How spinal cord injury affects bladder function – Can Inosine and PARP therapy help?

Amy Schwarz, BMA 22-25

Biomedizinische Analytik, HF

Department for Biomedical Research, University of Bern, Functional Urology

1. Abstract

Spinal cord injury (SCI) frequently leads to neurogenic bladder dysfunction, yet the early structural and molecular events remain poorly understood. This study investigated acute and subacute bladder remodeling in a mouse model and evaluated the therapeutic potential of inosine and poly(ADP-ribose) polymerase (PARP) modulation. Histological and immunofluorescence analyses revealed marked edema in the lamina propria and extracellular matrix accumulation within 72 hours after SCI, which largely subsided by one week. Vascular remodeling, smooth muscle disorganization, fibroblast activation, and increased DNA damage were also observed. PAR activity was significantly elevated at 72 hours and partially reduced by inosine treatment, accompanied by mild morphological improvements. These findings demonstrate that SCI rapidly induces dynamic bladder remodeling and highlight PARP signaling as a potential therapeutic target. Inosine showed protective effects by reducing PAR activity, supporting its relevance for early intervention in neurogenic bladder pathology.

2. Introduction

SCI often results in neurogenic bladder dysfunction, severely affecting quality of life [1]. While chronic remodeling of bladder tissue has been studied, the acute changes remain less defined. Early alterations in vascular integrity, smooth muscle structure, extracellular matrix composition, and DNA stability are thought to contribute to long-term dysfunction [1,4].

To capture these processes, specific molecular markers were applied: CD31 for vascular endothelial cells, α-smooth muscle actin (α-SMA) for smooth muscle, Pi16 for fibroblasts and extracellular matrix regulation, poly(ADP-ribose) (PAR) as a readout of PARP pathway activity [3], and γH2AX for DNA damage [4].

Inosine, an endogenous nucleoside, has shown protective effects by modulating PARP activity and reducing oxidative DNA damage in preclinical studies [2]. Together, these findings provided the rationale to investigate early bladder remodeling after SCI and evaluate inosine as a potential therapeutic modulator of PARP signaling.

3. Aims and leading questions

Aim 1: Investigate the acute and subacute effects of SCI on bladder tissue, focusing on morphological, functional, and neural alterations that may underlie the development of chronic dysfunction

- How does SCI affect bladder morphology, function, and neural integrity, leading to long-term dysfunction?

Aim 2: Understanding the involvement of PARP signaling in bladder dysfunction caused by SCI, specifically how it contributes to DNA damage and tissue remodeling.

- What is the role of PARP signaling in SCI-induced bladder pathology, and how does it contribute to DNA damage and tissue remodeling?

Aim 3: Exploring whether Inosine can alleviate bladder dysfunction by modulating PARP activity, reducing DNA damage, and preserving the structure and function of the bladder.

- Can Inosine mitigate bladder dysfunction by modulating PARP activity, reducing DNA damage, and preserving bladder structure and function?

4. Methods and material

A mouse model of spinal cord injury (SCI) with sham-operated controls was used. Bladders were collected at 72 hours post-injury. Tissue was processed by whole-organ preparation, cryosectioning, and histological staining with hematoxylin and eosin (H&E), Masson's trichrome (MTS), and Picro Sirius red (PS). Immunofluorescence labeling was performed for CD31, α-SMA, Pi16, PAR, and γH2AX. Staining was conducted under darkroom conditions to preserve fluorophores. Microscopy was used for image acquisition, and quantitative analyses were carried out in ImageJ. Group comparisons were evaluated statistically, and biological replicates (n=3 per group) ensured reproducibility.

5. Results

At 72 hours post-SCI, bladders showed edema, extracellular matrix accumulation, and increased weight.
Immunofluorescence revealed vascular disruption, smooth muscle disorganization, reduced Pi16, elevated PAR activity, and DNA damage.
Inosine partially reduced PAR intensity and improved morphology.

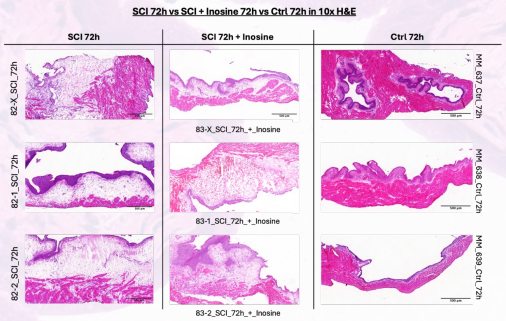

Fig. 1: Histological analysis of mouse urinary bladders (Schwarz, 2025)

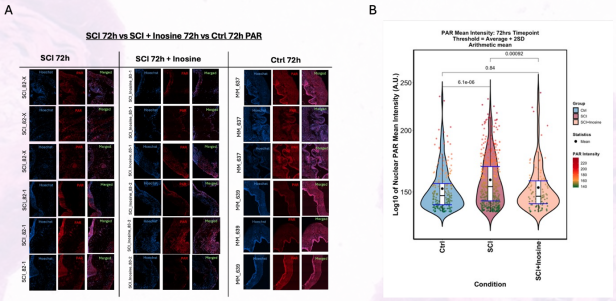

Fig. 2: Nuclear PAR expression in mouse bladder tissue (Schwarz, 2025)

6. Discussion and conclusion

SCI rapidly induces bladder remodeling, characterized by edema, extracellular matrix accumulation, vascular disruption, and smooth muscle disorganization. PARP signaling emerged as a central mechanism, linking SCI to increased DNA damage and impaired tissue stability. Inosine treatment showed a tendency to reduce PAR activity and mild structural protection, but its therapeutic effect could not be conclusively demonstrated.
Future studies should systematically investigate PARP inhibition and include additional markers (e.g., NF200, EpCAM, GLUT1) to clarify cellular mechanisms and identify potential therapeutic strategies

References

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Figures

Fig. 1: Own representation, Histological analysis of mouse urinary bladders (Schwarz, 2025)
Fig. 2: Own representation, Nuclear PAR expression in mouse bladder tissue (Schwarz, 2025)
Fig. 3: Own representation, Background (Schwarz, 2025)