RECOMMENDATIONS

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1- As there is a strong relationship between NES and BMI, psychiatrics must not neglect the major role of treatment of obesity hand in hand with the treatment of depression and NES.

2- There is an emphasis for the need to identify individuals with the atypical depression as it was found that the atypical subtype of MDD is a strong predictor of obesity and thereafter, therapeutic measures to diminish the consequences of increased appetite during depressive episodes with atypical features are advocated.

3- Future studies are needed to explore weight changes and the relationship between NES and BMI as possible risk factors for each other, especially among depressed patients of all weight ranges.

4- Further researches are essential to augment our understanding of NES as it occurs in conjunction with depression in order to discover the effects and causes of NES among depression patients.

5- Further researches are needed to study the relationship between NES and antidepressant drugs for the assessment of their effects, and how NES might be better managed and/or prevented with their use.

6- In patients with combined NES and depression it is preferred to consider the effect of certain types of SSRIs in the treatment.

7- Avoid as much as possible certain antidepressants as mirtazapine, clomipramine and trazodone in treatment of NES among patient with depression as they may have some risk in inducing NES which will make the treatment difficult.

8- Educate patients and family members on the side effects of antidepressants (change in appetite, weight gain, risk of glucose intolerance, and lipid abnormalities).

9- Adjust, if possible, the patient's antidepressant treatment in accordance with his or her metabolic profile.

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APPENDIX

NEQ

1. How hungry are you usually in the morning?

□ Not at all □ A little □ Somewhat □ Moderately □ Very

2. When do you usually eat for the first time?

□ Before 9 a.m □ 9:01 a.m. to 12:00 p.m □ 12:01 p.m. to 3:00 p.m.

□ 3:01 p.m. to 6:00 p.m. □ After 6:01 p.m

3. Do you have cravings or urges to eat snacks after supper but before bedtime?

□ Not at all □ A little □ Somewhat □ Very much so □ Extremely so

4. How much control do you have over your eating between supper and bedtime?

□ Not at all □ A little □ Somewhat □ Very much so □ Complete

5. How much of you daily food intake do you consume after suppertime?

□ 0% (none) □ 1-25% (Up to a quarter) □ 26-50% (About half) □ 51-75% (More than half) □ 76-100% (All)

6. Are you currently feeling blue or down in the dumps?

□ Not at all □ A little □ Somewhat □ Very much so □ Extremely so

7. When you are feeling blue, is your mood lower in the:

□ Early morning □ Late morning □ Afternoon □ Early evening

□ Late evening / nighttime □ Check if your mood doesn't change during the day

8. How often do you have trouble getting to sleep?

□ Never □ Sometimes □ About half the time □ Usually □ Always

9. Other than only to used the bathroom, how often do you get up at least once in the middle of the night?

□ None at all □ Less than once a week □ About once a week

□ More than once a week □ Every night

If 0 on # 9, Please stop here

10. Do you have cravings or urges to eat snacks when you wake up at night?

□ Not at all □ A little □ Somewhat □ Very much so □ Extremely so

11. Do you need to eat in order to get back to sleep when you awake at night?

□ Not at all □ A little □ Somewhat □ Very much so □ Extremely so

12. When you get up in the middle of the night, how often do you snack?

□ Never □ Sometimes □ About half the time □ Usually □ Always

If 0 on # 12, Please stop here

13. When you snack in the middle of the night, how aware are you of your eating?

□ Not at all □ A little □ Somewhat □ Very much so □ Completely

14. How much control do you have over your night-time eating?

□ Not at all □ A little □ Somewhat □ Very much □ Complete

PROTOCOL

STUDY OF THE PREVELANCE OF NIGHT EATING SYNDROME IN DEPRESSED PATIENTS AND ITS RELATION TO ANTIDEPRESSANT DRUGS

دراسة معدل انتشار متلازمة تناول الطعام ليلا في مرضى الاكتئاب و علاقته بالعقاقير المضادة للاكتئاب

Protocol of a thesis submitted
to the Faculty of Medicine
University of Alexandria
In partial fulfillment of the
requirements of the degree of
Master of neuropsychiatry

خطة بحث مقدمة
لكلية الطب
جامعة الإسكندرية
إيفاءً جزئياً
لشروط الحصول على درجة
الماجستيرفى أمراض المخ و الأعصاب و الطب النفسي

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INTRODUCTION

The reciprocal links associating obesity (whether general or central obesity) and depression (whether major or atypical) has been reported in many clinical and epidemiological studies, and seem to correlate more in adulthood, especially among women.[1-6]

Generally, both are major public health problems of high prevalence, that share leading threats being both associated with a number of chronic conditions as cardiovascular disease, metabolic disorders and cancers.[7-9]

Among their interlinking relations, some literature view obesity to be the clinical manifestation of a subtype of depression similar to that of atypical depression, while others view that they are separate constructs, having an influencing effect on each other; even being a risk factor to the development of one another.[10-12]

For instance, as far as obesity is concerned, in a prospective cohort of 74,332 men and women, it was reported that those with raised body mass index (BMI) were associated with an increased risk of depression,[13] while in another study elderly men with BMI over 30 had a 31% increased risk of developing depression.[14] In obese adolescences followed over a 4-year period, symptoms of depression were significantly related to increases in BMI for girls but not boys.[15] However, still, concrete data cannot as yet distinguish whether obesity is a consequence of, a contributor to, or a correlate of psychological disorders when linked to depression.[13-15]

Vice versa, from depression perspectives, combining data from 16 studies, confirmed that, depressed compared to non depressed people were at significantly higher risk for developing obesity[16] and that the risk among depressed people for later obesity was particularly high for adolescent females. This later was reported also in another study,[17] declaring that major depression in late adolescent girls was associated with a 2.3-fold increased risk of obesity in adulthood.[16,17]

Explanations have suggested some genetic and/or environmental cues that permit hypothalamic pituitary dysregulation, decrease physical activity, change the eating habits (especially become night eaters) use of antidepressants (more with tricyclic, monoaminoxidase inhibitors and some newer antidepressants), can all increase the risk of metabolic dysregulation in depressed individuals, ending in obesity.[18-20]

In this context, circadian desynchrony i.e disruption of circadian rhythmicity of the biological clock that fine tunes the sleep/wake cycle, has recently been nailed to the etiopathogenic links of depression, behavioral eating disorders specially night eating syndrome (NES) and obesity. Indeed, the association between NES and depressive symptoms in particular was noted in literature and has ranked up to 70% of NES subjects reporting a depressed mood in one of the studies.[21-24]

It's worth noting that depression in NES follows an atypical pattern with distinctive circadian features where by mood is usually better in the morning and worse during the evening and night, unlike depression which is worse in the morning and improves throughout the day.[10,21,24]

The denominator bottom line theme found in common in such association was the existence of hypothalamic-pituitary neurochemical dysregulation involving transmitters (monaminergic, gabergic,…etc), hormones (cortisol, insulin, leptin…etc), and cytokines and neuropeptides (interleukines, adiponectin,…etc.).[25-27]

From all aforementioned etiopathogenic raised links it was of interest to investigate in this study the relation between depression and obesity especially in subsets of patient presenting with NES and to correlate these findings to their anti-depressant drug treatment.

AIM OF THE WORK

This work aims to:

1- Evaluate the prevalence of night eating syndrome in patients with depression.

2- Study the relationship between night eating syndrome and antidepressant drugs.

SUBJECTS

After approval of Ethical Committee of Faculty of Medicine and written informed consent from patients, this study will be carried out among psychiatric outpatients in Alexandria Main University Hospitals over the period from February 2013 to July 2013 and patients will be divided into 2 groups (naïve and others receiving antidepressant therapy for at least 2 months)

Inclusion criteria

1. Patients diagnosed as having depression according to DSM "IV" TR criteria.
2. Patients aged from 18 – 60 years.
3. Both sexes are included.
4. Patients will be grouped into naïve and others receiving antidepressant therapy for at least 2 months.
5. Patients must be accepting by informed consent.

Exclusion criteria

1. Presence of organic illness contributes tc either obesity or depression eg. Thyroid dysfunction.
2. Refusal of participation (none consenting).
3. Depression with psychotic features.
4. Patients receiving more than one antidepressant.
5. Other axis I or II disorders according to DSM "IV" TR.

METHODS

All studied sample will be subjected to the following tools and techniques after the intake of f' nsent:

1. Structured interview to collect:
   A. Sociodemographic data as age, residence, educational level, marital status, occupation and socioeconomic status.
   B. Medical, psychiatric and drug history.
   C. Family history of psychiatric illness.
   D. Onset of increase in weight and its relation to the onset of antidepressant intake.
   E. The type of antidepressant in use.
   F. Patterns of eating adopted.
   G. Presence or absence of sleep disorders.
2. Clinical psychiatric assessment and diagnosis based on DSM-I VTR.
3. Weight and hight measurements to define BMI.

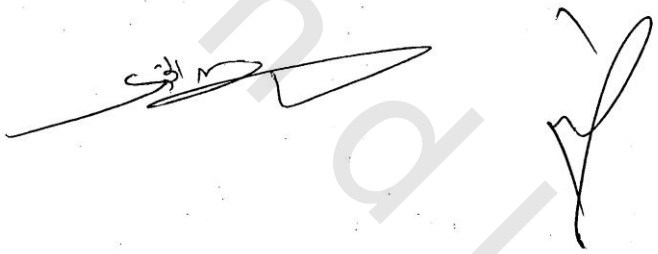
Accordingly patients will be categorized into:

- Very obese: from 35 and above.
- Obese: from 30 to 34.9.
- Overweight: from 25 to 29.9.

4. Analysis by Arabic version of night eating questionnaire to define whether or not he is NES.[28]

RESULTS

The results obtained from this study will be tabulated and statistically analyzed using the standard statistical methods.



DISCUSSION

The results obtained from this study will be discussed in view of achievement of the aim and compared with any available published data in the same field of the research.

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ARABIC SUMMARY

الملخص العربي

إن العلاقة المتبادلة التي تربط السمنة (سواء العامة او المركزية) بالاكتئاب قد وردت في العديد من الدراسات و يبدو انها ارتبطت أكثر بسن البلوغ و خاصة بين النساء.

عموما، كلاهما من الأسباب الضخمة لمشاكل صحية عالية الانتشار، و التي تشترك في تهديدات صحية، كونهما يرتبطان بالعديد من الأمراض المزمنة مثل أمراض القلب و الأوعية الدموية، اضرابات التمثيل الغذائي و السرطان.

في اطار هذه الروابط المتبادلة، البعض يرى السمنة أنها مظهر اكلينيكي لنوع فرعي من أنواع الاكتئاب مثل الاكتئاب الغير نمطي، في حين يرى البعض الآخر أنهما منفصلان بينما لهما تأثير على بعضهما البعض أو كون أحدهما عامل مسبب لتطور الآخر.

مؤخرا، دخلت متلازمة الأكل الليلي هذه الحلقة المفرغة كونها مرتبطة بقوة مع كل من السمنة و الاكتئاب في علاقة ثنائية الاتجاه مع كل واحد منهما.

لوحظت متلازمة تناول الطعام ليلا لأول مرة بين المرضى الذين يعانون من السمنة، كما تم دعم العلاقة بينهما مع تقديرات تشير الى أنها أكثر شيوعا بين الأشخاص البدناء (٦-١٦%) مقارنة مع عموم الناس (١.٥%).

و فيما يتعلق بعلاقة متلازمة تناول الطعام ليلا مع الاكتئاب، فانه ليس من الواضح ما اذا كان الاكتئاب هو سبب، هو نتيجة أو سمة من سمات متلازمة تناول الطعام ليلا.

على الرغم من أنه تم اجراء العديد من الدراسات على العلاقة بين متلازمة تناول الطعام ليلا و الاكتئاب، الا أن معظمهم كان من منظور متلازمة تناول الطعام ليلا. و في الوقت الحاضر هناك قليل من الدراسات بشأن معدل متلازمة تناول الطعام ليلا في مرضى الاكتئاب و علاقتها بمضادات الاكتئاب.

لذلك أجري هذا البحث لتقدير معدل انتشار متلازمة تناول الطعام ليلا بين مرضى الاكتئاب و علاقته بالعقاقير المضادة للاكتئاب. و قد أجريت هذه الدراسة على ٤٠٠ مريض نفسي تتراوح أعمارهم بين ١٨-٦٠ عاما، من الجنسين في مستشفيات جامعة الاسكندرية خلال الفترة من فبراير ٢٠١٣ حتى يوليو ٢٠١٣، و قد تم تقسيم المرضى الى مجموعتين متساويتين (٢٠٠ مريض في كل مجموعة). واحدة على مضى الاكتئاب دون علاج و الأخرى على مرضى الاكتئاب و على العلاج لمدة شهرين على الأقل.

وقد خضع المشاركون لما يلي:

١- استبيان معد ذاتيا لجمع كافة المعلومات المتعلقة بالامور الاجتماعية و الديموغرافية والصحية و النفسية و التاريخ الدوائي بما في ذلك نوع مضادات الاكتئاب المستخدمة، بداية زيادة الوزن و علاقته ببداية العلاج.

٢- التقييم النفسي على أساس (DSM-IV) لتشخيص اضراب الاكتئاب و استبعاد اضرابات محور١ (AXIS I) الأخرى.

٣- تم حساب القياسات الأنثروبومترية (قياسات الجسم البشري) و مؤشر كتلة الجسم.

٤- مقابلة نفسية لجميع الأشخاص الذين تم تحليلهم باستخدام معايير التشخيص المقترحة لمتلازمة تناول الطعام ليلا و هو ما كان مؤكدا باستبيان تناول الطعام ليلا الذي تم تعريبه ومن ثم تم جمع درجات جميع العناصر ما عدا سؤال ١٣ (عن الوعي اثناء تناول الطعام) للوصول الى الدرجة الكلية حيث تتراوح بين ٠-٥٢. و كانت الدرجة القطعية المستخدمة في هذه الدراسة من ٢٥.

ولقد اظهرت الدراسة النتائج التالية:

- ٢٦.٥ %من الحالات في المجموعة أ تم تشخيصهم بمتلازمة تناول الطعام ليلا في حين تم تشخييص ٩% فقط من حالات المجموعة ب.
- في كل مجموعة، كانت حالات زيادة الوزن و السمنة أعلى احصائيا من الحالات ذات الوزن الطبيعي.
- فيما يتعلق بمؤشر كتلة الجسم، كان هناك فروق ذات دلالة احصائية بين المجموعتين ($p<0.001$) كما كانت الفروق بين حالات زيادة الوزن و السمنة بين المجموعتين ذات دلالة احصائية (٨٣% و ٥٧%) على التوالي.
- حالات متلازمة تناول الطعام ليلا الايجابية في كلتا المجموعتين كانت ذات سن أصغر من الحالات السلبية.

- الفروق بين الحالات السلبية و الايجابية لمتلازمة الأكل الليلي فيما يتعلق بمؤشر كتلة الجسم، كانت ذات دلالة احصائية ($p<0.001$). بمعنى آخر، مؤشر كتلة الجسم أعلى في الحالات الايجابية لمتلازمة الأكل الليلي عن الحالات السلبية. وقد تم تأكيد ذلك بالعلاقة الطردية بين درجات استبيان الأكل الليلي و مؤشر كتلة الجسم حيث ازدادت الدرجات مع تزايد مؤشر كتلة الجسم.
- ارتبطت متلازمة تناول الطعام ليلا بشكل كبير مع الاكتئاب الغير نمطي في المجموعة أ، و هذا ما أكده درجات استبيان الأكل الليلي التي كانت ذات دلالة احصائية في المقارنة بين الاكتئاب الغير نمطي مع الأنواع الأخرى. في حين المجموعة ب ، ارتبطت حالات متلازمة الأكل الليلي بالاكتئاب الغير نمطي و الاكتئاب الأعظم.
- كان هناك فروق احصائية بين الحالات السلبية و الايجابية لمتلازمة تناول الطعام ليلا في المجموعة ب فيما يتعلق بنوع مضادات الاكتئاب المستخدمة. و قد وجد هذا مع ميرتازابين، ترازودون و كلوميبرامين.

وبناءا على نتائج الدراسة الحالية توصلت الدراسة إلى التوصيات التالية:

- بما أن متلازمة الأكل الليلي شائعة بين مرضى الاكتئاب ، لذلك يجب استبعادها من قبل الأطباء في مرضى الاكتئاب خاصة بين البالغين و الذين يعانون من الاكتئاب الغير نمطي.
- بما أن هناك علاقة قوية بين متلازمة تناول الطعام ليلا و مؤشر كتلة الجسم، لذا يجب ان لا يهمل الأطباء النفسيين الدور الرئيسي لعلاج السمنة جنبا الى جنب مع علاج الاكتئاب ومتلازمة تناول الطعام ليلا.
- هناك تأكيد على الحاجة لتحديد الأفراد ذات الاكتئاب الغير نمطي، حيث وجد أن هذا النوع من الاكتئاب كان مؤشرا قويا للسمنة و بالتالي أخذ التدابير العلاجية للتقليل من عواقب زيادة الشهية خلال نوبات الاكتئاب.
- هناك الحاجة لدراسات مستقبلية لدراسة تغيرات الوزن و العلاقة بين متلازمة الأكل الليلي و مؤشر كتلة الجسم كعوامل خطر محتملة لبعضهم البعض.
- المزيد من الأبحاث ضرورية لتأكيد فهمنا لمتلازمة تناول الطعام ليلا التي تحدث بالتزامن مع الاكتئاب من أجل اكتشاف أسباب و آثار متلازمة تناول الطعام ليلا بين مرضى الاكتئاب.
- هناك الحاجة لمزيد من الأبحاث لدراسة العلاقة بين متلازمة تناول الطعام ليلا و العقاقير المضادة للاكتئاب لتقييم آثارها و كيفية العلاج الأفضل لمتلازمة تناول الطعام ليلا أو منعه.
- في المرضى الذين يعانون من متلازمة تناول الطعام ليلا و الاكتئاب معا، يفضل أن ننظر الى تأثير بعض أنواع مثبطات امتصاص السيروتونين الانتقائية في العلاج.
- تجنب قدر الامكان مضادات اكتئاب معينة مثل ميرتازابين، كلوميبرامين و ترازودون في علاج متلازمة تناول الطعام ليلا بين مرضى الاكتئاب حيث قد يكون لديهم بعض المخاطر في احداث متلازمة تناول الطعام ليلا الأمر الذي سيجعل العلاج صعبا.
- تثقيف المرضى وأفراد الأسرة على الآثار الجانبية لمضادات الاكتئاب (تغيرات الشهية ، زيادة الوزن، خطر الحساسية المفرطة تجاه الجلوكوز و تشوهات الدهون).
- ضبط مضادات الاكتئاب للمرضى إن أمكن وفقاً للبيانات الأيضية للمرضى.

الملخص العربي

لجنة الإشراف

أ. د./ طارق كمال ملوخية .....
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د./ أسامة أبو المجد الخولي .....
أستاذ مساعد الطب النفسي
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جامعة الإسكندرية

دراسة معدل انتشار متلازمة تناول الطعام ليلا في مرضى الاكتئاب و علاقته بالعقاقير المضادة للاكتئاب

مقدمة من

مي عصام حامد رزق
بكالوريوس الطب والجراحة - جامعة الإسكندرية، ٢٠٠٦

للحصول على درجة

الماجستير

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أ. د./ طارق كمال ملوخية أستاذ الطب النفسي كلية الطب جامعة الإسكندرية	.....
د/ سها عبد اللطيف الغباشي أستاذ مساعد الطب النفسي كلية الطب جامعة الاسكندرية	.....

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رسالة

مقدمة الي كلية الطب – جامعة الأسكندرية

إستيفاء للدراسات المقررة للحصول على درجة

الماجستير

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أمراض المخ والأعصاب والطب النفسي

مقدمة من

مي عصام حامد رزق

بكالوريوس في الطب والجراحه- كلية الطب- جامعة الأسكندرية (٢٠٠٦)

كلية الطب

جامعة الإسكندرية

٢٠١٥