

Dr. Abbi Lulseged¹, Mr Alexander Bedu-Addo², Mr. Dr. Andy Zamar^{3*}

¹Consultant Endocrinologist, HEALTH121 Ltd. ²Medical Student. ³Consultant Psychiatrist, The London Psychiatry Centre.
email: ¹admin@health121.co.uk. • ³andy.zamar@psychiatrycentre.co.uk.

Introduction

- RCBPD & particularly episode of mixed affective states are dangerous conditions.
- RCBPD has a 1 : 6 mortality rate.
- Standard treatments are ineffective (average 3 drugs+).
- Homozygous polymorphism of DIO2 gene is associated 3.75-fold risk of bipolar disorder.
- We report a Retrospective analysis of 20 patients with RCBPD in full remission for a minimum of 6 moths consecutively tested for DIO1/DIO2 status.
- All fulfilled the ICD-10 criteria for bipolar disorder.
- All were severely symptomatic and resistant to treatment.

Discussion

- RCBPD is a treatment-resistant condition with high suicide rates. Standard treatments are ineffective.
- HDL is in the prescribing guidelines for RCBPD.
- However, the mechanism of action and absence of thyrotoxicosis despite large, unconventional doses remains unclear.
- This novel report shows a strong association with SNP of DIO2/DIO1 and RCBPD.
- Cell-specific deletion of DIO2 in mice astrocytes associated with anxiety/depression and reduced hippocampal cortex DIO2 but systemically euthyroid.

We speculate that

- (i) HDL helps to overcome relative deficiency (cerebral) and that the polymorphisms of DIO2 play a role in this deficiency.
- (ii) Robust inactivating deiodinases in the periphery help protect from systemic thyrotoxicosis. HDL can also downregulate DIO2/DIO1 activity in the periphery. Our patients have a high FT4:FT3.
- (iii) RCBPD might be a primary Thyroid (cerebral) problem.

Results

- 17 were female, average age 32.4 yrs.
- 19/20 had Single nucleotide polymorphisms (SNP) of either DIO1, DIO2 or both.
- All but two patients were treated with rTMS to induce cerebral neuroplasticity.
- Average pre-treatment FT4 was 17.0 pmol/L (12-22), and FT3 4.5 pmol/L (3.1-6.8)
- Post-treatment, FT4 was 59.7 pmol/L and FT3 5.3 pmol/L.
- Average FT4:FT3 ratio pre-treatment was 4:1, and post-treatment was 5:1.
- HDL range was 200-800 mcg daily for remission. Average dose 472 mcg daily.
- Discontinuation rate was 0%.
- All patients had ECG and cardiac review (normal)
- One patient required a dose reduction (750 mcg to 600mcg) because of side effects, namely palpitations and sweating.
- 12 patients needed one mood stabiliser

Conclusion

- Rapid cycling bipolar disorder and mixed state affective states are dangerous conditions with high mortality and morbidity rates.
- Standard treatments are often ineffective.
- Data highlights an association between polymorphisms of the DIO2 gene and bipolar disorder and previous studies have highlighted the safety and effectiveness of HDL in achieving remission.
- We speculate that BPD is a form of cerebral hypothyroidism and that HDL helps to overcome the deficit while robust inactivating deiodinases in the periphery protect from systemic thyrotoxicosis.
- This is evidenced by findings of normal clinical examination and elevated rT3.
- rTMS exercises its well established neuroplastic effect, helping to achieve and maintain remission as an adjunct to HDL.

References

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- * Declaration of interest: The London Psychiatry Centre has filed a patent application for the above protocol.