

Centrally acting antihypertensives

Agents that reduce sympathetic outflow from the central nervous system rather than blocking receptors in the periphery, valued in resistant hypertension and in pregnancy but defined by sedation and by rebound hypertension on abrupt withdrawal.

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Quick revision

One Liner: These agents work upstream of the vessel: by agonising central alpha-2 receptors they reduce sympathetic outflow from the brain, so blood pressure and heart rate fall - and stopping them suddenly releases that suppressed outflow as rebound hypertension.

1. Clonidine is a central alpha-2 adrenergic and imidazoline receptor agonist that lowers blood pressure and heart rate by decreasing sympathetic outflow. [1]
2. Methyldopa is converted centrally to methyl norepinephrine, which reduces adrenergic outflow through alpha-2 agonism and lowers total peripheral resistance. [2]
3. Alpha-2 receptors sit on peripheral nerve endings too, where activation inhibits norepinephrine release - the same feedback logic exploited centrally. [5]
4. Abrupt discontinuation of clonidine may induce a hypertensive crisis, so the drug is tapered to avoid rebound hypertension. [1]
5. Rebound hypertension is also listed among the adverse effects of methyldopa, so the withdrawal caution is not unique to clonidine. [2]
6. When clonidine is being withdrawn from a patient also taking a beta blocker, the beta blocker is stopped several days earlier. [1]
7. Rebound hypertension can be reversed with oral clonidine or with intravenous phentolamine. [1]
8. Clonidine is typically reserved for treatment-resistant hypertension and is regarded as a last-line antihypertensive because of central nervous system adverse effects. [1]
9. Central alpha-2 agonists appear in the Beers criteria as potentially inappropriate in older adults with hypertension. [1]
10. Methyldopa's alpha-2 action does not reduce cardiac output or renal blood flow, which is why it suits hypertension with renal insufficiency. [2]
11. Methyldopa remains a second-line agent used safely in pregnancy, where it has no teratogenic effects. [2]
12. Coombs-positive haemolytic anaemia, hepatotoxicity and a lupus-like syndrome are the rare but serious methyldopa reactions. [2]
13. Sedation, dry mouth, dizziness and fatigue are the everyday problems that limit how tolerable this class is. [1][2]
14. Guanfacine tablets are used alone or with other medicines to treat high blood pressure, lowering it by slowing heart rate and relaxing blood vessels. [3]

Overview

1. Centrally acting antihypertensives lower blood pressure by reducing sympathetic outflow from the central nervous system rather than by acting on a receptor in the vessel wall. Clonidine, the prototype, is an imidazoline derivative that agonises central alpha-2 adrenergic receptors; acting in the nucleus tractus solitarius it excites a pathway that inhibits excitatory cardiovascular neurons, and the resulting reduction in central sympathetic outflow produces a clinically significant fall in arterial pressure. [1]
2. Methyldopa reaches the same end by a different route. It is converted centrally to methyl norepinephrine, and that

metabolite decreases adrenergic outflow through alpha-2 agonism, lowering total peripheral resistance and systemic blood pressure. Notably, its alpha-2 activity does not affect cardiac output or renal blood flow, which is why it retains a role in hypertension complicated by renal insufficiency. [2]

3. The logic of alpha-2 agonism is familiar from the periphery, where alpha-2 receptors on nerve endings inhibit norepinephrine release when activated, forming a feedback loop that limits sympathetic transmission. Centrally acting agents simply harness that same braking mechanism at the level of the brainstem instead of the synapse. [5][1]

4. Neither drug is a modern first choice. Clonidine is typically reserved for treatment-resistant hypertension and is regarded as last-line because of central nervous system adverse effects, particularly in older adults, and central alpha-2 agonists appear in the Beers criteria as potentially inappropriate in that group. Methyldopa's use has fallen markedly in favour of better-tolerated alternatives, though it persists where cost matters and as a second-line agent used safely in pregnancy. [1][2]

5. What keeps the class examinable is the withdrawal problem. Sustained suppression of central sympathetic outflow leaves the system primed, and abrupt discontinuation releases it: clonidine withdrawal may induce a hypertensive crisis, and rebound hypertension is listed among methyldopa's adverse effects as well. Tapering, and getting the order right when a beta blocker is also being stopped, is therefore part of using these drugs at all. [1][2]

Classification and drug examples

Intro: A small class, most usefully divided by whether the agent is a direct central alpha-2 agonist or a prodrug converted to one centrally. The distinction matters because it explains why methyldopa carries an immunological adverse effect profile that clonidine does not.

1. Name: Direct central alpha-2 agonists

1. Note: Agonise central alpha-2 adrenergic receptors themselves, reducing sympathetic outflow without needing conversion.

1. Name: Clonidine

Clonidine hydrochloride

1. Route: Oral, transdermal, epidural

1. Note: Also an imidazoline receptor agonist. Approved for adult hypertension, attention-deficit hyperactivity disorder in children, tics in Tourette syndrome and as an adjunct in severe cancer-related pain. [1]

2. Name: Guanfacine

2. Route: Oral

2. Note: Tablets are used alone or with other medications for high blood pressure, which they lower by decreasing heart rate and relaxing blood vessels. [3]

3. Name: Moxonidine

3. Route: Oral

3. Note: A further centrally acting agent named here for completeness; it is not covered by the sources cited on this page and no claims about it are made. [1] [1]

2. Name: Centrally converted prodrug

2. Note: Requires central conversion to an active alpha-2 agonist metabolite, and carries a distinct set of rare immunological and hepatic reactions.

Name: Methyldopa

Alpha-methyldopa

Route: Oral, IV

Note: Converted centrally to methyl norepinephrine. Second-line overall but used safely in pregnancy, where it has no teratogenic effects; intramuscular and subcutaneous routes are not recommended because absorption is unpredictable. [2] [2]

Mechanism of action

Summary: These agents stimulate alpha-2 adrenergic receptors within the central nervous system, reducing sympathetic outflow to the heart and vasculature so that peripheral resistance, blood pressure and heart rate all fall.

Target: Central alpha-2 adrenergic receptors, and for clonidine imidazoline receptors as well

Cidal Static: receptor agonist

Kill Kinetics: sustained central sympathetic suppression

1. Step: 1

1. Title: Alpha-2 receptors act as a brake on sympathetic transmission

1. Detail: Alpha-2 adrenergic receptors on peripheral nerve endings inhibit norepinephrine release when activated, creating a feedback mechanism that regulates sympathetic output. [5]

2. Step: 2

2. Title: The drug reaches central alpha-2 receptors

2. Detail: Clonidine is highly lipid-soluble and readily distributed within the central nervous system, which is what allows a peripheral dose to act centrally. [1]

3. Step: 3

3. Title: Central agonism inhibits excitatory cardiovascular neurons

3. Detail: Acting as an alpha-adrenergic agonist in the nucleus tractus solitarii, clonidine excites a pathway that inhibits excitatory cardiovascular neurons and ultimately reduces sympathetic outflow from the central nervous system. [1]

4. Step: 4

4. Title: Methyldopa needs converting first

4. Detail: Methyldopa is converted centrally to methyl norepinephrine, and it is that metabolite whose alpha-2 agonism reduces adrenergic outflow. [2]

5. Step: 5

5. Title: Peripheral resistance and blood pressure fall

5. Detail: Reduced sympathetic outflow relaxes arterial smooth muscle and lowers total peripheral resistance; for methyldopa this occurs without an effect on cardiac output or renal blood flow. [2][1]

6. Step: 6

6. Title: Chronic suppression sets up the rebound

6. Detail: Because the suppression is of outflow rather than of a receptor at the effector, abrupt removal of the drug allows sympathetic activity to return sharply, producing rebound hypertension and withdrawal symptoms. [1]

Major clinical uses

1. Drug: Clonidine

1. Organism: Not applicable

1. Indication: Adult hypertension, typically treatment-resistant, alone or preferably alongside other antihypertensive agents

1. Line: last-line

1. Note: Reserved late because of central nervous system adverse effects, especially in older adults. [1]

2. Drug: Clonidine

2. Organism: Not applicable

2. Indication: Attention-deficit hyperactivity disorder in children, and tics associated with Tourette syndrome

2. Line: targeted

2. Note: The extended-release dose form and extended-release suspension carry the approval for the attention-deficit indication. [1]

3. Drug: Clonidine

3. Organism: Not applicable

3. Indication: Adjunct therapy in severe cancer-related pain
3. Line: adjunct
3. Note: Given by the epidural route in this setting, where alpha-2 receptors in the dorsal horn reduce pain transmission. [1]
4. Drug: Clonidine
4. Organism: Not applicable
4. Indication: Investigation of pheochromocytoma by the clonidine suppression test
4. Line: diagnostic
4. Note: Catecholamine levels are measured before and after an oral dose; in healthy individuals they fall. [1]
5. Drug: Methyldopa
5. Organism: Not applicable
5. Indication: Hypertension in pregnancy
5. Line: second-line
5. Note: Retained for this role because it has no teratogenic effects and can be used safely in pregnancy. [2]
6. Drug: Methyldopa
6. Organism: Not applicable
6. Indication: Hypertension complicated by renal insufficiency
6. Line: second-line
6. Note: Its alpha-2 agonism lowers peripheral resistance without affecting cardiac output or renal blood flow. [2]
7. Drug: Guanfacine
7. Organism: Not applicable
7. Indication: High blood pressure, alone or in combination with other medications
7. Line: second-line
7. Note: Lowers blood pressure by decreasing heart rate and relaxing blood vessels. [3]

Pharmacokinetics

1. Drug: Clonidine
1. Route: Oral, transdermal, epidural
1. Absorption: Rapidly absorbed orally within hours; the extended-release form is slower and the transdermal form is absorbed steadily across a week
1. Csf Penetration: Highly lipid-soluble and readily distributed within the central nervous system
1. Metabolism: Enterohepatic recirculation after oral administration, with CYP2D6 predominant in non-renal clearance
1. Elimination: Much of an oral dose recovered unchanged in the urine within a day
1. Half Life: Several hours to the better part of a day, and substantially longer in renal impairment
1. Dose Adjust: Renal impairment; start low and titrate cautiously with monitoring for hypotension and bradycardia [1]
2. Drug: Methyldopa
2. Route: Oral, IV
2. Absorption: About half of an oral dose is absorbed, with peak plasma concentrations within several hours
2. Csf Penetration: Acts centrally after conversion to methyl norepinephrine
2. Metabolism: Converted centrally to the active metabolite methyl norepinephrine
2. Elimination: See a current prescribing reference
2. Half Life: See a current prescribing reference
2. Dose Adjust: Avoid in active hepatic disease; intramuscular and subcutaneous routes are not recommended because absorption is unpredictable [2]
1. Clonidine is available as immediate-release tablets, extended-release tablets, transdermal patches, oral suspension and injectable solution, and the different formulations are not interchangeable on a milligram-for-milligram basis. [1]
2. Conversion between oral and transdermal clonidine follows a defined stepwise schedule over several days rather

than a straight substitution. [1]

3. Clonidine crosses the placental barrier, and product labelling advises use in pregnancy only if indicated; methyldopa by contrast is the member of this class with an established place in pregnancy. [1][2]

4. This page gives no dose regimens by design. Doses depend on the indication, the formulation, renal function, age and comorbidity, and belong in a prescribing reference used by the treating clinician.

Adverse effects

1. Effect: Sedation and fatigue

1. Detail: Among the central nervous system effects that make this class hard to tolerate and that drive its low position in treatment sequences. [1]

2. Effect: Dry mouth

2. Detail: Xerostomia is one of the commonly observed reactions to clonidine, and dry mouth is also reported with methyldopa. [1][2]

3. Effect: Hypotension and dizziness

3. Detail: Direct consequences of reduced sympathetic outflow. [1][2]

4. Effect: Gastrointestinal upset

4. Detail: Constipation, diarrhoea, nausea and abdominal pain are all reported. [1][2]

5. Effect: Headache

5. Detail: Reported with both clonidine and methyldopa. [1][2]

6. Effect: Sexual dysfunction and emotional instability

6. Detail: Listed among the commonly observed reactions to clonidine. [1]

1. Effect: Rebound hypertension on abrupt discontinuation

1. Detail: Abrupt discontinuation may produce rebound hypertension and withdrawal symptoms, and rare cases of hypertensive encephalopathy, stroke and death have been reported.

1. Action: Taper over several weeks; where a beta blocker is also being stopped, discontinue it several days earlier. Rebound can be reversed with oral clonidine or intravenous phentolamine. [1]

2. Effect: Bradycardia and atrioventricular block

2. Detail: Listed among the serious reactions to clonidine.

2. Action: Dose adjustment is needed in bradycardia, hypotension, cardiovascular disease and severe coronary artery disease. [1]

3. Effect: Syncope and severe hypotension

3. Detail: Serious reactions reflecting the same mechanism that produces the therapeutic effect.

3. Action: Caution in patients with a history of syncope or recent myocardial infarction. [1]

4. Effect: Angioedema, hypersensitivity and depression

4. Detail: Further serious reactions attributed to clonidine.

4. Action: Caution in patients with a history of depression. [1]

5. Effect: Coombs-positive haemolytic anaemia

5. Detail: A rare but clinically serious methyldopa reaction, and one that becomes a contraindication once established.

5. Action: Established direct Coombs-positive haemolytic anaemia contraindicates continued use. [2]

6. Effect: Hepatotoxicity, myocarditis and pancreatitis

6. Detail: Further rare but potentially fatal methyldopa reactions, alongside a lupus-like syndrome, immune thrombocytopenia and reversible leukopenia.

6. Action: Active hepatic disease, and liver disorders arising from previous therapy, contraindicate the drug. [2]

1. Drug: Clonidine

1. Effect: Overdose characteristically begins with hypertension from peripheral alpha-2 stimulation before progressing to hypotension, bradycardia, respiratory depression, drowsiness, coma, seizures, hypothermia and miosis. [1]

2. Drug: Methyldopa

2. Effect: Involuntary choreoathetotic movements and weight gain are listed among its recognised adverse effects. [2]
3. Drug: Clonidine in breastfeeding
3. Effect: Potential risk of infant sedation, hypotonia and apnoea, and a theoretical reduction in milk production through lowered prolactin, so other antihypertensives are generally preferred. [1]

Contraindications, precautions and interactions

1. Hypersensitivity to clonidine or to any excipient of its formulation. [1]
2. Epidural clonidine administered above the C4 dermatome. [1]
3. Active hepatic disease, or liver disorders arising from previous methyldopa therapy. [2]
4. Established direct Coombs-positive haemolytic anaemia, for methyldopa. [2]
5. Pheochromocytoma and a significant history of monoamine oxidase inhibitor therapy, for methyldopa. [2]
6. Known hypersensitivity to methyldopa in any form. [2]
1. Renal impairment, where clonidine's half-life lengthens substantially and cautious titration with monitoring for hypotension and bradycardia is required. [1]
2. Cardiovascular disease, bradycardia, hypotension and severe coronary artery disease, all of which require dose adjustment. [1]
3. A history of depression, recent myocardial infarction or syncope. [1]
4. Older adults, in whom central alpha-2 agonists are listed as potentially inappropriate for hypertension. [1]
5. Children on clonidine, in whom vomiting from common illnesses may precipitate withdrawal-related hypertensive episodes. [1]
6. Breastfeeding, where other antihypertensive medicines are generally preferred over clonidine. [1]
1. With: Beta blockers
1. Effect: Abrupt withdrawal of clonidine in a patient taking a beta blocker may precipitate rebound hypertension through unopposed sympathetic activity; the beta blocker is discontinued several days before the clonidine taper. [4][1]
2. With: Other antihypertensive agents
2. Effect: Additive blood pressure lowering; clonidine is preferably used alongside other agents in resistant hypertension, which makes hypotension a shared risk. [1]
3. With: Neuraxial opioids and fentanyl
3. Effect: Epidural clonidine enhances the effect of neuraxial opioids and interacts additively with fentanyl. [1]
4. With: Monoamine oxidase inhibitors
4. Effect: A significant history of monoamine oxidase inhibitor therapy contraindicates methyldopa. [2]

Comparison tables

Title: Clonidine and methyldopa side by side

Caption: Both reduce central sympathetic outflow, but they differ in whether conversion is needed, in where they sit in practice and in which serious reactions they carry. Actual therapy is governed by a current prescribing reference.

1. Key: feature
1. Label: Feature
1. Is Row Header: true
2. Key: clonidine
2. Label: Clonidine
3. Key: methyldopa
3. Label: Methyldopa
1. Feature: Mechanism
1. Clonidine: Direct central alpha-2 adrenergic and imidazoline receptor agonist
1. Methyldopa: Converted centrally to methyl norepinephrine, which is the alpha-2 agonist [1][2]
2. Feature: Position in practice

2. Clonidine: Treatment-resistant hypertension; regarded as last-line
2. Methyldopa: Second-line; retained for pregnancy and where cost matters [1][2]
3. Feature: Effect on cardiac output and renal blood flow
3. Clonidine: Reduces heart rate as well as blood pressure
3. Methyldopa: Alpha-2 activity does not affect cardiac output or renal blood flow [1][2]
4. Feature: Use in pregnancy
4. Clonidine: Crosses the placenta; labelling advises use only if indicated
4. Methyldopa: Used safely in pregnancy, with no teratogenic effects [1][2]
5. Feature: Distinctive serious reactions
5. Clonidine: Bradycardia, atrioventricular block, angioedema, severe hypotension
5. Methyldopa: Coombs-positive haemolytic anaemia, hepatotoxicity, lupus-like syndrome [1][2]
6. Feature: Withdrawal
6. Clonidine: Abrupt stop may induce hypertensive crisis; taper over several weeks
6. Methyldopa: Rebound hypertension is listed among its adverse effects [1][2]
7. Feature: Non-cardiovascular roles
7. Clonidine: Attention-deficit hyperactivity disorder, Tourette tics, severe cancer pain, substance withdrawal
7. Methyldopa: No comparable approved roles outside blood pressure [1][2]

High-yield exam pearls

1. Pearl: The site of action, not the receptor, is what defines this class.
1. Why: An alpha-2 agonist stimulating receptors in the brainstem reduces sympathetic outflow to the whole cardiovascular system, which is a fundamentally different lever from blocking a receptor on a single vessel wall. [1]
2. Pearl: Methyldopa is a prodrug in the truest sense.
2. Why: It is converted centrally to methyl norepinephrine, and it is that metabolite which produces the alpha-2 agonism responsible for reduced adrenergic outflow and lower peripheral resistance. [2]
3. Pearl: Rebound hypertension is the signature hazard of the class.
3. Why: Suppressed central sympathetic outflow is released when the drug stops abruptly; for clonidine this can amount to a hypertensive crisis, and rare cases of hypertensive encephalopathy, stroke and death have been reported. [1]
4. Pearl: The order of withdrawal matters when a beta blocker is also involved.
4. Why: Clonidine is tapered over several weeks with the beta blocker discontinued several days earlier, because abrupt clonidine withdrawal in the presence of beta blockade leaves the sympathetic surge acting on unopposed alpha receptors. [1][4]
5. Pearl: Methyldopa's selling point is what it does not do.
5. Why: Its alpha-2 agonism lowers total peripheral resistance without affecting cardiac output or renal blood flow, which is why it is described as useful in hypertensive patients with renal insufficiency. [2]
6. Pearl: A positive direct Coombs test is a methyldopa question until proven otherwise.
6. Why: Coombs-positive haemolytic anaemia is listed among its rare but clinically serious reactions, and established direct Coombs-positive haemolytic anaemia is a contraindication to the drug. [2]
7. Pearl: Clonidine has a diagnostic use as well as a therapeutic one.
7. Why: The clonidine suppression test measures catecholamine levels before and after an oral dose; in healthy individuals circulating catecholamines fall, which is the basis of its use in investigating pheochromocytoma. [1]
8. Pearl: Clonidine overdose starts by looking like the opposite of what the drug does.
8. Why: Early hypertension from peripheral alpha-2 stimulation precedes the expected hypotension, bradycardia, sedation and respiratory depression, so an early normal or high blood pressure does not exclude serious poisoning. [1]

Common exam traps

1. Trap: "Clonidine is a first-line antihypertensive."
1. Correction: It is typically used for treatment-resistant hypertension and is reserved as a last-line agent because of its central nervous system adverse effects, especially in older adults. [1]
2. Trap: "Only clonidine causes rebound hypertension."
2. Correction: Rebound hypertension is listed among the adverse effects of methyldopa as well, so the caution about abrupt withdrawal applies across the class rather than to one drug. [2][1]
3. Trap: "Stopping the beta blocker and the clonidine together is the tidy approach."
3. Correction: Clonidine is tapered over several weeks and the beta blocker is discontinued several days before that taper, not alongside it. [1]
4. Trap: "Methyldopa is obsolete."
4. Correction: Its use has fallen markedly, but it is still used where cost matters and it remains a second-line agent used safely in pregnancy, where it has no teratogenic effects. [2]
5. Trap: "Clonidine formulations can be swapped milligram for milligram."
5. Correction: Immediate-release and extended-release clonidine are not interchangeable, and conversion between oral and transdermal routes follows a defined stepwise schedule. [1]
6. Trap: "A hypertensive reading early after a clonidine overdose rules out toxicity."
6. Correction: Overdose characteristically begins with hypertension from peripheral alpha-2 stimulation before progressing to hypotension, bradycardia and central nervous system depression. [1]

Self-test questions

1. Question: How does clonidine lower blood pressure?
1. By blocking alpha-1 receptors on vascular smooth muscle
2. By agonising central alpha-2 adrenergic and imidazoline receptors, reducing sympathetic outflow from the central nervous system
3. By blocking calcium entry through L-type channels in the vessel wall
4. By inhibiting angiotensin-converting enzyme
1. Explanation: Clonidine is a central alpha-2 adrenergic and imidazoline receptor agonist. Acting in the nucleus tractus solitarius and reducing sympathetic outflow from the central nervous system produces a clinically significant fall in arterial blood pressure and in heart rate. [1]
2. Question: Why is methyldopa described as a centrally acting sympatholytic rather than a direct vasodilator?
1. It is converted centrally to methyl norepinephrine, which reduces adrenergic outflow by alpha-2 agonism
2. It dilates arterioles directly by opening potassium channels
3. It blocks the sodium-potassium pump in vascular smooth muscle
4. It acts only on the renal vasculature
2. Explanation: Alpha-methyldopa is converted centrally to methyl norepinephrine, and that metabolite decreases adrenergic outflow from the central nervous system through alpha-2 agonistic action, lowering total peripheral resistance and systemic blood pressure. [2]
3. Question: What is the principal hazard of stopping clonidine abruptly?
1. Profound and irreversible bradycardia
2. Rebound hypertension, potentially amounting to a hypertensive crisis
3. Acute renal failure within hours
4. Immediate loss of central alpha-2 receptors
3. Explanation: Abrupt discontinuation may induce a hypertensive crisis, so clonidine must be tapered to avoid rebound hypertension. Rare cases of hypertensive encephalopathy, stroke and death have been reported, and the rebound can be reversed with oral clonidine or intravenous phentolamine. [1]

4. Question: When clonidine is being withdrawn from a patient who is also taking a beta blocker, what is the correct sequence?

1. Both drugs are stopped on the same day
2. The clonidine is stopped first and the beta blocker continued indefinitely
3. The beta blocker is discontinued several days before the clonidine taper
4. Neither drug can ever be withdrawn

4. Explanation: Clonidine is tapered over several weeks and the beta blocker is discontinued several days earlier. Abrupt clonidine withdrawal in a patient on a beta blocker can precipitate rebound hypertension through unopposed sympathetic activity. [1][4]

5. Question: Which rare adverse effect is particularly associated with methyldopa?

1. Coombs-positive haemolytic anaemia
2. Irreversible cochlear hearing loss
3. Gingival hyperplasia
4. Photosensitive porphyria

5. Explanation: Coombs-positive haemolytic anaemia sits among methyldopa's rare but clinically serious reactions, alongside a lupus-like syndrome, myocarditis, pancreatitis, hepatotoxicity and immune thrombocytopenia. Established direct Coombs-positive haemolytic anaemia is also a contraindication to the drug. [2]

6. Question: Why is methyldopa still used in hypertensive patients with renal insufficiency?

1. Because it is renally excreted unchanged and so accumulates usefully
2. Because its alpha-2 agonistic activity does not affect cardiac output or renal blood flow
3. Because it increases glomerular filtration directly
4. Because it is the only antihypertensive that is dialysable

6. Explanation: The alpha-2 agonistic activity that lowers total peripheral resistance does not affect cardiac output or renal blood flow, which is the stated reason the drug is useful in hypertensive patients with renal insufficiency. [2]

7. Question: Which statement about clonidine in older adults is correct?

1. It is the preferred first-line antihypertensive in this group
2. Central alpha-2 agonists are listed as potentially inappropriate in older adults with hypertension because of the risk of bradycardia, hypotension and sedation
3. Age has no bearing on its adverse effect profile
4. It is contraindicated in anyone over sixty-five

7. Explanation: The American Geriatrics Society Beers Criteria list central alpha-2 agonists as potentially inappropriate for use in older adults with hypertension, and clonidine is not recommended as a first-line antihypertensive in that group because of bradycardia, hypotension and central nervous system effects such as sedation. [1]

8. Question: What is the management approach in clonidine overdose?

1. A specific competitive antidote is given immediately
2. Urgent dialysis, which markedly increases elimination
3. Supportive care, with atropine for bradycardia and fluids or vasopressors for hypotension
4. High-dose beta agonist infusion

8. Explanation: There is no specific antidote and treatment is primarily supportive: the airway is protected, bradycardia may be managed with atropine, and hypotension with intravenous fluids and vasopressors if needed. Dialysis is unlikely to increase elimination. [1]

Frequently asked questions

1. Question: Why are these called centrally acting antihypertensives?

1. Answer: Because they act on receptors inside the central nervous system rather than at the blood vessel. Reducing sympathetic outflow from the brain lowers vascular tone and heart rate throughout the body, which is a different lever from blocking a peripheral receptor. [1]

2. Question: Why must clonidine be tapered rather than stopped?

2. Answer: Because abrupt discontinuation may induce a hypertensive crisis. The drug is tapered over several weeks, and rare cases of hypertensive encephalopathy, stroke and death have been reported after sudden withdrawal. [1]

3. Question: What is done if rebound hypertension happens?

3. Answer: It can be reversed with oral clonidine or with intravenous phentolamine, the latter being a non-selective alpha blocker used for catecholamine-driven hypertension. [1][5]

4. Question: Why is methyl dopa still used in pregnancy?

4. Answer: It remains a second-line agent that can be used safely in pregnancy because it has no teratogenic effects, which is why it survives in that setting despite being displaced elsewhere by better-tolerated alternatives. [2]

5. Question: Does clonidine have uses beyond blood pressure?

5. Answer: Yes. It is approved for attention-deficit hyperactivity disorder in children, for tics associated with Tourette syndrome and as an adjunct in severe cancer-related pain, and it is used off-label in opioid, benzodiazepine and alcohol withdrawal among other settings. [1]

6. Question: Why are these drugs avoided in older adults?

6. Answer: Central alpha-2 agonists appear in the Beers criteria as potentially inappropriate in older adults with hypertension, because of a high risk of bradycardia, hypotension and central nervous system effects such as sedation. [1]

References

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