OPTIMIZATION OF A CHRONIC COLITIS MODEL IN MICE INDUCED BY DEXTRAN SULPHATE SODIUM (DSS) AND EFFECTS OF DRUGS THEREON

Harun Rashid and Rana Samadfam

Charles River Montreal, Quebec, Canada

1 INTRODUCTION

Ulcerative colitis is an inflammatory bowel disease that affects millions of people worldwide. Dextran Sulfate Sodium (DSS) model of colitis is widely used to explore disease mechanism and to evaluate potential new therapies. In the present study, a chronic version of the DSS-induced colitis model in mice has been optimized.

2 METHODS

Mice received DSS in sterile drinking water and underwent washout with sterile water in 6 different protocols as outlined below. Daily body weight taken and stool evaluation performed for softness and presence of occult blood. In-life data were summed to obtain a disease activity index (DAI) score. At necropsy, colons were collected

2 METHODS cont..

length and weight measured and processed for histopathological evaluation. Effects of three different test agents (Prednisolone 1mg/kg, Sulfasalazine 200mg/kg and Cyclosporine A 40mg/kg, once daily oral gavage) were also evaluated using the protocol 2A.

Group	DSS conc	Cycles	Necropsy
1. A	2%	**DSS: Day 1-7, 15-21, 29-35** Washout: Day 8-14, 22-28	Day 35
1. B	2%	**DSS: Day 1-7, 15-21, 29-35** Washout: Day 8-14, 22-28, 36-42	Day 42
2. A	2%	**DSS: Day 1-5, 13-17, 23-27** Washout: Day 6-12, 18-23	Day 27
2. B	2%	**DSS: Day 1-5, 13-17, 23-27** Washout: Day 6-12, 18-23, 28-34	Day 34
3. A	2%	**DSS: Day 1-4, 8-11, 15-18** Washout: Day 5-7, 12-14	Day 18
3. B	2%	**DSS: Day 1-4, 8-11, 15-18** Washout: Day 5-7, 12-14, 19-21	Day 21

4 CONCLUSIONS

Of the 6 different DSS treatment and washout protocols, 3 cycles of 5 days of DSS with 2 cycles of 7 days of washout in between has been chosen as the optimal for evaluation of effects of test agents based on in-life and histopathology results.

In terms of effects of the standard of care (SOC) treatment agents, sulfasalazine and prednisolone failed to produce any effects in-vivo while cyclosporine A was able to only partially reduce DAI scores in the early phase of the model.

3 RESULTS

DAI score from the 6 protocols

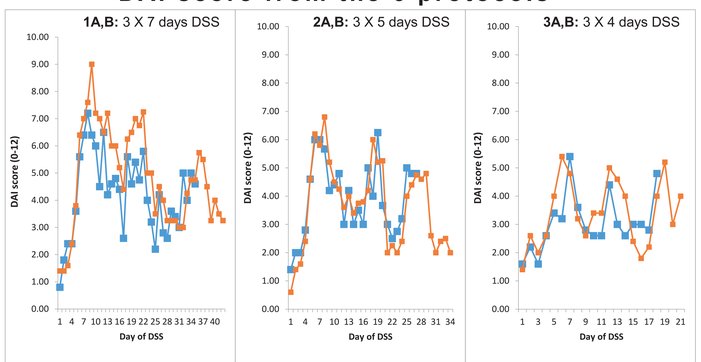

Figure 1: DSS exposure-dependent increase in DAI scores was observed. Animals with 7 days DSS cycles (1A and B) showed poor health conditions and while animals with 4 days DSS cycles (3A and B) had sub-optimal DAI scores. Protocol with 5 days DSS cycles were seemed optimal.

Colon macro and micro changes

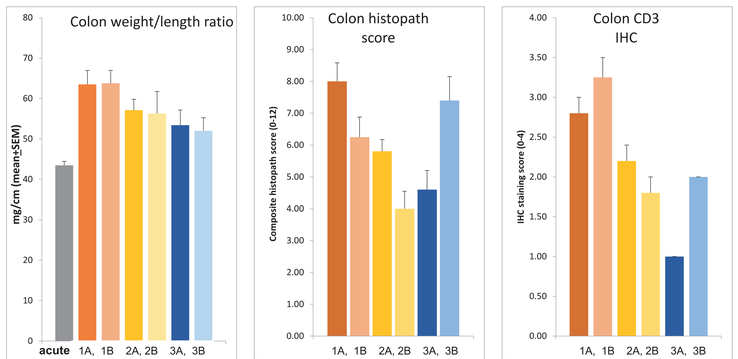

Figure 2: Macroscopic changes in colon as evidenced by increase in weight and decrease in length was observed in all three protocols. In microscopic evaluation, chronic colitic inflammation was observed with all three protocols in a DSS exposure-dependent manner.

Effects of SOCs

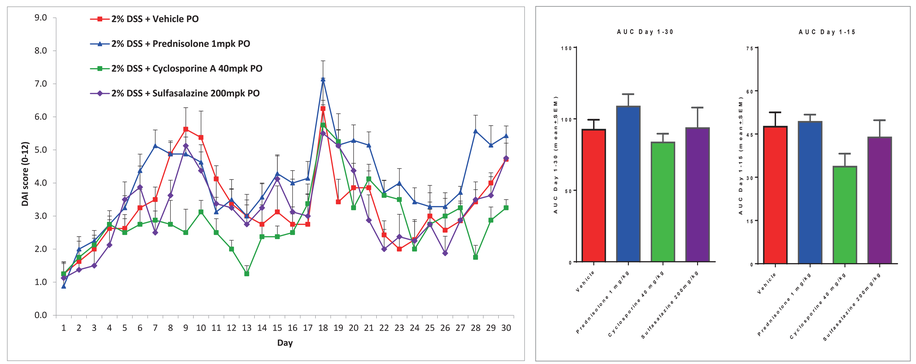

Figure 3: Among the three agents tested in the chronic 2A DSS protocol, Cyclosporine A produced some attenuation of colitis score in the early phase while Sulfasalazine and Prednisolone had no effect.