Involvement of HVDCCs in oxymatrine suppressing neuropathic pain

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Neuropathic pain as chronic medical condition is resistant to classic analgesics. Gabapentinoids are used as the first line drugs for neuropathic pain therapy through modulating calcium channels by associating with auxiliary subunit alpha2delta of voltage dependent calcium channels (VDCCs). Oxymatrine as one of main alkaloids of radix sophorae flavescentis was reported to have effects of anti-inflammation, anti-tumor, anti-HBV virus, immune regulation and so on. Present study showed analgesic effects of oxymatrine in partial sciatic nerve ligated (PSNL) mice, a classic neuropathic pain model. Study of the involvement of high-VDCCs in oxymatrine analgesic effect was then carried out. In oxymatrine treated PSNL mice, real-time PCR results showed that mRNA expressions of Cav1 and Cav2 family and the auxiliary subunit alpha2delta changed, and Western-blot results showed expression of Cav2.2 changed remarkably but not Cav1.3. Oxymatrine restored levels of p-CaMKII and p-CREB in brain and spinal cord tissues from PSNL mice. Meanwhile, oxymatrine, nifedipine (L-type calcium channel blocker) and omega-conotoxin GIVA (N-type calcium channel blocker) suppressed PSNL-induced increase of intracellular calcium ion concentration in cultured dorsal root ganglia cells. So did anticonvulsant Gabapentin, a gabapentinoid as first line drug for neuropathic pain. Also, oxymatrine blocked both L- and N-type calcium channel activators effects on intracellular calcium ion concentration, and similar effects of nifedipine and omega-conotoxin GIVA were detected. Therefore, oxymatrine suppressed neuropathic pain possibly by blocking calcium ion influx through L- and/or N-type calcium channels and reversing p-CaMKII/p-CREB signalings, and the role of auxiliary subunit alpha2delta of HVDCCs in the analgesis of oxymatrine needs to be explored further.