Molsidomine

Molsidomine is an orally active, long acting vasodilator. Molsidomine is metabolized in the liver to the active metabolite linsidomine. Linsidomine is an unstable compound that releases nitric oxide (NO) upon decay as the actual vasodilating compound.

Belongs to the drug class of sydnones . SIN-1A metabolite of Molsidomine has pharmacologically active group of NO, which by increasing levels of cGMP, decreases levels of intracellular calcium ions in smooth muscle cells. This effect leads to relaxation of smooth muscle vasculature, inhibits platelets aggregation and has indirect antiproliferative effect. In clinical observations no effect of tolerance to the drug was observed. Experimental data show additional mechanism of action of the drug: SIN-1C metabolites protects the reoxygenated cardiomyocyte from post-reperfusion damage. Indications for use of Molsidomine are: ischaemic heart disease, chronic heart failure and pulmonary hypertension. Effects of Molsidomine use in acute myocardial infarction and unstable angina were compared in clinical trials to effects of nitroglycerin use. Both drugs were found equally potent, but authors underline the fact of better Molsidomine tolerability comparing NTG, but longer serum half-time of Molsidomin effects that control of the treatment is worse. In clinical trials it was suggested that intravenous use of Molsidomine metabolite SIN-1 during PTCA procedures is more effective than use of isosorbide dinitrate in the same procedures. In other clinical trials molsidomin was found to produce beneficial effects in patients with heart failure due to ischaemic cardiomyopathy, dilatative cardiomyopathy, in essential hypertension, pulmonary artery hypertension in COPD patients and in congestive heart failure [1)].

Ehlers et al. examined the effects of treatment with molsidomine with regard to decreasing the incidence of spasm-related delayed cerebral infarctions and improving clinical outcome in patients with SAH.

Seventy-four patients with spontaneous aneurysmal subarachnoid hemorrhage (SAH) were included in this post hoc analysis. Twenty-nine patients with SAH and proven cerebral vasospasm (CVS) received molsidomine in addition to oral or intravenous nimodipine. Control groups consisted of 25 SAH patients with proven vasospasm and 20 SAH patients without. These patients received nimodipine therapy alone. Cranial computed tomography (CCT) before and after treatment was analyzed for CVS-related infarcts. A Modified National Institutes of Health Stroke Scale (mNIHSS) and the modified Rankin Scale (mRS) were used to assess outcomes at a 3-month clinical follow-up.

Four of the 29 (13.8%) patients receiving molsidomine plus nimodipine and 22 of the 45 (48%) patients receiving nimodipine therapy alone developed vasospasm-associated brain infarcts ($p < 0.01$). Follow-up revealed a median mNIHSS score of 3.0 and a median mRS score of 2.5 in the molsidomine group compared with scores of 11.5 and 5.0, respectively, in the nimodipine group with CVS ($p < 0.001$). One patient in the molsidomine treatment group died, and 12 patients in the standard care group died ($p < 0.01$).

In this post hoc analysis, patients with CVS who were treated with intravenous molsidomine had a significant improvement in clinical outcome and less cerebral infarction. Molsidomine offers a promising therapeutic option in patients with severe SAH and CVS and should be assessed in a prospective study [2)].

Durak et al., investigated the protective and therapeutic effects of molsidomine (MOL) in a rat model of whole brain radiotherapy (RT). Forty female rats were divided into five groups of eight: group 1,

control; group 2, 15 Gy single dose RT (RT); group 3, 4 mg/kg MOL treated for 5 days (MOL); group 4, 4 mg/kg MOL for 5 days, 10 days after RT treatment (RT + MOL); group 5, 4 mg/kg MOL treatment for 5 days before RT treatment and for 5 days after RT treatment (MOL + RT). All rats were sacrificed on day 16. Neurodegenerative changes in the brain and tissue levels of oxidants and antioxidants were evaluated. The oxidative parameters were increased and antioxidant status was decreased in group RT compared to groups MOL + RT and RT + MOL. Histopathological examination showed that treatment with MOL after RT application and treatment with MOL before RT treatment decreased neuronal degeneration. No difference in neuronal appearance was found between groups RT + MOL and MOL + RT. MOL treatment protected the nervous system of rats and may be a treatment option for preventing RT induced neural injury [3)]

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2)
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