Lack of Effect of the Direct Renin Inhibitor Aliskiren on Cardiac Mast Cells and Macrophages in an Acute Model of Fat Embolism in Rats

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INTRODUCTION

Fat embolism (FE) induced by Triolein injection causes both acute and chronic lung injury in rats and the histopathological damage is not limited to the lungs but also involves the heart (1). The renin-angiotensin system (RAS) plays a role in the pathogenesis of such damage. Captopril and losartan treatment prevented such damage both in lungs and heart at 10 weeks after Triolein injection (2). More recently we reported that the renin inhibitor aliskiren induced the same protective effect in the lungs (3) and reduced the number of mast cells 48 hours after Triolein (4). The hearts of the same Triolein treated rats however had a modest but statistically significant increase of alpha-smooth muscle actin (SMA) ($p<0.05$) versus controls but no fibrosis or vasculitis and no changes by aliskiren in the acute experiment (5). We measured the mast cells and the macrophages in the heart to delineate their potential role in this early cardiac damage.

METHODS

Twenty-two rats were divided into controls (n=4, Group A) and three FE groups (n=6, groups B,C &D). FE induction was done with Triolein 0.2 ml i.v at 0 hours, and an hour later animals received 0.2 ml i.p saline (Groups A&B), aliskiren at 50 mg/kg (group C) or at 100 mg/kg (Group D). Rats were euthanized at 48 hours and hearts were fixed and stained with H&E for general histopathology evaluation, Masson's Trichrome (MT) for collagen presence and distribution, and SMA for myofibroblasts incidence. Mast cells were stained with CD 117 and macrophages with CD 68.

RESULTS

The only damage observed in the experiment was a statistical significant increase ($P<0.05$) in SMA staining in the adventia of the coronary arteries, in the myocardium of the rats injected with Triolein + saline vs the controls. No other significant difference was observed for all the other parameters. Mast cells and macrophages did not show any statistical difference among the four groups. The macrophages did not show the two types of cells that we have observed in the lungs, one with large cytoplasm with small vacuoles and the second with small compact cytoplasm (6).

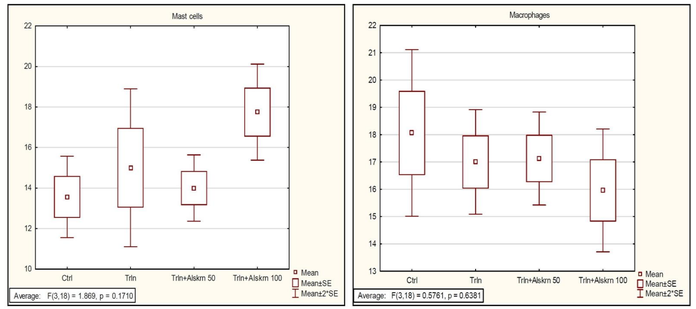

Fig 3. Mast cells and macrphages count of the four group. No statistical significant difference.

SUMMARY

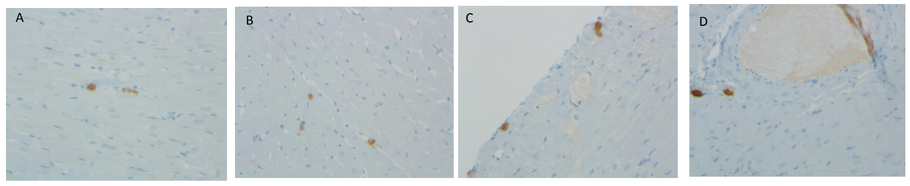

Fig 1. Representative section of Macrophages of Saline + Saline (A), Triolein + Saline (B), Triolein + Aliskiren 50 mg/kg (C), Triolein + Aliskiren 100 mg/kg (D). Staining CD68, 400x.

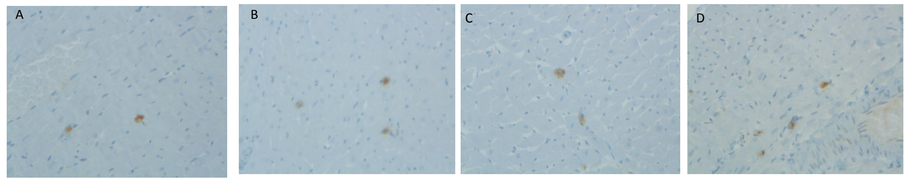

Fig 2. Representative section of Mast Cells of Saline + Saline (A), Triolein + Saline (B), Triolein + Aliskiren 50 mg/kg (C), Triolein + Aliskiren 100 mg/kg (D). Staining CD117, 400x.

CONCLUSION

Despite the significant cellular response in the lungs at 48 hours after Triolein, there were no alterations in mast cells or macrophages in the heart of the same animals either after Triolein alone or Triolein + aliskiren treatments. In contrast to the lungs, where we have observed two types of macrophages, only one type was present in the heart. The lack of change in mast cells and macrophages in the heart and the occurrence of no fibrosis with only a modest change in SMA at this early time suggests that such cellular response for the heart is happening only in a late phase following fat embolism.

CREDITS/DISCLOSURE/REFERENCES

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