DSS-induced colitis in mice: optimization and investigation of gender differences

I. Zini, A. Grandi, V. Vivo, L. Flammini, V. Ballabeni, E. Barocelli, S. Bertoni

Università degli Studi di Parma

BACKGROUND

It is well known that no single experimental model can fully recapitulate the complexity of human Inflammatory Bowel Disease (IBD) pathogenesis and development, yet each one of the available models may shed light only on some peculiar aspects of the disease providing clue on potential target of novel therapeutic agents.
The dextran sulphate sodium (DSS) model of colitis is considered a good model of experimental colitis because of its numerous similarities to human IBD: in particular, the loss of epithelial barrier integrity makes the DSS colitis model useful to study therapeutic agents aimed at barrier restitution and/or modulation of innate immune mechanisms (1).

AIM

Our aim was to develop and characterize a model of DSS-induced colitis in C57BL/6 mice by tuning the dosage and the duration of DSS exposure and by assessing the occurrence of gender differences.

METHODS

Colitis was induced in C57BL/6 mice of both sexes, 8-12 weeks old, giving them access to DSS solution *ad libitum*.
Male mice were randomly divided in 5 groups:

- S: no colitis (free access to water);
- 1M: DSS 2% w/v dissolved in water, free access for 5 days;
- 2M: DSS 3% for 5 days;
- 3M: DSS 3% for 7 days;
- 4M: DSS 4% for 7 days;

Female mice were randomly divided in 4 groups:

- S: no colitis (free access to water);
- 3F: DSS 3% for 7 days;
- 4F: DSS 4% for 7 days;
- 5F: DSS 5% for 5 days;

Colon length and thickness, colon and lung myeloperoxidase (MPO) activity, index of leukocyte recruitment, colon and liver edema, spleen and liver weight, disease progression (daily scored as Disease Activity Index (DAI)) and colon macroscopic damage (MS) were assessed in mice euthanized at the end of the treatment period.
All animal experiments were performed according to the guidelines for the use and care of laboratory animals and were authorized by Italian Ministry of Health (D.Lgs. 26/2014).

RESULTS

Among male mice, both DSS 2% and 3%, in groups 1M and 2M, led only to reduction in colon length ($p<0.05$, 0.01) and increase in colon MPO ($p<0.05$). On the contrary, DSS 4% 7d caused a too severe colitis, leading to the death of 90% of animals while DSS 3% 7d induced in group 3M a moderate to severe colitis, with a highly significant increase of DAI, MS, colon and lung MPO and spleen/bw ratio [$p<0.001$] and a marked decrease in colon length and liver/bw ratio [$p<0.01$], compared to S mice.
Among female mice, in 5F group only a slight increase in DAI, MS [$p<0.01$] and lung MPO [$p<0.05$] and the reduction of liver/body weight ratio [$p<0.001$] were observed compared to S animals.
DSS 3% 7d triggered in group 3F a moderate to severe colitis similar to that observed in group 3M although with a significantly lower decrease in colon length [$p<0.05$] and increase in MS [$p<0.001$] and lung MPO [$p<0.05$].
Similar results were obtained in group 4F with a more consistent increase of lung MPO [$p<0.01$].

CONCLUSIONS

On the whole, these preliminary findings indicate that: the administration of DSS 3% for 7 days to C57BL6 mice induces a reproducible condition of moderate to severe colitis with local and systemic inflammatory responses in both sexes; male

mice appear globally more susceptible than female ones to DSS-induced colitis; the evaluation of a conventional therapeutic agent for human IBD is required to fully validate this model.

REFERENCES

1. Kiesler P et al., Cell Mol Gastroenterol Hepatol. 2015 Mar 1;1(2):154-170.