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Lina González Cardona: Critical literature review; data collection, analysis, and interpretation; preparation and writing of the manuscript; study conception and planning.

Conflicts of interest

None declared.

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The effects of isotretinoin on serotonin: a prospective pilot study on acne patients ☆

Dear Editor,

Isotretinoin (13-cis retinoic acid) is a highly effective and commonly used treatment against acne vulgaris. Even though isotretinoin has been linked to low mood, depression, and suicidal ideation, a concrete link to adverse mood has not been proven yet, with some studies supporting this claim and others refuting it.[1–6]

Since isotretinoin crosses the blood-brain barrier, a biological mechanism linking isotretinoin to depression is plausible.[3,7–10] In the adult brain, receptors for retinoids are widely expressed, and isotretinoin could potentially regulate the expression of several neuronal genes.[8–10] Serotonin (5-HT) is a widely recognized neurotransmitter and a key mediator of mood. Imbalances in serotonin levels have been linked to low mood and depression.[7,8] The present work's objective was to pilot a study that tests the hypothesis that treatment with isotretinoin could lead to measurable changes in the concentration of key mood-related neurotransmitters. In order to do so, the authors performed a prospective cohort study assessing the effects of isotretinoin on the neurotransmitter's serotonin (5-HT) and 5-HIAA (the main serotonin metabolite) in patients with acne vulgaris. Plasma levels of 5-HT and 5-HIAA were measured before, during, and after treatment with isotretinoin. Data were collected prior to treatment initiation, at two and four months of treatment, and one month after treatment cessation. A total of 27 patients contributed blood prior to initiation of treatment. 24 and 22 patients had their serum measured at two and four months of treatment, respectively. Only

☆ Study conducted at the Department of Dermatology of University Hospitals Bristol NHS Foundation Trust, Bristol, UK.

Table 1 Total numbers of patients contributing data at each visit.

Time-points	5-HT & 5-HIAA
Baseline	27
2-months	24
4-months	22
1-month post-cessation	4

Table 2 Nonparametric summary of the findings for 5-HT (HT), 5-HIAA (HA), and their ratio (HTHA) at baseline (0), 2-months (2), and 4-months (4) of treatment.

Test results over time	Number of patients	Min	Lower quartile	Median	Mean	Upper quartile	Max	Wilcoxon matched-pairs signed-ranks tests
5-HT_0	27	0.61	4.59	8.70	10.66	13.04	36.78	Baseline comparator
5-HT_2	24	1.26	5.89	7.60	9.64	11.54	28.32	p=0.633
5-HT_4	22	1.07	6.34	9.78	13.07	14.77	56.10	p=0.349
5-HIAA_0	26	7.05	14.77	26.23	74.77	74.86	502.30	Baseline comparator
5-HIAA_2	24	3.11	13.19	23.05	44.31	29.03	548.20	p=0.082
5-HIAA_4	22	2.26	8.50	25.67	32.83	41.12	143.70	p =0.294
HTHA_0	26	0.012	0.098	0.249	0.605	0.527	5.220	Baseline comparator
HTHA_2	21	0.015	0.203	0.312	0.475	0.496	1.803	p=0.523
HTHA_4	20	0.015	0.246	0.490	0.749	0.761	2.854	p=0.244

four patients attended for blood testing one month after treatment cessation (Table 1).

At the pre-treatment baseline, the authors found the following mean values: 5-HT 10.66, 5-HIAA 74.77.

Mean values at 2-months of treatment were found to be: 5-HT 9.64 (p = 0.633), 5-HIAA 44.31 (p = 0.082). At 4-months of isotretinoin therapy values had changed to: 5-HT 13.07 (p = 0.349), 5-HIAA 32.83 (p = 0.294). These findings did not represent statistically significant changes from the baseline.

The disappointingly low numbers of patients that attended the follow-up appointment at one month after cessation of treatment did not allow for a meaningful statistical analysis of post-isotretinoin effects.

A detailed documentation of the findings over time, as well as the changing ratios of HT to HA, are presented in Table 2.

The relationship between isotretinoin and adverse mood changes is a highly debated aspect of isotretinoin therapy.

The authors did not find a significant link between treatment with isotretinoin and changes in the neurotransmitters 5-HT, 5-HIAA, or the ratio of the two. If a causal link is present between the two, it is likely mediated via a different neurochemical pathway.

Having said that, the pilot study has a small number of patients and significant attrition in follow-up. Therefore, even though it can act instructively, this work cannot fully support this claim. Larger, prospective, case-controlled studies will likely be required in order to address in detail the link between mood, isotretinoin, and neurotransmitters. The authors hope that this work will act as guidance and inspiration for such further undertakings.

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Authors' contributions

Adam P. Bray: Contributed to the design, recruitment, management, writing, and literature review associated with this study.

Georgios Kravvas: Contributed to the design, recruitment, management, writing, and literature review associated with this study.

Suzanne M. Skevington: Contributed to the design, recruitment, management, writing, and literature review associated with this study.

Christopher R. Lovell: Contributed to the design, recruitment, management, writing, and literature review associated with this study.

Conflicts of interest

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Using the internet to obtain dermatological information on patients from the public health network: a cross-sectional study☆

Dear Editor,

The internet is a powerful and accessible media, it can also offer knowledge in the health area so that users may understand the possible involvement by a disease and its outcomes.[1] Previous studies have shown that women, young people, university students, and individuals with higher incomes are more likely to seek health information on the internet.[2] However, there have been few studies on the influence of research on dermatological diseases. Thus, given the Brazilian profile of intensive use of the internet, including for health information, it is necessary to study the way people use this tool in their daily lives.[1,3]

Considering the abovementioned facts, this study aimed to evaluate the prevalence of internet access to obtain information on skin health among dermatological patients, their demographic and search profile, and their associations with internet use, as well as the interactions of the results with dermatological care.

This is a cross-sectional, descriptive and exploratory study, carried out with patients from a public hospital in the hinterland state of São Paulo, interviewed between July and September 2019. Participants were recruited for convenience in the waiting areas for scheduled outpatient dermatological care.

Patients over 18 years of age who were literate and had no communication problems, cognitive impairment, or psychiatric illness, that prevented the interview from being conducted, were included.

Data collection was carried out using a two-part investigation protocol: the first on patient demographics and the second on the use of the internet in health-related searches.

The study was approved by the institutional Ethics Committee (Counsel n. 3,661,913).

Continuous variables were analyzed as bivariate data using the parametric Student's *t* test after normal distributions were assessed using the Shapiro-Wilk test. Categorical variables were compared using the chi-square or Fisher's exact tests according to the lowest number of events in each analysis.

The variables indicating the type of researched information and the type of tool used in the search were analyzed using hierarchical clustering, linkages between groups, and Euclidean distance, represented by dendrograms using centroid linkage.

The minimum sample size consisted of 130 individuals for an exploratory analysis with up to 12 variables.

The categorical data were represented as absolute numbers and/or percentages, and non-categorical data as means and standard deviations.

The association between searching for skin-related health information on the internet and the other demographic variables was evaluated in a bivariate manner, and, subsequently, the significant variables were included in a multivariate logistic regression model.

Two-tailed values of $p \leq 0.05$ were considered significant.

Table 1 describes the socioeconomic data and the internet use of the 148 patients who agreed to participate in the research protocol.

Table 2 depicts the association of demographic variables with having obtained dermatological health information from the internet. Obtaining this information was associated with young individuals, women, higher education, and having access to the internet at home. However, in multivariate analysis by logistic regression, including variables with $p \leq 0.05$, only age remained significant ($p < 0.01$).

The reliability of the information was not associated with age, sex, education, or income; discussing the results with the physician was directly correlated with schooling ($p = 0.01$ – chi-square trend) and income ($p = 0.05$ – chi-square trend); eliciting conflict with the medical conduct was not associated with sex, age, schooling or income; the search for alternative treatments was associated with young individuals (36.82 [12.32] 43.33 [14.17] years; $p = 0.02$ – Student's *t* test) and a higher level of schooling ($p < 0.01$ – chi-square trend); and the performance of treatments based on virtual searches was associated only with young individuals (35.85 [13.21] $\times$ 42.80 [13.72] years; $p = 0.02$ – Student's *t* test).

The cluster analysis of information types showed two main independent search patterns, focusing on the diagnosis, treatments, and other information. The analysis of the