METABOLIC ABNORMALITIES IN A SUBGROUP OF THE CANADIAN BIPOLAR CONSORTIUM: A TWO-YEARS FOLLOW-UP STUDY

Beaulieu, S.[1]; Cervantes, P. [2]; Yatham, L.N.[3]; Belingard, L.[1]; Sablé, R.[1] ; Saury S.[1] & Maisy, N.[1]

[1] McGill University and Douglas Hospital Research Center, CANADA; [2] General Hospital of Montreal, CANADA; [3] University of British Columbia, CANADA.

ABSTRACT

There is increased evidence that bipolar patients are more sensitive to several metabolic abnormalities than the rest of the population. We have recorded several types of metabolic data on a three months basis for bipolar patients in several centers across Canada during two years, and compiled those results. We present the analysis of the data from two of those centers. For the first visit, only 28.4% of our bipolar patients (n = 95) have a normal Body Mass Index (BMI<25), 42.1% are overweight and 29.5% are obese (BMI>30), these ratios do not significantly change during the two-years follow-up. At the first visit, mean Fasting Glucose is 5.45 mmol/L (n = 64), mean Insulin is 70.1 pmol/L (N=42), mean Cholesterol is 5.1 mmol/L (n = 59), mean HDL is 1.17 mmol/L (n = 60), mean LDL is 3 mmol/L (n=59), mean Triglycerides are elevated at 2.02 mmol/L (n = 61) and mean Blood Pressure is 127/78 (n = 59). This data demonstrated the importance for the physician to monitor patient physical health as well as mental health and to create a strategy to reduce these metabolic abnormalities.

INTRODUCTION

The Canadian Network for Bipolar Disorder (CAN-BD) began collecting prospective data about 4 years ago tracking treatment patterns, clinical outcomes, quality of life and resource utilization of bipolar patients treated at 14 centers across Canada. The main objective of the CAN-BD is to gather the effectiveness of various treatment interventions on symptomatic and functional outcomes in patients with bipolar disorder. We present here the preliminary results concerning the metabolic abnormalities in a subgroup of participants (two centers).

OBJECTIVES

The goal of the present study is to monitor prospectively metabolic and physiological variables in bipolar patients within a naturalistic follow-up.

METHOD

Patients diagnosed with bipolar I/II disorder who required a change in treatment within 3 months prior to enrollment were eligible. At the first visit, data collected included demographics, clinical/medical history, psychiatric medications, life events, symptom rating scales such as the HAM-D 21, MADRS, YMRS, CGI, CGI-I, GAF, and side effect scales. Patients were also asked to do blood tests at the first visit and at every 3-months visits in order to monitor ALP, ALT, Amylase, Bilirubin total, lipid profile (Triglycerides, Cholesterol, HDL, LDL), CK, Creatinine, GGT, Glucose AC, Potassium, Urea, Thyroid Profile, CBC + 5 Part Diff., Insulin and Cortisol levels. Patients were managed under routine clinical practice conditions and all behavioural scales were administered as well as weight and blood pressure measured at least every 3 months. In addition, YMRS, MADRS and CGI were administered at each intermediate clinical visit. Data was collected in a database designed for psychiatric disorders : PQM (Lundbeck). Some variables were collected using paper CRFs and monthly patient diaries.

RESULTS

133 patients were available for analysis, however the number of patients available to each parameter varies.

Demographics	(N=133)				
Gender	**N**	**%**	**Age (mean ± SD)**	46	±14
Male	62	53	**Diagnosis (N=154)**	**N**	**%**
Female	71	47	Bipolar type 1	82	53
Education level	**N**	**%**	Bipolar type 2	51	33
High school or less	49	37	**Marital Status**	**N**	**%**
College or University attended	82	62	Unmarried	34	26
Studying	2	2	Married	38	29
Professional Situation	**N**	**%**	Divorced/Separated	37	28
Full Time	47	35	Living Together	24	18
Part Time	16	12	**Living Arrangement**	**N**	**%**
Unemployed	27	20	Alone	54	41
Retired	11	8	Partner	60	45
Studying	10	8	With relatives (parents, children, other)	12	9
Other	22	17	Other	7	5

Table 1. Demographic characteristics on patients enrolled in CAN-DB, Montreal centers.

Intra-Individual variability

Statistical Design : Repeated Measures (General Linear Model) SPSS 11.5

One-Year Follow Up		BMI (n=95)	Fasting Glucose (n=64)	Insulin (n=42)	Cholesterol (n=59)	HDL (n=60)	Tchol/HDL (n=58)	LDL (n=59)	TG (n=61)	Systolic BP (n=59)	Diastolic BP (n=59)
Within Subject	Simple (ddl =1)	NO p=.56	NO p=.56	NO p=.60	NO p=.34	NO p=.18	NO p=.16	NO p=.45	NO p=.11	NO p=.90	NO p=.26
Between Subject	* Bipolar Dis (ddl = 1)	NO p=.08	NO p=.61	NO p=.48	NO p=.71	NO p=.20	NO p=.40	NO p=.33	NO p=.30	NO p=.27	NO p=.42
	* Gender (ddl = 1)	NO p=.56	NO p=.29	NO p=.56	NO p=.32	NO p=.47	NO p=.14	NO p=.18	NO p=.87	NO p=.32	NO p=.18
	* Smoking (ddl = 1)	NO p=.70	NO p=.73	NO p=.86	NO p=.98	NO p=.28	NO p=.99	NO p=.69	NO p=.46	NO p=.92	NO p=.39
	* BMI Cat (ddl = 2)	---------- --	YES F=4.07 (p<.05)	NO p=.92	NO p=.70	NO p=.53	NO p=.24	NO p=.23	NO p=.64	NO p=.17	NO p=.87

Table 2: One-Year Intra-Individual Variability for BMI, Glucose, Cholesterol, HDL, Ratio Tchol/HDL, LDL, TG, Insulin, Systolic and Diastolic Blood Pressure.
Within Subject factors : Time (t = 0, t = 1 Year)
Between Subjects Factors : Bipolar Disorder Type (Bip I, Bip II), Gender (Female, Male), Smoking (No, Yes), Body Mass Index category (Obese, Overweight, Normal).

Two-Years Follow-Up		BMI (n=49)	Fasting Glucose (n=24)	Insulin (n=21)	Cholesterol (n=24)	HDL (n=22)	Tchol/HDL (n=21)	LDL (n=22)	TG (n=24)	Systolic BP (n=29)	Diastolic BP (n=29)
Within Subject	Simple (ddl =1)	NO p=.43	NO p=.95	NO p=..58	NO p=.39	YES F=4.6 (p<.05)	NO p=.85	NO p=.55	NO p=.85	NO p=.78	NO p=.72
Between Subject	* Bipolar Dis (ddl = 1)	NO p=.85	NO p=.72	NO p=.82	NO p=.92	NO p=.22	NO p=.42	NO p=.68	NO p=.82	NO p=.09	NO p=.46
	* Gender (ddl = 1)	NO p=.08	NO p=.81	NO p=.65	NO p=.72	NO p=.95	NO p=.27	NO p=.89	NO p=.51	YES F=4.12 (p<.05)	NO p=.82
	* Smoking (ddl = 1)	NO p=.28	NO p=.749	NO p=.84	NO p=.77	NO p=.28	NO p=.92	NO p=.85	NO p=.49	NO p=.54	NO p=.69
	* BMI cat (ddl = 2)	---------- --	NO p=.99	NO p=.97	NO p=.38	NO p=.30	NO p=.41	NO p=.67	NO p=.82	YES F=2.77 (p<.05)	NO p=.50

Table 3: Two-Years Intra-Individual Variability for BMI, Glucose, Cholesterol, HDL, Ratio Tchol/HDL, LDL, TG, Insulin, Systolic and Diastolic Blood Pressure.
Within Subject factors : Time (t = 0, t = 1 Year, t = 2 Years)
Between Subjects Factors : Bipolar Disorder Type (Bip I, Bip II), Gender (Female, Male), Smoking (No, Yes), Body Mass Index category (Obese, Overweight, Normal).

Distribution of BMI

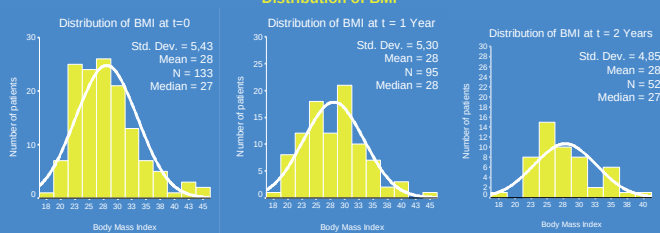


Figure 1: Distribution of Body Mass Index (BMI) at t=0, t=1 Year and t=2 Years.
Within a period of 2 years, BMI does not significantly change (Mean (SD) = 28 (±5.43) at t= 0 ; Mean (SD) = 28 (±5.30) at t=1 Year ; Mean (SD) = 27 (±4.85) at t= 2 Years).

Blood results vs BMI

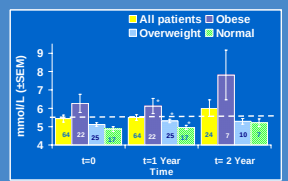


Figure 2: Fasting glucose vs BMI
*Fasting glucose significantly varies depending on the BMI between t=0 and t=1 year (F=4.07 ; p<.05).

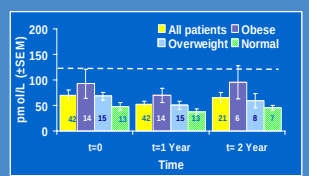


Figure 3: Insulin vs BMI
No statistical intra-individual change over a period of 2 years.

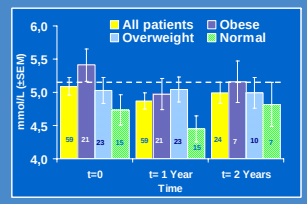


Figure 4: Cholesterol vs BMI
No statistical intra-individual change over a period of 2 years.

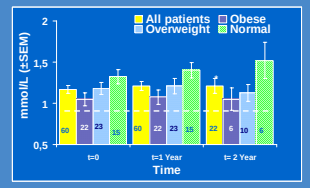


Figure 5: HDL vs BMI
* A significant HDL intra-individual variation is observed within a two-years period (F=4.6 ; p<.05) when all patients are considered in the analysis.

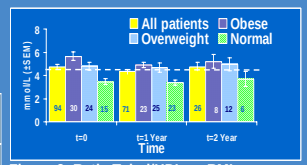


Figure 6: Ratio Tchol/HDL vs BMI
No statistical intra-individual change over a period of 2 years.

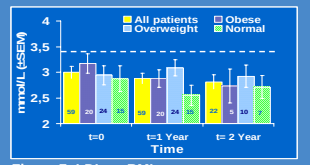


Figure 7: LDL vs BMI
No statistical intra-individual change over a period of 2 years.

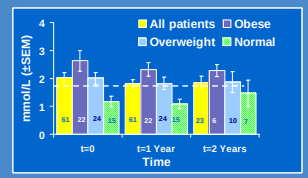
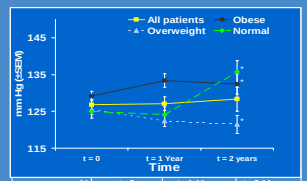


Figure 8: TG vs BMI
No statistical intra-individual change over a period of 2 years.

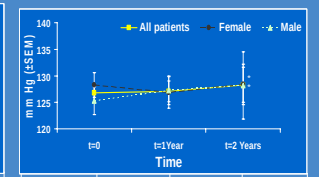
Blood Pressure



N	t=0	t=1 Year	t=2 Years
All patients	59	59	29
Obese	23	23	9
Overweight	22	22	13
Normal	14	14	7

Figure 9: Systolic Blood Pressure vs BMI

* Systolic Blood Pressure significantly varies depending on the BMI between t=0 and t=2 years (F=2.77 ; p<.05). Despite statistical variation at t= 2 years, this change, based on a small number of patients, is to be interpreted cautiously.



N	t=0	t=1 Year	t=2 Years
All patients	59	59	29
Female	29	29	18
Male	30	30	11

Figure 10: Systolic Blood Pressure vs Gender

* Systolic Blood Pressure significantly varies depending on the Gender between t=0 and t=2 years (F=4.12 ; p<.05).

CONCLUSIONS

Despite the presence of metabolic and/or weight difficulties among this cohort of patients, we have demonstrated that there are only a few changes occurring over a period of 2 years. This underlines the possibility of preventing a deterioration of the metabolic parameters when patients are followed with a regular monitoring of these variables and that proper psycho-education and dietary advices and/or change of medications are made to prevent further deterioration.
One of the limits of this study is the small number of patients available at 2 years follow-up. We are also in the process of analyzing our database to study more specifically the relationship with the type of medications prescribed and the metabolic parameters.

REFERENCES

T. Baptista, N. M. Kin, S. Beaulieu, and E. A. de Baptista. Obesity and related metabolic abnormalities during antipsychotic drug administration: mechanisms, management and research perspectives. *Pharmacopsychiatry* 35 (6):205-219, 2002.

For further reading on subject:

T. Baptista, J. Martinez, A. Lacruz, N. Rangel, S. Beaulieu, A. Serrano, Y. Arape, M. Martinez, Mendoza S. de, L. Teneud, and L. Hernandez. Metformin for prevention of weight gain and insulin resistance with olanzapine: a double-blind placebo-controlled trial. Can.J.Psychiatry 51 (3):192-196, 2006.

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