Can Adrenomedullin be a potential Osteoarthritis treatment?


BACKGROUND & METHODS

Chondrolysis, chondrocyte apoptosis and local inflammation are described to exacerbate osteoarthritis (OA) development. We therefore aimed to investigate the effects of adrenomedullin (AM) and its truncated peptide (22-52AM) on in vitro and in vivo OA models. Both have exhibited anti-apoptotic and anti-inflammatory properties in collagen-induced arthritis (CIA) in mice.

IN VITRO METHODS

- Bovine articular chondrocytes (BACs)

IN VIVO METHODS

- Murine OA instability model (meniscectomy)

IP injections, 3 times a week, 8 weeks

IN VITRO RESULTS

1. AM and its receptor components are constitutively expressed in BACs. In physiological hypoxic environment, CLR-RAMP2 association is enhanced, as visualized by colocalized pixels. Moreover, inflammatory environment increases extensively this association. IL-1β stimulation also induces an increased AM secretion in chondrocyte conditioned media and cAMP production suggests that AM receptor is functional, both in normoxia and hypoxia (3).

2. Exogenous AM treatment (10⁻⁶M) leads to a decreased caspase-3 activity, assuming AM could modulate chondrocyte apoptosis during OA. Given the AM effects and the AM receptor functionality, we address AM as a preventive OA treatment in vivo.

IN VIVO RESULTS

Neither AM nor (22-52)AM have a protective effect on apoptosis and chondrolysis.

CONCLUSION

In « physiological environment », BACs were able to produce both ADM and functional receptor components. In addition, ADM treatment prevented FasL-induced apoptosis in hypoxia. Contrary to our expectations based on the CIA model, ADM or its derived peptide 22-52ADM administered systemically did not disclose any effect on OA progression. Direct intra-articular effects of ADM might be investigated.

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