Drug Effects		
System	**Effect**	**Test**
CV	Tachycardia, palpitations, Htn with other cardiac stimulants, edema	HR, BP
HEME	Decreases effectiveness of warfarin, inhibits coagulation cascade	INR, PT, PTT
NEURO	Excessive use: Somnolence, hypertonia, nervousness, and excitability mania in pts on phenelzine Reduces analgesic effect of morphine	
ENDO	Hypoglycemia	Blood glucose
GYN	Mastalgia, postmenopausal bleeding	Hct

Key References: Volger BK, Pittler MH, Ernst E: The efficacy of ginseng. a systematic review of randomized clinical trials, *Eur J Clin Pharmacol* 55(8):567–575, 1999; Tokuyama S, Takahashi M: Pharmacological and physiological effects of ginseng on actions induced by opioids and psychostimulants, *Japan J Pharm* 117(3):195–201, 2001.

Perioperative Implications

Preoperative Concerns
- Check coagulation studies; monitor blood glucose.

Monitoring
- Standard

Induction
- Increased amounts of opioids may be required to blunt adrenergic response to intubation.

Airway
- No specific concerns

Postoperative Concerns
- Monitor blood glucose level, monitor for signs of excessive postop bleeding.
- Increased amounts of opioids may be required to manage postop pain.

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Glucosamine Sulfate

Bridget Perrin Pulos

Uses
- For pain associated with OA, particularly of the knee
- IBD
- Other inflammatory disorders, such as rheumatoid arthritis, psoriasis
- Possible benefits for wound healing and prevention of migraines

Perioperative Risks
- No convincing evidence of increased periop risk owing to glucosamine therapy
- No known significant interactions with commonly administered anesthetic drugs

Worry About
- Potential increase in INR in pts on warfarin who initiate glucosamine therapy, or increase glucosamine dose

Overview
- Available without a prescription in North America.
- Classified as a food additive, not regulated by the USA FDA, made from crustacean skeletons.
- As monotherapy, little consistent evidence of therapeutic effect.
- Often used in combination with other drug supplements, such as chondroitin.
- In combination with chondroitin, may prolong the time to total knee replacement in those with severe OA.
- Side-effect profile is indistinguishable from placebo and better than that of NSAIDs.
- High oral bioavailability with substantial first-pass metabolism, freely diffusable with a 28- to 58-h half-life.

Drug Class/Mechanism of Action/Usual Dose
- Glucosamine is a component of the extracellular matrix of articular cartilage, found naturally in the body.
- Recommended oral dose is 1500 mg/d or 500 mg 3 times per d.
- Precise mechanism of action of glucosamine is unknown; thought to aid in cartilage repair, normalize cartilage metab, and have mild anti-inflammatory properties.

Assessment Points		
System	**Effect**	**Test**
HEME	May potentiate warfarin or increase risk of bleeding when taken with other drugs that increase risk of bleeding	PT/INR if pt is on warfarin
ENDO	No consistent effect	Glucose if otherwise indicated

Key References: Fransen M, Agaliotis M, Nairn L, et al.: Glucosamine and chondroitin for knee osteoarthritis: a double blind randomized placebo-controlled clinical trial evaluating single and combination regimens, *Ann Rheum Dis* 74(5):851–858, 2015; Altman RD: Glucosamine therapy for knee osteoarthritis: pharmacokinetic considerations, *Expert Rev Clin Pharmacol* 2(4):359–371, 2009.

Perioperative Implications
- Glucosamine therapy has no significant periop or anesthetic implications. No need to interrupt therapy for a surgical procedure, no reason to modify an anesthetic plan due to glucosamine, and there is no urgency with regard to restarting therapy postop.

Glycine

Alan David Kaye | Rachel J. Kaye | Mark R. Jones

Uses
- Inhibitory neurotransmitter in the brain stem and spinal cord.
- Glycine and GABA receptors may mediate the effects of inhaled anesthetics.
- A nonessential amino acid sold as a natural sugar substitute, a sedative, and an antacid; used to promote muscle growth and decrease Sx of BPH; also as a polyphenol and an antipsychotic.
- Glycine 1.5% used as a nonhemolytic irrigation solution during TURP.
- Antagonists of glycine binding to NMDA receptor complex are used as anticonvulsants.
- Attempts to use glycine and other NMDA agonists in schizophrenia have had little success.
- Intrathecal glycine is not different from placebo in the treatment of complex regional pain syndrome.

Perioperative Risks

- Incidence of TURP syndrome, a complication of TURP surgery, is 0.5–8%; mortality rate is 0.2–0.8%, even up to 25% in severe cases.
- Operative hysteroscopy intravascular absorption syndrome (OHIAS) can rarely result during hysteroscopy for endometrial ablation, septum resection, myomectomy, or polypectomy. The thick uterine wall necessitates distention pressures higher than those required for irrigation during TURP.
- Clinical presentation of glycine toxicity and hyponatremia may be difficult to distinguish from sepsis or DIC; most commonly presents 30–45 min after the completion of surgery, although can occur from 15 min after starting irrigation up to 24 h postop.
- Glycine metabolized to ammonia can lead to hyperammonemic encephalopathy.

Worry About

- Glycine irrigation is contraindicated in pts with anuria.
- TURP syndrome is thought to be due to hyponatremia, hypoosmolality, and elevated glycine levels due to absorption of irrigation fluid. Manifestations probably related to the glycine load include myocardial depression, hemodynamic changes, and visual disturbances. Other symptoms include burning sensations in the face, N/V, weakness, confusion, seizure, and coma.
- Glycine irrigation should be used with caution in pts with CHF.
- Recent case reports have demonstrated transient postop blindness following use of large quantities of glycine delivered through a rotatory pump set at an inappropriately high pressure and OHIAS, similar to TURP syndrome with hyponatremia, hypoosmolality, hyperglycinemia, and volume overload, including pulm edema.

Overview/Pharmacology

- Smallest amino acid; glycogenic; major inhibitory neurotransmitter.
- Glycine is inhibitory on ligand-gated, strychnine-sensitive Cl^- channel receptors but excitatory on strychnine-insensitive NMDA receptors, where it is a cofactor for activation of the NMDA receptor by L-glutamate.
- Glycine metabolism: Primarily transamination to serine and deamination to ammonia, which is converted to urea and excreted by the kidneys. A portion of absorbed glycine is excreted unchanged by the kidneys.
- Studies indicate that there are better irrigating fluids than glycine solution during monopolar TURP. In some studies, glycine has been at best equal but never superior to alternative fluids. Unlike alternate solutions, glycine has toxic properties that add to patient safety concerns associated with massive fluid absorption.

Drug Class/Usual Dose

- Glycine 1.5% solution is used as an irrigation solution during endoscopic procedures, especially TURP. It is nontoxic, has a refractive index close to that of water, and is nonhemolytic despite a hypotonic osmolality of 200–220 mOsm/L.
- Homeopathic use for BPH at 780 mg/d for 2 wk and then 390 mg for the next 3 mo.
- Glycine 30–60 g/d improves negative symptoms of schizophrenia.
- NMDA receptor allows influx of Na^+ and Ca^{2+}. Overstimulation of this channel leads to Ca^{2+} overload in neurons, which has been shown to be neurotoxic. Glycine antagonists at the NMDA receptor potentiate GABA receptor-mediated events, leading to increased Cl^- conductance, membrane hyperpolarization, and neuroprotection. Glycine site antagonists decrease the release of excitatory amino acids, such as glutamate, which are known to potentiate cerebral ischemic injury.
- Possible drug interactions: Clozapine, haloperidol, olanzapine, risperidone.

Hyperekplexia

- Hereditary disorder characterized by exaggerated startle reflex in response to unexpected acoustic, tactile, and other stimuli.
- Neonates with hyperekplexia may present with hypertonia, developmental delays, apnea, and sudden death.
- In some cases, a mutation encoding the postsynaptic inhibitory glycine receptors (GLRA1, GLRB) or presynaptic glycine transporter (SLC6A5), resulting in abnormal glycinergic neurotransmission, is present.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	T-wave depression or inversion, increased long-term risk of MI Htn or hypotension may occur in TURP syndrome	Homeopathic use or glycine 1.5% irrigation		BP, HR, ECG
HEME	Antagonists associated with aplastic anemia	Homeopathic glycine use	Skin/mucous membranes for infection/petechiae	CBC, peripheral smear, bone marrow biopsy
GU	Metabolites oxalate and glycolate may produce renal failure	TURP with glycine irrigation or homeopathic use		Chem 7
GI	Gastric antacid			
CNS	Glycine accumulates in cells, which increases cerebral edema, hyponatremia, hypotonicity. Direct toxicity account for neurologic symptoms in TURP syndrome Encephalopathy through ammonia metabolite; mitigates negative Sx of schizophrenia	Headache, N/V, visual changes, seizure, weakness, encephalopathy, lethargy	Mental status, visual acuity, strength	Serum, Na serum osmolality
RESP	Pulm edema (decreased with spinal anesthesia)	TURP	SOB, wheeze, frothy sputum	CXR, SpO_2

Key References: Hawary A, Mukhtar K, Sinclair A, et al.: Transurethral resection of the prostate syndrome: almost gone but not forgotten, *J Endourol* 23(12):2013–2020, 2009; Chau A, Roitfarb M, Carabuena JM, et al.: Anesthetic management of a parturient with hyperekplexia, *A A Case Rep* 4(8):103–106, 2015.

Perioperative Implications

Preoperative Period

- Elicit recent Hx of glycine use as homeopathic treatment.
- Anuria is a contraindication to use of glycine irrigation; caution with oliguric pts.

Induction/Maintenance

- No known interactions with homeopathic doses of glycine
- If pt is using glycine as a homeopathic antipsychotic, affect/mental status may be problematic given underlying disease and side-effect profile of this drug.
- Risk of TURP syndrome/OHIAS. Be aware of the degree of blood loss and amount of irrigation used. If RA used, monitor for symptoms of glycine toxicity: N/V, visual changes, weakness. Also monitor for hemodynamic instability; ECG changes, hypotension or Htn.
- With intraop onset of TURP syndrome/OHIAS, surgery should be terminated as soon as possible.

Postoperative Concerns

- TURP syndrome can occur within 15 min of beginning irrigation or as late as 24 h postop. Monitor for signs of changing mental status, hemodynamic instability, and seizures.
- Seizures, if caused by glycine activity on NMDA receptors, can be treated with NMDA receptor antagonists or glycine antagonists. Mg^{2+}, which may be low after TURP, exerts a negative effect on NMDA receptors, so a trial of Mg^{2+} therapy may be warranted.