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Monocytes and T Cells in Haemochromatosis

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Background

Haemochromatosis (HH) is an iron overload disorder where too much dietary iron is absorbed through the intestine. The body has no way of removing the excess iron so it accumulates initially in the liver parenchymal cells and then in other organs.

The large majority of HH patients are homozygous for the mutation but are clinically heterogeneous.

There have been questions over whether or not inflammatory processes play a role in the pathogenesis of Haemochromatosis.

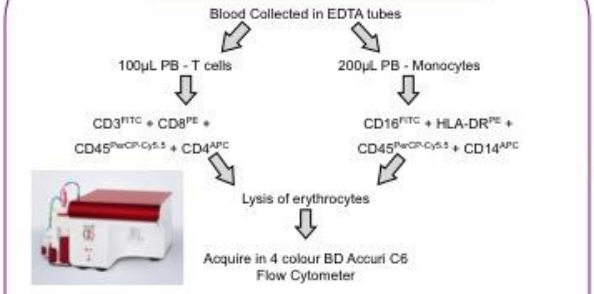
In 2010 Zimmermann *et al* claimed that non-classical monocytes were involved in inflammation and contributed to liver fibrosis. Cruz *et al* showed CD8+ T lymphocyte numbers can be correlated with the severity of clinical expression.

Leicester *et al* indicated no change in total numbers of monocyte/macrophages in the liver but histological staining indicated an increase in CD14+ moncoytes/macrophages.

Aim of the study

To explore whether monocyte or lymphocyte numbers were raised, in particular if certain subsets were expanded or diminished.

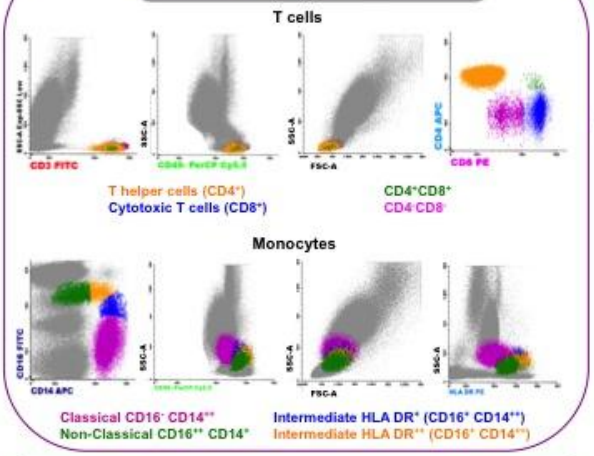
Method



Analysis:

Flow files were analysed in Infinicyt 1.7.0 software (Cytognos) and Cflow Sample (Accuri). The statistic analysis was done with GraphPad Prism software .

Gating strategy



References

- Zimmermann, H. W., et al. Functional Contribution of Elevated Circulating and Hepatic Non-Classical CD14+CD16+ Monocytes to Inflammation and Human Liver Fibrosis. PLoS ONE. Public Library of Science, 5: 1-15.
- Leicester, K. L., et al. (2004). "CD14-positive hepatic monocytes/macrophages increase in hereditary hemochromatosis." Liver International 24 (5): 446-451.
- Cruz, E., et al. (2008). "A new 508 kb haplotype associated with high CD8+ T-lymphocyte numbers predicts a less severe expression of hereditary hemochromatosis." BMC Medical Genetics 9: 1-12.

T cell Results

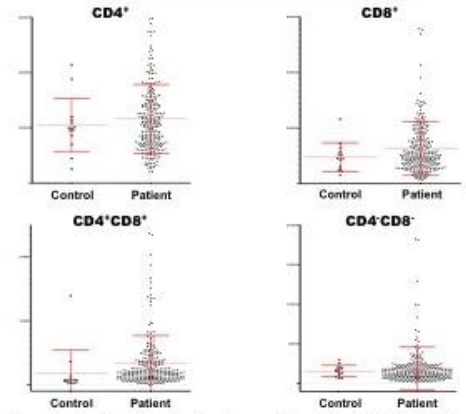


Figure 1 – Number of T cells subsets per mL in peripheral blood. 255 HH patient and 12 control samples were analyzed (healthy donors).

Monocyte Results

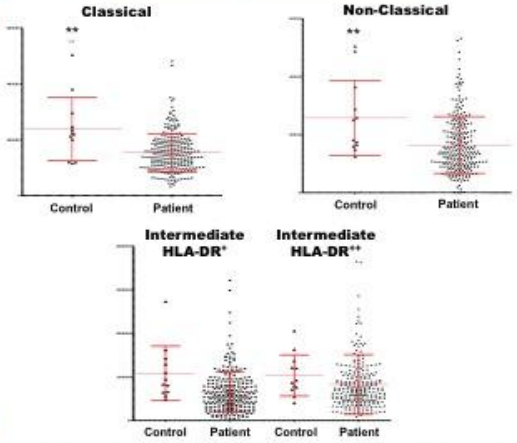


Figure 2 – Number of monocytes subsets per mL in peripheral blood. 255 HH patient and 12 control samples were analyzed (healthy donors)** $p < 0.005$

Conclusion

- There was a significant decrease found in classical and non- classical monocyte cell counts between the control group and patients with HH. This implies that monocytes may be implicated in the development of the complications of haemochromatosis.
- There was however a large spread in cell numbers between patients which may be related to the pathogenesis of HH.
- A change in T lymphocyte numbers in haemochromatosis was not observed. However a subset of patients appear to have elevated CD4-CD8- cell numbers.
- Correlating our results with clinical data from the patients may help to further explain the reasons for variation in patient cell counts.
- Cell numbers in peripheral blood may not be indicative of changes occurring in monocyte or T lymphocyte number or activity within the organs suffering from iron overload. This is important to take into account.
- These conclusions are tempered by the fact that the control group is not age-matched with the patient group.

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