Platelet-Rich Plasma (PRP) Exerts Anti-inflammatory Effects on Injured Tendons

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INTRODUCTION

Autologous platelet-rich plasma (PRP) is widely used to repair injured tendons in clinics. While the efficacy of PRP treatment is still a matter of debate, many publications have reported that PRP treatment may improve pain in patients with tendon injury. It is known that tendon pain is associated with tissue inflammation, which is characterized by the presence of high levels of inflammatory agents such as IL-β1 and prostaglandin E2 (PGE2). Therefore, we hypothesized that PRP exerts anti-inflammatory effects on injured tendons. To test this hypothesis, we used an in vitro culture model.

METHODS

PRP preparation − PRP was prepared from autologous blood of 12 New Zealand white rabbits (female, 4-6 months) according to an established protocol [1]. The resulting PRP product was also referred to as platelet-rich clot releasates (PRCR).

Tendon stem cell isolation -Tendon stem cells (TSCs) were isolated from rabbit patellar tendon samples based on our published protocol [2]. The identity of TSCs was verified by immunostaining of several stem cell markers, including Oct-4, SSEA-4 and nucleostemin (data not shown).

Cell culture experiments − TSCs at passage 2 were seeded in 6-well plates at a density of 6×10^4/dish and cultured in growth medium (20% FBS-DMEM) for 3 days (at which point cells had reached about 90% confluence). Then the growth medium was replaced by serum-free medium (Sigma), and the cells were subjected to the following treatments for 4 hours. Group #1: serum free medium only (Cont); group #2: serum free medium + 1 ng/ml IL-β1 (IL-β1); group #3: serum free medium + 10% PRP (PRP); and group #4: serum free medium + 1 ng/ml IL-β1 + 10% PRP (PRP+IL-β1). At the end of each treatment, cellular expression of COX-1, COX-2, and membrane-associated PGE synthase (mPGES) genes was measured by real time quantitative RT-PCR. In addition, the production of PGE2 in culture media was determined using an ELISA kit (Cayman).

RESULTS

After addition of PRP to cell cultures with IL-1β treatment, both COX-1 and COX-2 expression were markedly decreased compared to the IL-1β treatment condition (**Figs. 1, 2**). PRP treatment also significantly suppressed mPGES expression (**Fig. 3**). Finally, PRP treatment markedly decreased PGE2 production induced by IL-1β treatment (**Fig. 4**).

DISCUSSION

This study showed that PRP treatment, in the form of PRCR, suppresses inflammation of TSCs, in terms of COX-1, COX-2, and mPGES expression, as well as PGE2 production, thus supporting our hypothesis that PRP exerts anti-inflammatory effects on injured tendons. The findings of this study also explain why PRP treatment in clinics can improve functional scores of patients [3], because it may relieve pain through the reduction of COX and mPGES expression and resulting production of PGE2, which is a known inflammatory mediator involved in pain [4]. Further study will investigate the PRP-anti-inflammatory effects on an animal model and also elucidate the factors in PRP that are responsible for inflammation-suppressing effects.

SIGNIFICANCE

This study provides new basic scientific data justifying the use of PRP to treat injured tendons at least in terms of relieving pain, thus improving tendon function in tendon injury patients.

ACKNOWLEDGEMENTS

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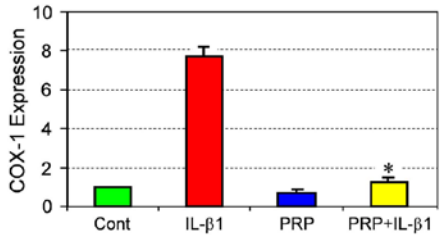

Fig. 1 The effect of PRP treatment on COX-1 expression. PRP treatment suppressed COX-1 expression to near base-line levels under control and PRP conditions (*P < 0.05, with respect to IL-1β treatment condition).

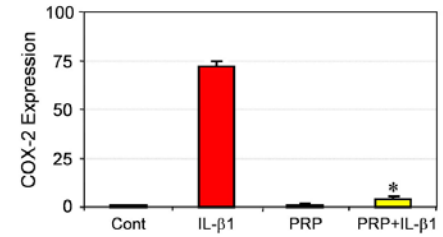

Fig. 2 The effect of PRP treatment on COX-2 gene expression. PRP treatment markedly decreased COX-2 expression induced by IL-1β treatment of TSCs (*P < 0.05, with respect to IL-1β treatment). Note that under control culture conditions and addition of PRP, COX-2 expression was minimal.

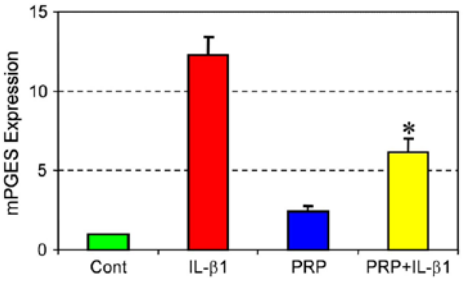

Fig. 3 The effect of PRP treatment on mPGES gene expression. IL-1β treatment of TSCs increased mPGES expression, but it was significantly suppressed by PRP treatment (*P < 0.05, with respect to IL-1β treatment).

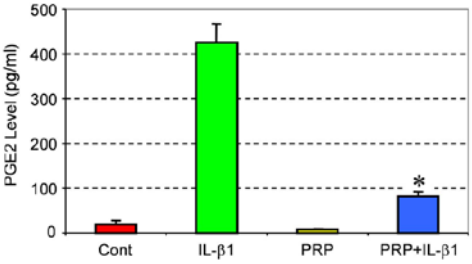

Fig. 4 The effect of PRP treatment on PGE2 production. IL-1β treatment induced high levels of PGE2 production in cells compared to the control condition; however, such an increase in PGE2 was markedly reduced by PRP treatment (*P < 0.05, with respect to IL-1β treatment).