SUMMARY

Acute lung injury (ALI) has been reported to be associated with secondary organ dysfunction and the molecular factors behind such extra pulmonary manifestations are not clearly known. Hence, the present study was designed to investigate the ALI associated secondary organ dysfunction (brain and kidney), utilizing mouse model of ALI using either HCl or LPS or combination of both with an aim to develop appropriate experimental conditions which can mimic the clinical observations. Interestingly, the ‘two hit’ induced ALI was found to be associated with exaggerated pulmonary inflammation which may lead to the leakage as well as production-expression of inflammatory factors primarily TNF-α and IL-1β in the systemic circulation. These systemic inflammatory factors in turn, trigger the disruption of tight junctions of blood brain barrier (BBB) leading to the cognitive deficits. Also, the ‘two hit’ induced ALI was found to be associated with renal dysfunction and the increased renal mRNA expression of pro-inflammatory factors suggested the induction of inflammation in the kidney. Additionally, our results have also demonstrated the protective effects of olaparib on ALI associated lung inflammation, as evident by reduced neutrophil infiltration, decreased alveolar damage and production of pro-inflammatory cytokines. Olaparib plays a pivotal role as neuro-protective agent by maintaining the BBB integrity as well as preventing neuro-inflammation via inhibiting NF-κB activation. Also, olaparib pre-treatment improved the renal function, assessed by serum creatinine and urea. Therefore, pharmacological inhibition of PARP-1 might be a potential approach in the therapy of cognitive impairment/renal dysfunction associated with ALI mediated via ‘two hits’.