SyncView™ Pain

Phenomics HEALTH

JOHN DOE
Specimen No: 700361
Physician: Dr. Alice Jones

DOB: 01-01-46
Sex: M

Sample Collection: Apr. 11, 2021 13:16 EDT
Sample Analysis: Apr. 13, 2021 11:35 EDT

MEDICATION	DOSAGE FREQUENCY	RESULT	DDI*	INDICATION
IN THE MEDICAL RECORD:				
ALPRAZOLAM Xanax	0.5 mg PRN QD	−	▲	Central nervous system agents/Anxiolytics, sedatives, and hypnotics
AMITRIPTYLINE Elavil	10 mg QHS	+	▲	Psychotherapeutic agents/Antidepressants
CYCLOBENZAPRINE Flexeril	10 mg PRN TID	+	▲	Central nervous system agents/Muscle relaxants
ESCITALOPRAM Lexapro	10 mg QD	+	▲	Psychotherapeutic agents/Antipsychotics
NOT IN THE MEDICAL RECORD:				
ACETAMINOPHEN Tylenol	Unknown	+		Central nervous system agents/Analgesics
OXYCODONE Roxicodone	Unknown	+	▲	Central nervous system agents/Analgesics
TRAMADOL Ultram	Unknown	+	▲	Central nervous system agents/Analgesics

Result:

+ Detected

− Not Detected

***Drug-Drug Interaction (DDI):** See details on the following pages.

Severe - The use of these medications together is contraindicated. Rare exceptions may exist.

Major - The use of these medications together may be contraindicated in a select group of patients. The patient should be monitored for possible manifestations of the interaction.

MEDICATIONS NOT IN ASSAY:

MELATONIN

Phenomics Health Inc. 46701 Commerce Center Dr Plymouth, MI 48170 734.233.3070

Report Released: April 14, 2021 13:44 EDT
Analysis: Phenomics Health Inc.
Certified: SN001

Interaction Details

ALPRAZOLAM

Interacting Drug OXYCODONE

Alert level MAJOR

Documentation Level Established

Professional Notes

Concomitant use of opiate agonists with benzodiazepines may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with benzodiazepines to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone is initiated in a patient taking a benzodiazepine, reduce dosages and titrate to clinical response. For acetaminophen; oxycodone extended-release tablets, start with 1 tablet PO every 12 hours, and for other oxycodone products, use an initial dose of oxycodone at one-third to one-half the usual dosage. If a benzodiazepine is prescribed for an indication other than epilepsy in a patient taking an opiate agonist, use a lower initial dose of the benzodiazepine and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Clinical Management

monitor blood pressure :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for an increase in CNS/respiratory depression

References

Ibuprofen and oxycodone tablet package insert. Elizabeth, NJ: Actavis Elizabeth LLC; 2017 Jan. :: OxyContin (oxycodone HCl extended-release) package insert. Stamford, CT: Purdue Pharma L.P.; 2016 Dec. :: Xartemis XR (acetaminophen; oxycodone) extended-release tablets. Hazelwood MO: Mallinckrodt Brand Pharmaceuticals, Inc.; 2016 Dec. :: Percodan (aspirin; oxycodone) tablet package insert. Malvern, PA: Endo Pharmaceuticals Inc.; 16 Dec. :: Troxyca ER (oxycodone hydrochloride; naltrexone hydrochloride) extended-release capsules package insert. New York, NY: Pfizer, Inc.; 2016 Dec. :: Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

Interacting Drug TRAMADOL

Alert level MAJOR

Documentation Level Established

Professional Notes

Concomitant use of opiate agonists with benzodiazepines may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with benzodiazepines to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a benzodiazepine, use a lower initial dose of the opiate and titrate to clinical response. If a benzodiazepine is prescribed for an indication other than epilepsy in a patient taking an opiate agonist, use a lower initial dose of the benzodiazepine and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Clinical Management

consider alternative drug therapy :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for an increase in CNS/respiratory depression

References

Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

AMITRIPTYLINE

Interacting Drug CITALOPRAM

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Citalopram causes dose-dependent QT interval prolongation and tricyclic antidepressants are associated with a possible risk of QT prolongation and torsade de pointes (TdP). According to the manufacturer, concurrent use of citalopram with other drugs that prolong the QT interval is not recommended. If concurrent therapy is considered essential, ECG monitoring is recommended. In addition, because of the potential risk and severity of serotonin syndrome, caution should be observed when administering citalopram with other drugs that have serotonergic properties such as tricyclic antidepressants. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. Clinicians should also be alert for pharmacokinetic interactions between tricyclic antidepressants (TCAs) and SSRIs. Citalopram is a weak inhibitor of CYP2D6, the isoenzyme responsible for metabolism of many of the tricyclic antidepressants. Coadministration of citalopram and imipramine did not significantly affect the plasma concentrations of either drug. However, the concentration of desipramine, the primary metabolite of imipramine, was increased by 50%. The clinical significance of the elevation in desipramine concentration is unknown. However, symptoms of toxicity, including seizures, have been reported when drugs from these 2 classes were used together. A decreased dosage of the TCA or the avoidance of concomitant SSRI therapy should be considered.

Clinical Management

avoid combination unless benefit outweighs potential risk :: monitor for signs or symptoms of serotonin syndrome :: monitor ECG :: monitor for fast, irregular heartbeat :: dosage reduction may be required

References

CredibleMeds. Drugs to avoid in congenital long QT. Available on the World Wide Web at http://www.crediblemeds.org. :: Celexa (citalopram) package insert. Irvine, CA: Allergan USA, Inc.; 2017 Jan. :: Nora Goldschlager, Andrew E Epstein, Blair P Grubb, et al. Etiologic considerations in the patient with syncope and an apparently normal heart. Arch Intern Med 2003;163:151-62. :: Hansten PD, Horn JR. Drug Interactions with Drugs that Increase QTc Intervals. In: The Top 100 Drug Interactions - A Guide to Patient Management. 2007 Edition. Freeland, WA: H&H Publications; 2007:144-8.

Interacting Drug CYCLOBENZAPRINE

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

The concomitant use of tryptophan with tricyclic antidepressants should be avoided. Since tryptophan is converted to serotonin (5-hydroxytryptamine), the use of tryptophan in patients receiving drugs with serotonergic activity could lead to serotonin syndrome. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. If serotonin syndrome is suspected, the tricyclic antidepressant and concurrent serotonergic agents should be discontinued.

Clinical Management

avoid combination unless benefit outweighs potential risk :: monitor for signs or symptoms of serotonin syndrome

References

Ener RA, Meglathery SB, Van Decker WA, et al. Serotonin syndrome and other serotonergic disorders. Pain Med 2003;4:63-74.

Interacting Drug TRAMADOL

Alert level MAJOR

Documentation Level Established

Professional Notes

Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering tricyclic antidepressants (TCAs) with other drugs that have serotonergic properties such as tramadol. Both tramadol and TCAs inhibit the central reuptake of serotonin. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. In addition, in vitro drug interaction studies in human liver microsomes indicate that amitriptyline may inhibit the metabolism of tramadol via CYP2D6, suggesting that concomitant administration of TCAs could result in increases in tramadol concentrations and decreased concentrations of M1. The full pharmacological impact of these alterations in terms of either efficacy or safety is unknown. Tricyclic antidepressants may decrease the seizure threshold and have been associated with increased risk of seizures when given concurrently with tramadol.

Clinical Management

monitor for signs of drug toxicity :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for signs or symptoms of serotonin syndrome :: monitor for seizure activity

References

Kahn LH, Alderfer RJ, Graham DJ. Seizures reported with tramadol. JAMA 1997;278:1661. :: Ultram (tramadol hydrochloride) tablets package insert. Titusville, NJ; Janssen Pharmaceuticals, Inc.; 2017 Aug. :: Ener RA, Meglathery SB, Van Decker WA, et al. Serotonin syndrome and other serotonergic disorders. Pain Med 2003;4:63-74.

CITALOPRAM

Interacting Drug AMITRIPTYLINE

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Citalopram causes dose-dependent QT interval prolongation and tricyclic antidepressants are associated with a possible risk of QT prolongation and torsade de pointes (TdP). According to the manufacturer, concurrent use of citalopram with other drugs that prolong the QT interval is not recommended. If concurrent therapy is considered essential, ECG monitoring is recommended. In addition, because of the potential risk and severity of serotonin syndrome, caution should be observed when administering citalopram with other drugs that have serotonergic properties such as tricyclic antidepressants. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. Clinicians should also be alert for pharmacokinetic interactions between tricyclic antidepressants (TCAs) and SSRIs. Citalopram is a weak inhibitor of CYP2D6, the isoenzyme responsible for metabolism of many of the tricyclic antidepressants. Coadministration of citalopram and imipramine did not significantly affect the plasma concentrations of either drug. However, the concentration of desipramine, the primary metabolite of imipramine, was increased by 50%. The clinical significance of the elevation in desipramine concentration is unknown. However, symptoms of toxicity, including seizures, have been reported when drugs from these 2 classes were used together. A decreased dosage of the TCA or the avoidance of concomitant SSRI therapy should be considered.

Clinical Management

avoid combination unless benefit outweighs potential risk :: monitor for signs or symptoms of serotonin syndrome :: monitor ECG :: monitor for fast, irregular heartbeat :: dosage reduction may be required

References

CredibleMeds. Drugs to avoid in congenital long QT. Available on the World Wide Web at http://www.crediblemeds.org. :: Celexa (citalopram) package insert. Irvine, CA: Allergan USA, Inc.; 2017 Jan. :: Nora Goldschlager, Andrew E Epstein, Blair P Grubb, et al. Etiologic considerations in the patient with syncope and an apparently normal heart. Arch Intern Med 2003;163:151-62. :: Hansten PD, Horn JR. Drug Interactions with Drugs that Increase QTc Intervals. In: The Top 100 Drug Interactions - A Guide to Patient Management. 2007 Edition. Freeland, WA: H&H Publications; 2007:144-8.

Interacting Drug CYCLOBENZAPRINE

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Concurrent use of tryptophan and a selective serotonin reuptake inhibitor (SSRI) is not recommended. Since tryptophan is converted to serotonin, the use of tryptophan in patients receiving SSRIs could lead to serotonin excess and, potentially, the serotonin syndrome presenting as agitation, restlessness, aggressive behavior, insomnia, poor concentration, headache, paresthesia, incoordination, worsening of obsessive thoughts or compulsive behaviors, nausea, abdominal cramps, diarrhea, palpitations, or chills. Discontinuation of tryptophan usually resolves symptoms.

Clinical Management

never use this combination :: avoid combination unless benefit outweighs potential risk :: monitor for signs or symptoms of serotonin syndrome

References

Zoloft(R) (sertraline) package insert. New York, NY: Pfizer; 2003 Sept. :: Prozac(R) (fluoxetine hydrochloride). Indianapolis, IN: Eli Lilly and Company; 2003 Nov. :: Stahlmann R, Lode H: Toxicity of quinolones. Drugs. 1999;58(Suppl 2):37-42.

Interacting Drug TRAMADOL

Alert level MAJOR

Documentation Level Established

Professional Notes

Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering citalopram with other drugs that have serotonergic properties such as tramadol. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. Several cases of serotonin syndrome have been reported after the administration of tramadol with an SSRI. The combination of SSRIs and tramadol has also been associated with an increased risk of seizures. Post-marketing reports implicate the concurrent use of SSRIs with tramadol in some cases of seizures. Lastly, citalopram is a weak inhibitor of CYP2D6. The analgesic activity of tramadol is due to the activity of both the parent drug and the O-desmethyltramadol metabolite (M1), and M1 formation is dependent on CYP2D6. Therefore, use of tramadol with a CYP2D6-inhibitor may alter tramadol efficacy. In addition, inhibition of CYP2D6 metabolism is expected to result in reduced metabolic clearance of tramadol. This in turn may increase the risk of tramadol-related adverse events including serotonin syndrome and seizures. If serotonin syndrome is suspected, citalopram and concurrent serotonergic agents should be discontinued.

Clinical Management

monitor for signs of drug toxicity :: monitor for altered clinical response to drug therapy :: monitor for signs or symptoms of serotonin syndrome :: monitor for seizure activity

References

Celexa (citalopram) package insert. Irvine, CA: Allergan USA, Inc.; 2017 Jan. :: Ultram (tramadol hydrochloride) tablets package insert. Titusville, NJ; Janssen Pharmaceuticals, Inc.; 2017 Aug. :: Kesavan S, Sobala GM. Serotonin syndrome with fluoxetine plus tramadol. J R Soc Med. 1999;92:474-5. :: Egberts AC, ter Borgh J, Brodie-Meijer CC. Serotonin syndrome attributed to tramadol addition to paroxetine therapy. Int Clin Psychopharmacol 1997;12:181-2.

CYCLOBENZAPRINE

Interacting Drug AMITRIPTYLINE

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

The concomitant use of tryptophan with tricyclic antidepressants should be avoided. Since tryptophan is converted to serotonin (5-hydroxytryptamine), the use of tryptophan in patients receiving drugs with serotonergic activity could lead to serotonin syndrome. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. If serotonin syndrome is suspected, the tricyclic antidepressant and concurrent serotonergic agents should be discontinued.

Clinical Management

avoid combination unless benefit outweighs potential risk :: monitor for signs or symptoms of serotonin syndrome

References

Ener RA, Meglathery SB, Van Decker WA, et al. Serotonin syndrome and other serotonergic disorders. Pain Med 2003;4:63-74.

Interacting Drug CITALOPRAM

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Concurrent use of tryptophan and a selective serotonin reuptake inhibitor (SSRI) is not recommended. Since tryptophan is converted to serotonin, the use of tryptophan in patients receiving SSRIs could lead to serotonin excess and, potentially, the serotonin syndrome presenting as agitation, restlessness, aggressive behavior, insomnia, poor concentration, headache, paresthesia, incoordination, worsening of obsessive thoughts or compulsive behaviors, nausea, abdominal cramps, diarrhea, palpitations, or chills. Discontinuation of tryptophan usually resolves symptoms.

Clinical Management

never use this combination :: avoid combination unless benefit outweighs potential risk :: monitor for signs or symptoms of serotonin syndrome

References

Zoloft(R) (sertraline) package insert. New York, NY: Pfizer; 2003 Sept. :: Prozac(R) (fluoxetine hydrochloride). Indianapolis, IN: Eli Lilly and Company; 2003 Nov. :: Stahlmann R, Lode H: Toxicity of quinolones. Drugs. 1999;58(Suppl 2):37-42.

Interacting Drug OXYCODONE

Alert level MAJOR

Documentation Level Established

Professional Notes

Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone or oxycodone; naloxone is initiated in a patient taking a skeletal muscle relaxant, use an initial dose of oxycodone at one-third to one-half the usual dosage and titrate to clinical response; reduced initial doses of oxycodone; naltrexone, aspirin, ASA; oxycodone, and ibuprofen; oxycodone are also recommended. If a decision is made to start treatment with acetaminophen; oxycodone extended-release tablets, start with 1 tablet PO every 12 hours. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Clinical Management

monitor blood pressure :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for an increase in CNS/respiratory depression

References

Ibuprofen and oxycodone tablet package insert. Elizabeth, NJ: Actavis Elizabeth LLC; 2017 Jan. :: OxyContin (oxycodone HCl extended-release) package insert. Stamford, CT: Purdue Pharma L.P.; 2016 Dec. :: Xartemis XR (acetaminophen; oxycodone) extended-release tablets. Hazelwood MO: Mallinckrodt Brand Pharmaceuticals, Inc.; 2016 Dec. :: Targiniq ER (oxycodone; naloxone) extended-release tablet package insert. Stamford, CT: Purdue Pharma L.P.; 2016 Dec. :: Percodan (aspirin; oxycodone) tablet package insert. Malvern, PA: Endo Pharmaceuticals Inc.; 16 Dec. :: Troxyca ER (oxycodone hydrochloride; naltrexone hydrochloride) extended-release capsules package insert. New York, NY: Pfizer, Inc.; 2016 Dec. :: Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

Interacting Drug TRAMADOL

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Additionally, concurrent use of tramadol and cyclobenzaprine increases the possibility of developing serotonin syndrome. If these drugs must be used together, closely monitor the patient for signs and symptoms of serotonin syndrome. If such a reaction develops, immediately discontinue cyclobenzaprine and tramadol. Cyclobenzaprine may enhance the risk of seizures in patients taking tramadol.

Clinical Management

consider alternative drug therapy :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for signs or symptoms of serotonin syndrome :: monitor for an increase in CNS/respiratory depression

References

Flexeril (cyclobenzaprine) package insert. Fort Washington, PA: McNeil Consumer Healthcare; 2013 Apr. :: Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

OXYCODONE

Interacting Drug ALPRAZOLAM

Alert level MAJOR

Documentation Level Established

Professional Notes

Concomitant use of opiate agonists with benzodiazepines may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with benzodiazepines to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone is initiated in a patient taking a benzodiazepine, reduce dosages and titrate to clinical response. For acetaminophen; oxycodone extended-release tablets, start with 1 tablet PO every 12 hours, and for other oxycodone products, use an initial dose of oxycodone at one-third to one-half the usual dosage. If a benzodiazepine is prescribed for an indication other than epilepsy in a patient taking an opiate agonist, use a lower initial dose of the benzodiazepine and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Clinical Management

monitor blood pressure :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for an increase in CNS/respiratory depression

References

Ibuprofen and oxycodone tablet package insert. Elizabeth, NJ: Actavis Elizabeth LLC; 2017 Jan. :: OxyContin (oxycodone HCl extended-release) package insert. Stamford, CT: Purdue Pharma L.P.; 2016 Dec. :: Xartemis XR (acetaminophen; oxycodone) extended-release tablets. Hazelwood MO: Mallinckrodt Brand Pharmaceuticals, Inc.; 2016 Dec. :: Percodan (aspirin; oxycodone) tablet package insert. Malvern, PA: Endo Pharmaceuticals Inc.; 16 Dec. :: Troxyca ER (oxycodone hydrochloride; naltrexone hydrochloride) extended-release capsules package insert. New York, NY: Pfizer, Inc.; 2016 Dec. :: Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

Interacting Drug CYCLOBENZAPRINE

Alert level MAJOR

Documentation Level Established

Professional Notes

Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone or oxycodone; naloxone is initiated in a patient taking a skeletal muscle relaxant, use an initial dose of oxycodone at one-third to one-half the usual dosage and titrate to clinical response; reduced initial doses of oxycodone; naltrexone, aspirin, ASA; oxycodone, and ibuprofen; oxycodone are also recommended. If a decision is made to start treatment with acetaminophen; oxycodone extended-release tablets, start with 1 tablet PO every 12 hours. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Clinical Management

monitor blood pressure :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for an increase in CNS/respiratory depression

References

Ibuprofen and oxycodone tablet package insert. Elizabeth, NJ: Actavis Elizabeth LLC; 2017 Jan. :: OxyContin (oxycodone HCl extended-release) package insert. Stamford, CT: Purdue Pharma L.P.; 2016 Dec. :: Xartemis XR (acetaminophen; oxycodone) extended-release tablets. Hazelwood MO: Mallinckrodt Brand Pharmaceuticals, Inc.; 2016 Dec. :: Targiniq ER (oxycodone; naloxone) extended-release tablet package insert. Stamford, CT: Purdue Pharma L.P.; 2016 Dec. :: Percodan (aspirin; oxycodone) tablet package insert. Malvern, PA: Endo Pharmaceuticals Inc.; 16 Dec. :: Troxyca ER (oxycodone hydrochloride; naltrexone hydrochloride) extended-release capsules package insert. New York, NY: Pfizer, Inc.; 2016 Dec. :: Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

Interacting Drug TRAMADOL

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Concomitant use of tramadol increases the seizure risk in patients taking opiate agonists. Also, tramadol can cause additive CNS depression and respiratory depression when used with opiate agonists; avoid concurrent use whenever possible. If used together, extreme caution is needed, and a reduced tramadol dose is recommended.

Clinical Management

avoid combination unless benefit outweighs potential risk :: monitor for an increase in CNS/respiratory depression :: dosage reduction may be required

References

Ultram (tramadol hydrochloride) tablets package insert. Titusville, NJ; Janssen Pharmaceuticals, Inc.; 2017 Aug.

TRAMADOL

Interacting Drug ALPRAZOLAM

Alert level MAJOR

Documentation Level Established

Professional Notes

Concomitant use of opiate agonists with benzodiazepines may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with benzodiazepines to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a benzodiazepine, use a lower initial dose of the opiate and titrate to clinical response. If a benzodiazepine is prescribed for an indication other than epilepsy in a patient taking an opiate agonist, use a lower initial dose of the benzodiazepine and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Clinical Management

consider alternative drug therapy :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for an increase in CNS/respiratory depression

References

Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

Interacting Drug AMITRIPTYLINE

Alert level MAJOR

Documentation Level Established

Professional Notes

Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering tricyclic antidepressants (TCAs) with other drugs that have serotonergic properties such as tramadol. Both tramadol and TCAs inhibit the central reuptake of serotonin. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. In addition, in vitro drug interaction studies in human liver microsomes indicate that amitriptyline may inhibit the metabolism of tramadol via CYP2D6, suggesting that concomitant administration of TCAs could result in increases in tramadol concentrations and decreased concentrations of M1. The full pharmacological impact of these alterations in terms of either efficacy or safety is unknown. Tricyclic antidepressants may decrease the seizure threshold and have been associated with increased risk of seizures when given concurrently with tramadol.

Clinical Management

monitor for signs of drug toxicity :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for signs or symptoms of serotonin syndrome :: monitor for seizure activity

References

Kahn LH, Alderfer RJ, Graham DJ. Seizures reported with tramadol. JAMA 1997;278:1661. :: Ultram (tramadol hydrochloride) tablets package insert. Titusville, NJ; Janssen Pharmaceuticals, Inc.; 2017 Aug. :: Ener RA, Meglathery SB, Van Decker WA, et al. Serotonin syndrome and other serotonergic disorders. Pain Med 2003;4:63-74.

Interacting Drug CITALOPRAM

Alert level MAJOR

Documentation Level Established

Professional Notes

Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering citalopram with other drugs that have serotonergic properties such as tramadol. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. Several cases of serotonin syndrome have been reported after the administration of tramadol with an SSRI. The combination of SSRIs and tramadol has also been associated with an increased risk of seizures. Post-marketing reports implicate the concurrent use of SSRIs with tramadol in some cases of seizures. Lastly, citalopram is a weak inhibitor of CYP2D6. The analgesic activity of tramadol is due to the activity of both the parent drug and the O-desmethyltramadol metabolite (M1), and M1 formation is dependent on CYP2D6. Therefore, use of tramadol with a CYP2D6-inhibitor may alter tramadol efficacy. In addition, inhibition of CYP2D6 metabolism is expected to result in reduced metabolic clearance of tramadol. This in turn may increase the risk of tramadol-related adverse events including serotonin syndrome and seizures. If serotonin syndrome is suspected, citalopram and concurrent serotonergic agents should be discontinued.

Clinical Management

monitor for signs of drug toxicity :: monitor for altered clinical response to drug therapy :: monitor for signs or symptoms of serotonin syndrome :: monitor for seizure activity

References

Celexa (citalopram) package insert. Irvine, CA: Allergan USA, Inc.; 2017 Jan. :: Ultram (tramadol hydrochloride) tablets package insert. Titusville, NJ; Janssen Pharmaceuticals, Inc.; 2017 Aug. :: Kesavan S, Sobala GM. Serotonin syndrome with fluoxetine plus tramadol. J R Soc Med. 1999;92:474-5. :: Egberts AC, ter Borgh J, Brodie-Meijer CC. Serotonin syndrome attributed to tramadol addition to paroxetine therapy. Int Clin Psychopharmacol 1997;12:181-2.

Interacting Drug CYCLOBENZAPRINE

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Additionally, concurrent use of tramadol and cyclobenzaprine increases the possibility of developing serotonin syndrome. If these drugs must be used together, closely monitor the patient for signs and symptoms of serotonin syndrome. If such a reaction develops, immediately discontinue cyclobenzaprine and tramadol. Cyclobenzaprine may enhance the risk of seizures in patients taking tramadol.

Clinical Management

consider alternative drug therapy :: decrease drug dosage :: warn against driving or operating machinery or performing other hazardous tasks until drug effects are known :: monitor for signs or symptoms of serotonin syndrome :: monitor for an increase in CNS/respiratory depression

References

Flexeril (cyclobenzaprine) package insert. Fort Washington, PA: McNeil Consumer Healthcare; 2013 Apr. :: Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm. Retrieved August 31, 2016.

Interacting Drug OXYCODONE

Alert level MAJOR

Documentation Level Likely Established

Professional Notes

Concomitant use of tramadol increases the seizure risk in patients taking opiate agonists. Also, tramadol can cause additive CNS depression and respiratory depression when used with opiate agonists; avoid concurrent use whenever possible. If used together, extreme caution is needed, and a reduced tramadol dose is recommended.

Clinical Management

avoid combination unless benefit outweighs potential risk :: monitor for an increase in CNS/respiratory depression :: dosage reduction may be required

References

Ultram (tramadol hydrochloride) tablets package insert. Titusville, NJ; Janssen Pharmaceuticals, Inc.; 2017 Aug.