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Melatonin protects kidney grafts from ischemia/reperfusion injury in rat kidney transplantation

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Ischemia/reperfusion injury (IRI) is one of the most determining factors for outcome in organ transplantation. The hypoxic storage of graft limits the possibility of successful transplantation, and cellular damage due to insufficient organ preservation is a major cause for the loss or dysfunction of transplanted organs. Severe ischemia reperfusion injury of cadaveric kidney grafts is supposed to contribute to delayed graft function with subsequent acute rejection, and early nonspecific IRI is thought to influence long-term graft survival by enhancing host alloresponsiveness.

Some of the determining factors of the extent of cold ischemia and I/R-induced cellular deterioration are the energy deficiency, intracellular calcium overload, osmoregulatory dysfunction, the “oxygen paradox” and membrane oxidation induced by toxic metabolites and free oxygen radicals. Because melatonin can modulate transmembraneous Ca^{2+} transport, act as an osmoregulator, and a free radical scavenger, it seems to be a suitable protective agent against renal cold IRI.

This study demonstrates for the first time the protective effects of melatonin in experimental kidney transplantation. Also the oral application of melatonin to the donor by gavage is a new approach. Melatonin led to better graft function (decreased creatinine, BUN, LDH, AST, and ALT after reperfusion) and survival through reduction of the activity of prooxidant enzymes (LPO), the induction of the antioxidant enzyme systems (SOD), and the reduction of IRI (downregulation of NF-kBP65 and iNOS expression) and the subsequent cellular apoptosis (inhibition of caspase-3 expression) compared to controls.

In summary, melatonin proved to be beneficial in reducing IRI to rat kidney grafts. Investigations are still needed to fully explore protective effects and useful applications of melatonin. This work offers new insights and thoughts for the prevention of renal IRI after

kidney transplantation.