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luigi.naldi@gised.it

Floating numerators on photopatch tests: how to interpret them?

MADAM, we read with interest the paper from the European Multicentre Photopatch Test Study (EMCPPTS) Taskforce in the May issue of the Journal [1]. The study analyzed the results of Photopatch testing (PPT) on patients referred for suspected Photocontact dermatitis (PACD) to selected reference centres in Europe. The PPT series included a list of ultraviolet (UV) absorbers commonly found in sunscreens, and 6 selected non-steroidal anti-inflammatory drugs (NSAIDs). The main goal of the study was, in the words of the Authors, “to obtain current information on the frequency of PACD” to selected allergens in common usage in Europe.

The term “frequency” is loosely defined in epidemiology, summarizing the occurrence of a disease in a population without distinguishing between incidence and prevalence. In any case, its use implies some reference to an underlying at risk population. In the EMPTS paper no such a reference was made and the “frequency” measures were obtained by calculating proportions over the sample of people referred for suspected PACD. Similar measures are sometimes referred to in epidemiology as “floating numerators”, i.e. numerators floating without their appropriate denominators [2]. Epidemiological conclusions on risks cannot be drawn from purely clinical data on the number of sick people seen as it is proposed in the EMCPPTS paper. There is a need to refer measures to the underlying at risk population. It was not surprising that the observed proportions of PACDs per allergen in the EMCPPTS paper varied significantly among centers as shown in Appendix 4, and it was quite plausible that, as suggested by the authors, such variations were at least partly related to differences in subject selection in each center.

The photosensitizing potential of ketoprofen is an issue worth of being scrutinized by formal epidemiologic methods. To this end we are implementing a Europe-wide case control study especially aimed at estimating the risk of PACD linked with the use of ketoprofen and other NSAIDs. The study, entitled "Surveillance study of photocontact dermatitis leading to hospitalization in Europe with a special focus on topical ketoprofen and other topical NSAIDs, including evaluation of photosensitivity reactions", responds to a precise request made by the European Medicines Agency (EMA), and it is funded by a temporary holding of the ketoprofen's Marketing Authorization Holders. It will provide odds ratio estimates for developing PACD due to exposure to ketoprofen and other NSAIDs. In addition, the study will provide estimates of the attributable population risk of PACD for exposure to ketoprofen, i.e. the portion of incidence of PACD in the general population related to that exposure. Such a population attributable risk will be calculated by using the odds ratio estimates obtained in the case-control study and exposure rates in the control group according to the indirect method proposed by McMahon and Cole [3]. In a pilot feasibility study currently ongoing several centers are involved in different geographic areas throughout Europe, each covering a comparable population size to estimate the **exposure** rate to topical ketoprofen and other NSAIDs among controls admitted to hospitals for acute conditions or elective procedures, according to the methodology proposed by the Slone Epidemiology Unit of Boston and to compare it with available population-based drug consumption data [4]. A proportionate stratified sampling design without replacement [5] will be used in order to ensure that the sampled controls are comparable, in terms of age and gender distribution, with the underlying population of interest. In addition, an estimate of the **incidence** rate of severe PACD leading to hospitalization will be obtained by surveying hospital departments in selected geographic areas. The data obtained in the pilot phase will be used to refine the design of the case-control study. Hopefully such a case-control study will provide statistically sound data that will integrate data from case series such as those from the EMCPPTS Taskforce and will allow to better evaluate the risk benefit balance related to the use of ketoprofen and other NSAIDs with regards to PACD.

L. Naldi
S. Lecchi
Centro Studi GISED

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