**Objectives** Intravenous and intratracheal implantation of mesenchymal stem cells (MSCs) may offer ameliorating effects on pulmonary hypertension (PH) induced by monocrotaline (MCT) in rats model. The aim of this study was to explore the anti-remodelling effect of MSCs and whether it is related to the inhibition of Smad axis during PH development.

**Methods** MSCs were isolated from rat bone marrow. PH was induced in rats by intraperitoneal injection of MCT. One week after MCT administration, the rats received 3 different treatments: intravenous injection of MSCs (VMSCs group), intratracheal injection of MSCs (TMSCs group), and non-treatment (PH group). As the negative control, rats received saline instead of MCT (control group). Pulmonary arterial structure and dynamics, as well as remodelling-associated cytokine Smad2, 3 in the lungs were evaluated 3 weeks after MCT injection.

**Results** PH group versus control group had higher pulmonary arterial pressure (PAP) and wall thickness index (WTI) 21 days after MCT treatment. Phosphorylated (p)-Smad2 and ratio of p-Smad2/Smad2 were higher in PH group than control group. Widespread lung distribution of fluorescence labelled MSCs were viewed in VMSCs and TMSCs group rats' lungs both 3 and 14 days after transplantation, but not found in the media of pulmonary artery. WTI and PAP in both VMSCs and TMSCs groups were significantly lower than the PH group 3 weeks after MCT injection, while p-Smad2 and ratio of p-Smad2/Smad2 were obviously reduced among MSCs treated rats than their counterpart in control group.

**Conclusions** In conclusion, both intravenous and intratracheal transplantation of MSCs attenuate MCT-induced PH by the induction of therapeutic anti-remodelling, which may be associated with the early suppression of Smad2 phosphorylation via paracrine pathways.