Ibuprofen reduces spontaneous activity and enhances nerve evoked contractions to minimise mitomycin C induced bladder dysfunction

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Background
Inflammation may play a causal role in the urological side effects reported by bladder cancer patients receiving intravesical treatment with mitomycin C (MMC). The aim of this study was to determine the effects of intravesical MMC on voiding behaviour and murine bladder function and also to investigate whether ibuprofen (IBU) can be used to minimise the bladder dysfunction associated with MMC treatment.

Methods
Female mice (36 weeks, n=6 per group) received a 1 hour intravesical treatment with Saline or MMC (1mg/mL), while mice in IBU groups also received 1mg/mL IBU in drinking water for 7 days following MMC treatment. Voiding pattern analysis was conducted prior to and at 1, 3 and 7 days following intravesical treatment. A whole bladder preparation was used to assess spontaneous contractile activity, and intravesical pressure changes in response to bladder filling, electrical field stimulation and pharmacological agents.

Results
MMC treatment significantly increased the number of voiding events (p<0.001) at 24 hours and at 3 days post treatment (p<0.01). Ibuprofen reduced the effect of intravesical MMC on urinary frequency and increased recovery rate with a significant decrease in the number of voiding events at 3 days in the MMC + IBU group (p<0.05) compared to MMC alone. While intravesical pressure responses to carbachol, ATP, isoprenaline and electric field stimulation were not affected by MMC at 7 days following treatment, significant changes in spontaneous phasic activity was observed. Compared to the Saline control (2.3±0.5 contractions/min), MMC significantly increased the frequency of spontaneous contractions (4.8±0.16 contractions/min), amplitude was also increased (p<0.05). Ibuprofen protected against this change in spontaneous activity. Interestingly, while responses to electric field stimulation were not altered by MMC treatment, they were increased in both Saline + IBU and MMC + IBU groups.

Conclusions
MMC resulted in bladder overactivity in mice, an effect that may be due to increased spontaneous non-voiding contractions. Ibuprofen improved voiding symptoms through reducing spontaneous activity and enhancing nerve evoked contractile responses. These results indicate that use of ibuprofen in patients following intravesical MMC treatment may help to minimise the urological adverse effects associated with treatment.