Group	Edema (grade)		Vascular congestion (grade)		PMN count (median)		Mast cell count (median)		LMN count (median)	
	1 day	7 days	1 day	7 days	1 day	7 days	1 day	7 days	1 day	7 days

241

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THE EFFECT OF DMSO ON BLADDER INFLAMMATION AFTER PROTAMINE SULFATE INSTILLATION AND ON NORMAL BLADDER MUCOSA

Hypothesis / aims of study

In patients with interstitial cystitis (IC), DMSO has been used to provide symptomatic relief of chronic pain. An extraordinary variety of actions have been attributed to DMSO. It has anti-inflammatory and reactive oxygen scavenger actions, impairs the nerve conduction of C-fibers and has local anesthetic properties, but its mechanism of action and effects on bladder tissue function are poorly understood. We previously described a sequential inflammatory infiltrate evolution through the days, with infiltrate mainly neutrophilic or lymphocitic on the 1st and 7th, respectively, after intravesical instillation of protamine sulfate (PS). PS neutralizes the electronegative surface polysaccharide and leads to increased urothelium permeability. As increased permeability and inflammation are well-described components of IC, we used this experimental model to study the effect of DMSO in treating bladder inflammation.

Study design, materials and methods

Cystitis was induced in adult female Wistar rats by bladder instillation of 200 µL PS (10 mg) for 30 minutes. After 6 hours PS group was intravesically instilled with 200 µL of either 50% DMSO (n=5 per day) or saline (n=5 per day) for 30 minutes. To evaluate the effect of DMSO in healthy bladders, rats (n=5 per day) were instilled with 200 µL 50% DMSO and controls (n=5 per day) with 200 µL saline for 30 minutes. One and seven days afterwards, the animals (n=40) were sacrificed and their bladders were removed for histopathological analysis. Edema and vascular congestion were graded from 0 to 3, signifying none to severe, respectively. Each inflammatory cell type (polymorphonuclear, mast cell and lymphomononuclear cells) was counted in five cross sections at the most infiltrated area. The median cell number for all the animals was calculated by counting the different inflammatory cells in 25 areas for each group. Mann-Whitney non-parametric test was performed for statistical analysis.

Results

Rats treated with DMSO had significant reduced grade of edema and vascular congestion on the first day after PS instillation, compared to animals treated with saline ($p<0.05$). At this day DMSO also reduced the median PMN infiltrate per cross section (3, range:0-23) when compared to saline treatment (20, range:0-120) ($p<0.05$). On the 7th day edema, vascular congestion and inflammatory infiltrate (LMN) were also significantly reduced in the DMSO treated-group. On the other hand, when DMSO was injected in healthy bladders, there was a more pronounced PMN infiltrate on the 1st and 7th days and edema on the 1st day compared to saline group.($p<0.05$). Mast cell count was increased only on the 7th day of DMSO group when compared to saline group (table).

Interpretation of results

Intravesical instillation of PS caused bladder inflammation and we could observe that DMSO significantly reduced the inflammatory process on both 1st and 7th days after the urothelium injury. Conversely, this drug provoked mild inflammation in normal mucosa.

Concluding message

DMSO reduced inflammation in a rat model of PS induced cystitis. This local anti-inflammatory action may be one of the mechanisms by which it exerts a beneficial effect on IC. On the other hand, it caused inflammation in normal mucosa which could explain the initial flare-up of symptoms that some patients relate, sometimes leading to discontinuation of the treatment.

Saline	0.6±0.5	0.4±0.5	1.2±0.4	1.0±1.2	0	0	1	0	0	0
DMSO	1.8±0.8*	1.0±1.0	2.0±0.7	1.8±0.8	3*	1*	1	1*	0	0
PS/Saline	3.0±0*	1.4±0.5*	2.6±0.5*	2.2±0.4*	20*	0	0	0	3*	0
PS/DMSO	1.6±0.5	0.4±0.5	1.4±0.5	1.2±0.4	3	0	0	0	0	0

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