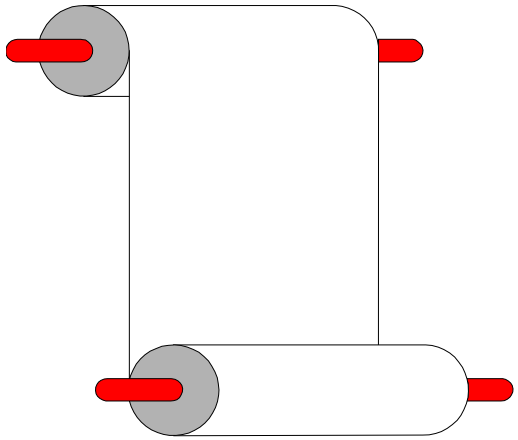
- Different SSRIs increase the blood levels and half-lives of different beta blockers.
- This can result in bradycardia and hypotension (and falls and fractures), and even in heart block
- This can also result in dose-dependent adverse effects like loss of cardioselectivity.
- E.g. Paroxetine raises metoprolol levels and triggers clinically relevant adverse effects.

Metabolism of Beta Blockers
(Andrade, J Clin Psychiatry 2013)

- Predominantly 2D6: carvedilol, metoprolol, nebivolol
- Multiple enzymes (1A2, 2C19, 2D6, 3A4): propranolol
- 50% 2D6 and 3A4, 50% renal excretion: bisoprolol
- Mainly renal excretion: atenolol, nadolol, sotalol
- 2D6 inhibited by paroxetine, fluoxetine (sertraline)
- 1A2, 3A4 inhibited by fluvoxamine
- 2C19 inhibited by fluoxetine, fluvoxamine

The Story so Far

- In IHD patients,
  - SSRIs may do good
  - SSRIs may be responsible for adverse drug interactions
- Do SSRIs have a direct effect on the heart?



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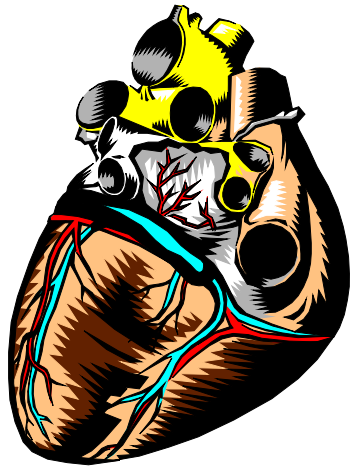
QTc

- What is the importance of the QT interval?
- What is QTc?
- How is QTc calculated?
- What values indicate QTc prolongation?
- What risk is associated with QTc prolongation?



Notes on the QTc: 1

- QRS waves: Ventricular depolarization
- T wave: Ventricular repolarization
  - QT interval: Time taken for ventricular repolarization
  - QT prolongation increases risks of arrhythmias
- QTc: QT interval corrected for heart rate
  - Why this is an issue
  - Bazett's correction: QT / Square root of RR
  - Fridericia's correction: QT / Cube root of RR (more accurate when bradycardia/tachycardia are present)

Notes on the QTc: 2

- Normal QTc:
  - <430 ms in men and <450 ms in women
- Prolonged QTc:
  - >450 ms in men and >470 ms in women
- Prolonged QTc (especially >500 ms):
  - Risk of torsades de pointes syndrome and sudden death due to ventricular tachyarrhythmia/fibrillation

Notes on the QTc: 3

- Risk factors for QTc prolongation:
  - Female gender, older age
  - Drugs (thioridazine, sertindole, ziprasidone, TCA, citalopram, terfenadine, astemizole, cisapride etc.)
  - Hypokalemia, hypomagnesemia
  - Cardiac failure and other heart diseases
  - Congenital long QT syndrome

SSRIs and QTc: 1

(Mago, Tripathi, Andrade, Expert Rev Neurother 2014)

- QTc is abnormal in about 20% of patients receiving antidepressants.
- Citalopram, escitalopram, and amitriptyline dose-dependently increase the QTc.
- With citalopram, increase is by about 10 ms between 10 and 20 mg/day; and between 20 and 40 mg/day.
- Bupropion dose-dependently decreases the QTc.

Castro et al, BMJ 2013

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SSRIs and QTc: 2

(Mago, Tripathi, Andrade, Expert Rev Neurother 2014)

FDA warnings:

- Do not use citalopram in doses >40 mg/day
- Do not use citalopram in doses >20 mg/day
  - In patients >60 years
  - In patients receiving 2C19 inhibitors (e.g. omeprazole)
  - In patients at risk of QTc prolongation due to other factors (what are these?)
- 2013 label change: Fluoxetine may also prolong the QTc.

Have we left out any Drug Interactions?

- What other medications do IHD patients take?

SSRIs and Statins: 1
(Andrade, J Clin Psychiatry 2014)

- Patients with diabetes and IHD almost always receive statins for primary or secondary prevention.
- New statin guidelines (Stone et al, Circulation 2013)
- Depression may complicate diabetes (reasons).
- Depression in diabetes is associated with an increased risk of CVS and all-cause mortality (van Dooren et al, PLoS One 2013; Hofmann et al, PLoS One 2013).
- Need for weight-neutral, heart-safe antidepressants.

SSRIs and Statins: 2
(Andrade, J Clin Psychiatry 2014)

- Most SSRIs are enzyme inhibitors.
- If statin levels are raised, there is a risk of myopathies, including rhabdomyolysis.
  - Myalgia, myositis, rhabdomyolysis: definitions and risks
- Questions:
  - What do these terms mean?
  - How common are these conditions with statin therapy?

SSRIs and Statins: 3
(Andrade, J Clin Psychiatry 2014)

- Myopathies:.
  - Myalgia: muscle complaints without CPK elevation
  - Myositis: myalgia with CPK up to 10x maximum normal
  - Rhabdomyolysis: CPK >10x maximum normal
- Myalgia with statins in about 10%
  - But also common with placebo!
  - Myositis in 0.1-0.5%; rhabdomyolysis in 0.02-0.04%
  - Bellosta and Corsini, Expert Opin Drug Saf 2012
  - Real life risks may be lower (Valiyil and Christopher-Stine, Curr Rheumatol Rep 2010)

SSRIs and Statins: 4
(Andrade, J Clin Psychiatry 2014)

- Questions
  - Which CYP enzymes metabolize the common statins?
  - Which CYP enzymes do the SSRIs inhibit?

SSRIs and Statins: 5
(Andrade, J Clin Psychiatry 2014)

- Metabolized
  - Atorvastatin 3A4, 3A5
  - Lovastatin 3A4, 3A5
  - Simvastatin 3A4, 3A5
  - Fluvastatin 2C9; 3A4 (minor), 2C8 (minor)
- Negligibly metabolized
  - Rosuvastatin 3A4, 3A5 (both minor)
  - Pitavastatin 2C9, 2C8 (both minor)
  - Pravastatin 3A4, 3A5 (both minor)

SSRIs and Statins: 4
(Andrade, J Clin Psychiatry 2014)

- 3A4/5:
  - Minor inhibition by fluvoxamine
  - Weak or questionable inhibition by fluoxetine, sertraline
  - No evidence of inhibition by paroxetine, citalopram, escitalopram
  - No data on 3A5

SSRIs and Statins: 5
(Andrade, J Clin Psychiatry 2014)

- 2C9:
  - Minor inhibition by fluvoxamine
  - Even smaller inhibition by sertraline
  - Weak or questionable inhibition by remaining SSRIs
- 2C8
  - Weak inhibition by fluvoxamine
  - No evidence of inhibition by fluoxetine
  - No data on remaining SSRIs

SSRIs and Statins: 6
(Andrade, J Clin Psychiatry 2014)

- Weak or modest 3A4 inhibitors can be used cautiously with 3A4-dependent statins (Neuvonen et al, Clin Pharmacol Ther 2006).
  - Applies to fluvoxamine with atorvastatin, lovastatin, and simvastatin.
  - Other SSRIs are safe with these statins.
- 2C9 inhibitors have negligible effects and can be ignored.

SSRIs and Statins: 7
(Andrade, J Clin Psychiatry 2014)

- Paroxetine, citalopram, escitalopram can be safely given with all statins
  - Possibly, fluvoxetine and sertraline, as well.
- All SSRIs can be given safely with rosuvastatin, pitavastatin, and pravastatin.
- Note: SSRIs and statins have been available for decades, and there have been no reports of adverse myopathy interactions.

SSRIs and Statins: 8
(Andrade, J Clin Psychiatry 2014)

- No data on organic anion transporting polypeptide (OATP) and p-glycoprotein (p-gp) interactions
  - Statins are substrates for both OATP and p-gp.
  - However, so far no evidence from fruit juice studies that OATP interactions affect statin absorption

SSRIs and Statins: 8
(Andrade, J Clin Psychiatry 2014)

- Pharmacodynamic interaction?
  - FDA AERS database mining showed that paroxetine and pravastatin were associated with an increased risk of elevated blood glucose.
  - Not a class effect for SSRIs and statins, in general.
  - This could have been a chance finding in a data mining study and needs to be confirmed prospectively.

Take-Home Messages: 1

- In an elderly patient with depression, take precautions against risk of IHD events.
  - Refer for cardiological work-up .
  - Monitor BP, lipids, other risk factors for IHD.
  - If you do not, and the patient has a critical event, you would never know that you might have been responsible.
- In an elderly patient with IHD, evaluate periodically for depression.

Take-Home Messages: 2

- Use SSRIs to treat depression in patients with IHD
  - Not TCA
  - Guard against venlafaxine and other SNRI use if hypertension is present
  - With SSRIs, warn about bleeds, watch for melena, test periodically for occult blood.
  - Take especial care about bleeds if aspirin, clopidogrel are also used

Take-Home Messages: 3

- In patients at risk of bleeds in whom the antidepressant cannot be changed
  - E.g. A depressed patient who is responding to an SSRI and in whom change of antidepressant may result in loss of antidepressant action.
  - Use rabeprazole, pantoprazole or ranitidine (but not omeprazole, esomeprazole) to prevent bleeds if there is risk, as indicated by development of gastric acidity or occult blood in stools. Change SSRI after patient becomes stable.
  - Use mirtazapine if the risk of bleeds is unacceptable

Take-Home Messages: 4

- Avoid fluoxetine, fluvoxamine if clopidogrel is used
- When combining an SSRI with a beta blocker
  - Avoid potentially interacting drugs
  - If interaction is unavoidable, titrate beta blocker dose to heart rate and blood pressure
  - No need for concern with atenolol
- Avoid citalopram, escitalopram, and perhaps fluoxetine if there is a risk of QTc prolongation.

Take-Home Messages: 5

- Paroxetine, citalopram, escitalopram can be safely given with all statins
  - Possibly, fluvoxetine and sertraline, as well.
- All SSRIs can be given safely with rosuvastatin, pitavastatin, and pravastatin.
- Weak or modest 3A4 inhibitors can be used cautiously with 3A4-dependent statins

  (Neuvonen et al, Clin Pharmacol Ther 2006).
  - Applies to fluvoxamine with atorvastatin, lovastatin, and simvastatin.

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Cardiovascular mechanisms of SSRI drugs and their benefits and risks in ischemic heart disease and heart failure

Andrade Chittaranjan, Kumar B. Chethan and Surya Sandarsh

Depression and heart disease are commonly comorbid. Selective serotonin reuptake inhibitors (SSRIs) are commonly used to treat depression. In March 2011, we carried out a 15-year search of PubMed for preclinical and clinical publications related to SSRIs and ischemic heart disease (IHD) or congestive heart failure (CHF). We identify and discuss a number of mechanisms by which SSRIs may influence cardiovascular functioning and health outcomes in patients with heart disease; many of the mechanisms that we present have received little attention in previous reviews. We examine studies with positive, neutral, and negative outcomes in IHD and CHF patients treated with SSRIs. SSRIs influence cardiovascular functioning and health through several different mechanisms; for example, they inhibit serotonin-mediated and collagen-mediated drug interactions with medications that influence cardiovascular functions. The clinical evidence suggests that, in general, SSRIs are safe in patients with IHD and may, in fact, exert a cardioprotective effect. The clinical data are less clear in patients with heart failure, and the evidence for benefits with SSRIs is weak. *Int Clin Psychopharmacol* 28:145–155 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

International Clinical Psychopharmacology 2013, 28:145–155

Keywords: cardiovascular disease, heart failure, ischemic heart disease, platelets, selective serotonin reuptake inhibitors

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Serotonin Reuptake Inhibitor Antidepressants and Abnormal Bleeding: A Review for Clinicians and a Reconsideration of Mechanisms

Chittaranjan Andrade, MD; Surya Sandarsh, MBBS;
Kumar B. Chethan, MBBS; and Koregala S. Nagesh, MPharm

Background: It is generally believed that selective serotonin reuptake inhibitor (SSRI) drugs increase the risk of abnormal bleeding and decrease the risk of ischemic heart disease events by blocking the uptake of serotonin into platelets, leading to an impairment in the platelet hemostatic response.

Objective: To perform a detailed qualitative review of existing literature on the association of abnormal bleeding with the use of SSRIs.

Data Sources: We conducted a PubMed search during June 2009 using the search terms *antidepressants* and *SSRIs* (including the names of individual SSRIs: *fluoxetine*, *sertraline*, *paroxetine*, *fluvoxamine*, *citalopram*, and *escitalopram*) in association with *bleeding*, *platelets*, *hemostasis*, *nonsteroidal anti-inflammatory drugs* (*NSAIDs*), *aspirin*, *antiplatelet drugs*, *proton pump inhibitors*, *peptic ulcer*, *premenstrual dysphoric disorder*, *menstruation*, *pregnancy*, *postpartum hemorrhage*, *surgery*, *tooth extraction*, *dental bleeding*, *stroke*, *ischemic heart disease*, and other terms related to the field. We then searched the reference lists of identified studies

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Selective serotonin reuptake inhibitor (SSRI) drugs are used in the treatment of diverse disorders in psychiatry, including depression, generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, premenstrual dysphoric disorder, and other conditions.[1] During the past decade, much literature has been published on the risk of abnormal gastrointestinal (GI) bleeding as an infrequent adverse effect of SSRI treatment. During the past decade, studies have also indicated that SSRIs may protect against ischemic heart disease events. Both effects have been suggested to arise from impaired hemostasis because serotonin weakly potentiates platelet aggregation and because SSRIs inhibit the uptake of serotonin into platelets.

Serotonin Reuptake Inhibitors and Risk of Abnormal Bleeding

Chittaranjan Andrade, MD[a,*], Eesha Sharma, MD[b]

KEYWORDS

- Antidepressant • Serotonin reuptake inhibitor • Selective serotonin reuptake inhibitor
- Bleeding • Postpartum hemorrhage • Intracranial hemorrhage
- Nonsteroidal anti-inflammatory drugs • Antiplatelet drugs

KEY POINTS

- Antidepressants with potent serotonin reuptake inhibitor (SRI) activity increase the risk of bleeding through different mechanisms.
- The upper gastrointestinal (GI) tract is the commonest site of SRI-related abnormal bleeding.
- The risk of SRI-related upper GI bleeding is raised by concurrent treatment with nonsteroidal anti-inflammatory drugs, antiplatelet drugs, and anticoagulant drugs; the risk is low-

Drug Interactions in the Treatment of Depression in Patients With Ischemic Heart Disease

Chittaranjan Andrade, MD

Each month in his online column, Dr Andrade offers practical knowledge, ideas, and tips in psychopharmacology to *JCP* readers in psychiatric and general medical settings.

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J Clin Psychiatry 2012;73(12):e1475–e1477 (doi:10.4088/JCP.12f08248)

Clinical Problem

Mr K is 67 years old. He has been diagnosed with major depressive disorder. He has a history of ischemic heart disease (IHD). What might be the concerns associated with treating his depression with a selective serotonin reuptake inhibitor (SSRI)?

The Relationship Between Depression and Ischemic Heart Disease

Patients with depression are at increased risk of IHD events, and patients who have IHD are at increased risk of depression; the presence of each condition worsens the course and outcome of the other.[1] It is important, therefore, for depression to be identified early and treated effectively in patients with IHD.[2,3] Given that SSRIs are commonly used antidepressants, clinicians should be aware that SSRIs may have effects beyond antidepressant action in patients with IHD.

Possible Benefits of SSRIs in Patients With Ischemic Heart Disease

SSRIs effectively attenuate depression, including depression that complicates the course of IHD.[4] SSRIs may also improve the course of IHD[5–10] through multiple mechanisms (Table 1)[11–17]—this is an important consideration, given that tricyclic antidepressants have been associated with an increased risk of IHD events.[18,19]

Drug Interactions in the Treatment of Depression in Patients Receiving β-Blocker Drugs

Chittaranjan Andrade, MD

Each month in his online column, Dr Andrade offers practical knowledge, ideas, and tips in psychopharmacology to *JCP* readers in psychiatric and general medical settings.

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J Clin Psychiatry 2013;74(1):e75–e78 (doi:10.4088/JCP.12f08323)

Clinical Problem

Last month's column examined potential selective serotonin reuptake inhibitor (SSRI) interactions with antiplatelet drugs (aspirin, clopidogrel) in a hypothetical 67-year-old man with major depressive disorder comorbid with ischemic heart disease (IHD).[1] This month, we continue the discussion on possible concerns associated with using an antidepressant to treat depression in this patient.

Patients with IHD commonly receive β-blocker drugs. β-Blockers are also used in the treatment of hypertension, heart failure, anxiety, migraine, essential tremor, and other conditions. Commonly used β-blockers include atenolol, metoprolol, nebivolol, carvedilol, bisoprolol, and propranolol.[2–5] Many antidepressants inhibit the cytochrome P450 (CYP) enzymes that metabolize certain β-blocker drugs. If the metabolism of β-blockers is inhibited, their peak blood level and half-life will increase, resulting in an increase in dose-dependent adverse effects. Prominent among these adverse effects are bradycardia, heart block, hypotension, and loss of cardioselectivity associated with an increased risk of bronchoconstriction and altered glucose homeostasis.[6,7]

Drug Interaction: Paroxetine and Metoprolol

Several studies illustrate the interaction between paroxetine a

Selective Serotonin Reuptake Inhibitor Drug Interactions in Patients Receiving Statins

Chittaranjan Andrade, MD

Each month in his online column, Dr Andrade offers practical knowledge, ideas, and tips in psychopharmacology to *JCP* readers in psychiatric and general medical settings.

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ABSTRACT

Elderly patients commonly receive statin drugs for the primary or secondary prevention of

Clinical Problem

A 51-year-old man with type 2 diabetes mellitus has been receiving atorvastatin 10 mg/d for the past year for the treatment of elevated low-density lipoprotein (LDL) cholesterol levels. He has been newly diagnosed with major depressive illness. Are there statin drug interactions that may limit the choice of antidepressant drugs that he can safely receive?

Statins and Primary Prevention

Statin therapy is associated with primary prevention benefits in cardiovascular and cerebrovascular disease; the 5-year numbers needed to treat range from 49 to 155, depending on the outcomes examined.[1] Recent guidelines from the American College of Cardiology and the American Heart Association encourage primary prevention with moderate- to high-intensity statin therapy in diabetic patients aged 40–75 years in whom LDL cholesterol levels are 70 mg/dL and above.[2]

EXPERT REVIEWS

Cardiovascular adverse effects of newer antidepressants

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Newer antidepressants that are more selective in their neurotransmitter effects include the selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and others (agomelatine, bupropion, mirtazapine, reboxetine, vilazodone, vortioxetine). This article systematically reviews data from a variety of sources regarding the potential adverse effects of these medications on various cardiovascular parameters. Potential biochemical mechanisms by which these antidepressants may adversely affect the cardiovascular system are also discussed. Antidepressants that are associated with higher cardiovascular risk (SNRIs, reboxetine), lower risk (SSRIs), and without current evidence of cardiovascular risk (agomelatine, mirtazapine, vilazodone, vortioxetine) are identified. The FDA's recommendations regarding citalopram are organized and summarized, and situations with higher risk of cardiovascular adverse effects are identified.

KEYWORDS: adverse effects • antidepressants • blood pressure • cardiovascular • electrocardiogram • orthostatic hypotension • QT interval • side effects • serotonin-norepinephrine reuptake inhibitors • selective serotonin reuptake inhibitors

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BIPOLAR DISORDERS

Review Article

Primary prevention of cardiovascular events in patients with major mental illness: a possible role for statins

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Objectives: To examine the need for and the possible benefits and risks of statin therapy in patients with major mental illness.

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ENFIN…

That's it, folks; thanks for listening!