Metformin

Metformin is the first-line medication for the treatment of type 2 diabetes.

This is particularly true in people who are overweight.

It is also used in the treatment of polycystic ovary syndrome.

Limited evidence suggests metformin may prevent cardiovascular disease and cancer complications of diabetes.

It is not associated with weight gain. It is taken by mouth.

Metformin is generally well tolerated.

It has a low risk of developing low blood sugar.

High blood lactic acid level is a concern if the drug is prescribed inappropriately and in overly large doses. It should not be used in those with liver disease or kidney problems.

While no clear harm comes from use during pregnancy, insulin is generally preferred for gestational diabetes.

Metformin is in the biguanide class.

It works by decreasing glucose production by the liver and increasing the insulin sensitivity of body tissues.

Metformin was discovered in 1922.

French physician Jean Sterne began study in humans in the 1950s.

It was introduced as a medication in France in 1957 and in the United States in 1995.

It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic healthcare system.

Metformin is believed to be the most widely used medication for diabetes which is taken by mouth.

Side effects

Common side effects include diarrhea, nausea, and abdominal pain.

Myelopathy chronic use of metformin (> 4 months).

Interactions

The manufacturer recommends withholding metformin 48 hrs prior to and following contrast

administration (or longer if there is evidence of declining renal function following the use of contrast). Metformin should also be held ≈ 48 hours before any surgery, and should not be restarted post-op until the patient has fully recovered and is eating and drinking normally.

Iodinated contrast (IV or intra-arterial) may delay the excretion of metformin (Glucophage®, Avandamet®), an oral hypoglycemic agent used in type 2 diabetes, and can be associated with lactic acidosis and renal failure (particularly in patients with CHF or those consuming alcohol). The maximum dose of iodine with normal renal function is ≈ 86 gm in a 24-hour period.

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iodinated contrast (IV or intra-arterial) may delay excretion of metformin (Glucophage®, Avandamet®), an oral hypoglycemic agent used in diabetes type II, and can be associated with lactic acidosis and renal failure (particularly in patients with CHF or those consuming alcohol). The manufacturer recommends withholding metformin 48 hrs prior to and following contrast administration (or longer if there is evidence of declining renal function following use of contrast). Metformin should also be held ≈ 48 hours before any surgery, and should not be restarted post-op until the patient has fully recovered and is eating and drinking normally. Maximum dose of iodine with normal renal function is ≈ 86 gm in a 24 hour period.

Cao et al. aimed to investigate the effects of metformin on Intraventricular Hemorrhage in adult male mice and further explored the underlying molecular mechanisms of these effects. In the acute phase, metformin treatment exerted dose-dependent neuroprotective effects by reducing periependymal apoptosis and neuronal degeneration and decreasing brain edema. Moreover, high-dose metformin reduced inflammatory cell infiltration and the release of pro-inflammatory factors, thus protecting ependymal structure integrity and subependymal neurons. In the chronic phase, metformin administration improved neurocognitive function and reduced delayed hydrocephalus. Additionally, metformin significantly inhibited basal subarachnoid fibrosis and ependymal glial scarring. The ependymal structures were partially restored. Mechanically, IVH reduced phospho-AMPK (p-AMPK) and SIRT1 expression and activated the phospho-NF-κB (p-NF-κB) inflammatory signaling pathway. However, metformin treatment increased AMPK/SIRT1 expression and lowered the protein expression of p-NF-κB and its downstream inflammation. Compound C and EX527 administration reversed the anti-inflammatory effect of metformin. In conclusion, metformin attenuated neuroinflammation and subsequent fibrosis after IVH by regulating AMPK /SIRT1/ NF-κB pathways, thereby reducing delayed hydrocephalus. Metformin may be a promising therapeutic agent to prevent delayed hydrocephalus following IVH [1)]

Metformin and glioblastoma

see Metformin for glioblastoma multiforme.

Neural repair

Resident neural precursor cells (NPCs) activation is a promising therapeutic strategy for brain repair. This strategy involves stimulating multiple stages of NPCs development, including proliferation, self-

renewal, migration, and differentiation. Metformin, an FDA-approved diabetes drug, has been shown to promote the proliferation and differentiation of NPCs. However, it is still unclear whether metformin promotes the migration of NPCs. EVOS living cell imaging system was used for observing the migration of primary NPCs dynamically in vitro after metformin treatment. For in vivo study, a mouse model of ischemic stroke was established through middle cerebral artery occlusion (MCAO). To label the proliferating cell in the subventricular zone, BrdU was injected intraperitoneally into the mice. After co-staining with BrdU and doublecortin (DCX), a marker for NPCs, the migration of BrdU and DCX double-positive NPCs were detected along the rostral migratory stream (RMS) and around the infarct area using frozen brain sections. Finally, the rotarod test, corner test, and beam walking were performed to evaluate the motor functions of the mice after stroke in different groups. The results showed that metformin enhanced NPCs migration in vivo and in vitro by promoting F-actin assembly and lamellipodia formation. What's more, metformin treatment also significantly reduced the infarct volume and alleviated functional dysfunction after stroke. Mechanistically, metformin promoted NPCs migration via up-regulating the CDC42 expression. Taken together, metformin represents an optimal candidate agent for neural repair that is capable of not only expanding the adult NPC population but also subsequently driving them toward the destination for neuronal differentiation [2)]

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Cao Y, Liu C, Li G, Gao W, Tang H, Fan S, Tang X, Zhao L, Wang H, Peng A, You C, Tong A, Zhou L. Metformin Alleviates Delayed Hydrocephalus after Intraventricular Hemorrhage by Inhibiting Inflammation and Fibrosis. Transl Stroke Res. 2022 Jul 19. doi: 10.1007/s12975-022-01026-3. Epub ahead of print. PMID: 35852765.
2)
Zhang L, Zhang J, Zhu X, Jiao W, Yang Y, Wu Y, Yang L, Wang Y. Metformin enhances neural precursor cells migration and functional recovery after ischemic stroke in mice. Exp Brain Res. 2023 Jan 8. doi: 10.1007/s00221-023-06547-3. Epub ahead of print. PMID: 36611122.