

Analyzing electronic momentary assessment data on chronic pain and weather conditions: a first look

V. Edefonti¹, F. Bravi^{1,2}, M. Ferraroni¹ AND A. Decarli^{1,3}

¹Dipartimento di Medicina del Lavoro “Clinica del Lavoro L. Devoto”, Università degli Studi di Milano, Milan, Italy.

²Dipartimento di Epidemiologia, Istituto di Ricerche Farmacologiche “Mario Negri”, Milan, Italy.

³S.C. Statistica Medica, Biometria e Bioinformatica, Fondazione IRCSS Istituto Nazionale Tumori di Milano, Milan, Italy.

Abstract

Although scientific evidence is scarce, patients affected by chronic masticatory muscle pain often report increased pain in response to changes in weather conditions. The aim of the present study was to assess a potential relationship between pain intensity and meteorological factors, through a newly developed, portable device, in this population.

Seven female subjects diagnosed with myofascial pain of the masticatory muscles participated in the study. Each patient was provided with a portable data logger that recorded and stored weather variables every 15 minutes. Patients were asked to record the level of perceived pain on an electronic visual analogue scale (VAS) every hour. The relationship between meteorological variables and pain scores was investigated using separate generalized least squares regression models with a correlation structure estimated via autoregressive integrated moving average models.

1 Introduction

Although the etiopathology of masticatory muscle pain is still unclear (Cairns (2010)) and evidence supporting a possible relationship between weather changes and masticatory muscle pain is scarce in the literature, patients with chronic myofascial pain often report increased pain symptoms in response to worst weather conditions. The present preliminary study used electronic momentary assessment (EMA), a methodology in which data are collected in “real-time”, in the respondent’s usual environment, using handheld computers. Given the preliminary nature of this study and the lack of existing empirical data, this study just attempted to answer the question of whether there seems to be possible legitimacy to the claim that changes in the weather are predictive of variations in chronic pain in adults with masticatory myofascial pain.

2 Materials and Methods

The study was designed to include patients a) suffering from masticatory muscle pain (diagnosis Ia/Ib, Research Diagnostic Criteria for Temporomandibular disorders), for at least six months and still in the last month, b) with a perceived pain intensity $> 3/10$ as measured on a Visual Analogue Scale (VAS) at their initial study visit at University of Naples “Federico II”, Italy, c) who were willing to participate in the study. Pregnant women and subjects with systemic diseases or undergoing therapies that might affect pain perception were excluded. Since two subjects refused to go further in the study, the final study sample included seven females (median age = 27, first quartile = 22, third quartile = 38 years, age range 18-68 years) suffering from myofascial pain.

In order to collect VAS scores and sample weather variables, a portable data logger was delivered to each participant, together with its battery charger. In this study, the device was set up to sample temperature ($^{\circ}\text{C}$), atmospheric pressure (kPa), and absolute (g/m^3) and relative humidity (compensated and uncompensated) every fifteen minutes. A beeper promoted patients to insert the perceived masticatory muscle pain on the VAS scale (0=minimum perceived pain – 10=maximum perceived pain) every hour during waking hours (intended as 8 am – 8 pm in the protocol). When the VAS score was not entered, the data logger automatically stored the previous record.

The accuracy of the weather sensors was checked by locating the device for 2 weeks at the meteorological station of the University of Naples “Parthenope” and by calculating cross-correlations between data collected with the data logger and data sampled by the local station. The correlations showed fairly good consistency for the overall recording period.

Each patient was invited to collect data during daytime for at least three consecutive weeks starting from the day of device delivery. The protocol allowed patients to insert VAS scores during the night (8 pm – 8 am). Night time VAS scores were included in the analysis when the difference between night time VAS scores and the last daytime VAS score (the last measurement before 8 pm) was greater than 2.

Although meteorological variables were measured every fifteen minutes and VAS scores were entered by the subjects once in a hour, the device software provided corresponding VAS scores for the complete series of meteorological observations. We, therefore, decided to keep all the available information and to base our analyses on measurements obtained fifteen minutes apart from each other.

After editing procedures, the dataset included a total of 8898 observations, with a minimum of 1102 observations (22 days) for subject 7, and a maximum of 1659 observations (36 days) for subject 1.

Descriptive analyses on pain intensity and meteorological variables of interest, including temperature ($^{\circ}\text{C}$), pressure (kPa), and uncompensated relative humidity (%), were carried out on each subject. The relationship between meteorological variables and pain scores was investigated using separate generalized least squares (GLS) regression

models provided with a correlation structure estimated via AutoRegressive Integrated Moving Average models, to account for the presence of autocorrelated errors in ordinary regression models (Box et al. (1994)). In detail, for each subject and for each possible model, we preliminary fitted an ordinary least squares (OLS) regression. We, then, examined the residuals autocorrelation from the OLS fitting: firstly, we identified potential sources of nonstationarity of the residuals time series; secondly, we applied the one-parameter Box-Cox transformation (y^λ , where λ and its 95% confidence interval were estimated through a maximum likelihood approach) and/or difference operators (Box et al. (1994)) to get a stationary time series; thirdly, we identified a reasonable form for the error-generating process of the GLS model through fitting of a suitable AutoRegressive Moving Average (ARMA) model on the residuals (Hyndman and Khandakar (2008)). Finally, we fitted a GLS regression model on the potentially transformed dependent variable and with the identified ARMA(p,q) correlation structure. The most appropriate parameters p and q for the ARMA models were selected using a combination of visual inspection of autocorrelation/partial autocorrelation plots on the residual time series and information criteria. For each subject, we repeated the described procedure for each of the seven additive models and for the model including the three main effects and the three two-way interaction terms.

3 Results

Patients reported to suffer from masticatory muscle pain from a minimum of 6 months to a maximum of 40 years, with a median value of 12 months. Moreover, all subjects suffered from other painful conditions. Individual VAS trajectories differ across subjects in terms of period of observation, range of observed values, and type of trend over time. Minimum and maximum values of temperature and pressure were comparable across subjects with comparable periods of observation. Uncompensated relative humidity showed the highest standard deviations across subjects.

For every study participant, we detected nonstationarity in mean and/or variance in the residuals time series of the corresponding OLS regression models. To account for this effect, we applied the one-parameter Box-Cox transformation in all the individual GLS regression models, with values of λ ranging from -0.25 to 1.50 across subjects; we also applied the difference operator to the transformed VAS scores for three subjects. The selected correlation structures, generally, showed higher orders for the AR component, compared to the MA component. Five subjects presented at least one significant parameter ($p < 0.05$) in the selected GLS regression model. Subjects 2 and 3 ended up with just one significant parameter that was the interaction term involving temperature and uncompensated relative humidity. For subject 4's pain, it seemed to be important both the independent effects of pressure and uncompensated relative humidity and their interaction effect, although pressure was only of borderline significance. Subjects 6 and 7 shared a common set of significant parameters including temperature, the interaction between

temperature and pressure, and the interaction between temperature and uncompensated relative humidity. Subject 6 added the single effect of pressure to the previous set.

4 Discussion

To our knowledge, the present study is the first one that evaluates whether changes in weather actually predicts increased pain perception in adults with chronic masticatory muscle pain. Compared to similar studies on different diseases, our study used the more rigorous prospective methodology of EMA, which avoids to collect information retrospectively and from local meteorological stations. The results provided empirical support for the possibility that some weather variables, together with all their two-way interactions, may in fact reliably predict an increased pain perception on the VAS scale for patients affected by chronic masticatory muscle pain. They, also, suggest to extend the use of EMA methodology, and of the developed device, to larger samples, for a better assessment of the relationship under examination.

A first limitation of our analysis is that we did provide separate GLS regression models for each subject and, therefore, we were not allowed to derive an overall estimate for the effect of each meteorological variable on pain intensity. However, the study was a pilot study including only seven subjects, assessing a definitely new research question on a clinically complex disease, and using a newly developed tool. Study subjects appeared to be different as to clinical characteristics and pain perception, and, therefore, deserve separate analyses on a first basis. The developed device was programmed to collect information on meteorological variables every fifteen minutes for at least three weeks. This leaves the statistician with a cumbersome number of time-related observations for seven subjects only. Time series approaches with regressors, or equivalent GLS regression models with a suitable ARMA correlation structure, were then preferred to repeated measurement approaches. With a higher number of subjects and a far smaller number of measurements per day, the application of a multilevel modeling approach would have provided us with the overall effect estimates of the meteorological variables.

A second major limitation of our analysis is that we were not able to model directly a putative relationship between VAS scores at time t and meteorological variables at times $t-1, t-2, \dots, t-k$, for some limit k . Functional data analysis and polynomial distributed lag regression models will be considered in the next future to overcome this limitation.

References

- Box G. E. P., Jenkins G. M. and Reinsel G. C. (1994) *Time series analysis: forecasting and control*, 3rd edition, Englewood Cliffs, NJ: Prentice Hall.
- Cairns B. E. (2010) Pathophysiology of TMD pain--basic mechanisms and their implications for pharmacotherapy. *J Oral Rehabil*, **37**, 391-410.
- Hyndman R. J. and Khandakar Y. (2008) Automatic time series forecasting: the forecast package for R. *J Statis Software*, **27(3)**.