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A Screening Technique for Antiperspirant Testing

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Key words

antiperspirant, testing, aluminum chlorohydrate, intraindividual design, screening

Abstract

A standardized in vivo test design for screening up to eight antiperspirant formulations in one panel is described. Dose-response curves for new raw materials or formulations can be performed in the same panel.

Designs for clinical evaluation of antiperspirant effectiveness are mostly based on the FDA guideline for effectiveness testing of OTC antiperspirant products. The guideline sets forth criteria for the test subjects, test conditions, test procedures and statistical analysis of the data.[1] Gravimetric methods are employed to measure perspiration reduction following once daily application of the product to the axilla for two to four days.

Testing in the axillae as outlined in the guideline is important to ensure that there will be a relevant perspiration reduction in a majority of consumers, not just a minimum reduction in sweat production that is statistically significant but not noticeable in practice. However, for routine use in formulation development, clinical testing in the axillae is impractical for several reasons:

- Antiperspirant products may not be used in the test axillae for 17 days before the first treatment with the test products. In practice, this means that the test duration from start of screening is approximately three weeks.
- Only two test areas, the left and right axillae, are available. A test formulation may be compared with only one control in a single panel.
- Differences between panels make comparisons of antiperspirant activity collected in separate panels difficult.

In 1998, a screening method allowing parallel comparison of up to eight antiperspirant formulations in a single panel was developed in our institute.[2] Test fields located on the back are treated on four consecutive days prior to collection of sweat approximately 24 hours after the last treatment. Since its introduction, we have collected experience and data from more than 100 antiperspirant tests in this model. Over the years, improvements in the methodology have prompted additional validation tests.

Materials and Methods

Subjects: Each panel includes 20 to 22 female subjects, aged 18 to 60 years. The women must be experienced sauna users and must have healthy skin on their backs.

Exclusion criteria include known allergic reactions to cosmetic leave-on products, deodorants or antiperspirants; symptoms or illnesses that may lead to adverse events resulting from sauna use (cardiovascular diseases, thyroid diseases, atopic dermatitis); participation in another study involving application of antiperspirants on the back in the four weeks preceding the study; evidence of drug or alcohol abuse; serious illness within the previous four weeks; and pregnancy or nursing.

The use of cosmetics or other topical products is not allowed within the test area (back) for the duration of the study. Written informed consent is obtained before inclusion in the study.

Treatments: Sixteen test fields (size 4 x 5 cm) are arranged on the back in a 4 x 4 matrix (Figure 1). All eight test fields located on one side of the back are treated with the test products. In half of the subjects treatments are on the left side of the back, in the other half on the right side. The corresponding contralateral field serves as the individual untreated control for each treatment field. Treatments are randomly assigned to the test fields on the left or right side. For example, if field 1-1 is treated, field 1-4 is the corresponding control; if field 3-3 is treated, field 3-2 is the corresponding control (Figure 1).

A defined amount of test product is applied to each of the treated test fields. Even distribution over the test field is performed in a standardized manner depending on the type of product (so-

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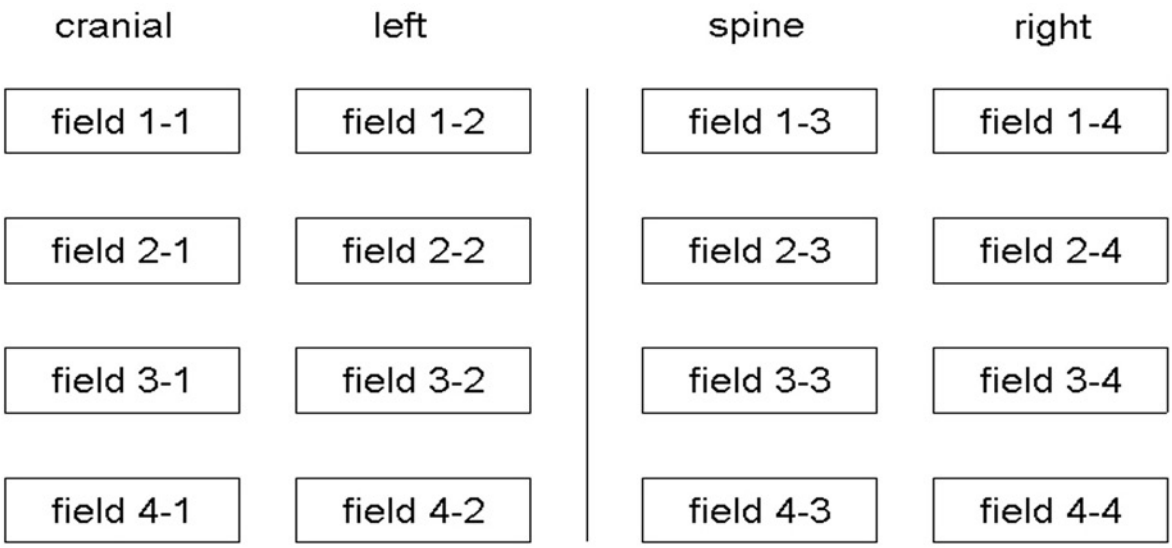

Figure 1. Arrangement of test fields on the back

lution, stick, spray, powder). The test fields are left open to air for five minutes before covering with occlusive patches. The conditions during occlusion and the length of occlusion varied according to the study protocol. Treatments are performed on four consecutive days.

Thermal stimulation: Approximately 24 hours after the last application, preweighed pads for absorption of sweat and an occlusive covering to prevent evaporation of sweat are fixed over the test fields. Thermal stimulation is then performed in a sauna at 80°C for 15 minutes. Immediately after leaving the sauna, the pads are removed and weighed.

Statistical analysis: The variable for statistical analysis is the relative reduction of sweat in the treated test area compared to the corresponding untreated control area. Descriptive statistics including mean, median, standard deviation, minimum, maximum and the 95% confidence interval are calculated. Effectiveness is proven if the lower 95% confidence limit is greater than zero. Products are ranked according to percent reduction of sweat. Comparisons between products are made using inferential methods defined in the study protocol (e.g., paired t-test, ANOVA).

Results and Discussion

Standardization of treatment conditions: The occlusion time following product application was initially set at two hours without standardized conditions for environmental temperature and humidity. At the end of this period the occlusive coverings were removed by study staff. A meta-analysis of data from more than 30 studies revealed that studies performed during cold, dry periods often showed an increased number of outliers. Therefore standardization of the environmental conditions during occlusion was undertaken using a standard marketed antiperspirant.

In order to simulate humid conditions such as found in the axillae, the subjects were placed in a room with 30°C, 50% humidity for 10-90 minutes. On the basis of the data presented in Figure 2, 60 minutes at 30°C, 50% humidity was chosen for the occlusion period. Significant differences between the fields occluded for 30, 60 and 90

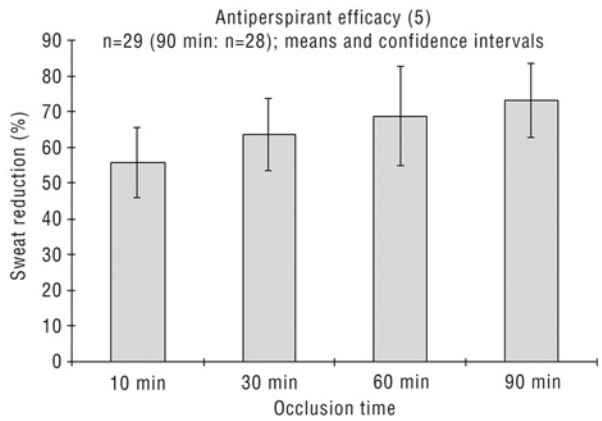

Figure 2. Relation of efficacy (sweat reduction) and occlusion time following application of a standard antiperspirant product to test fields on the back

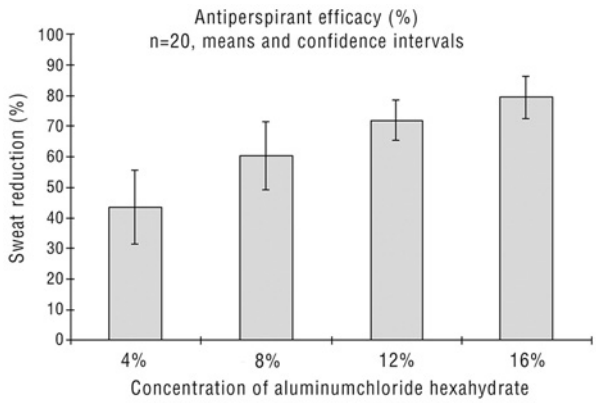

Figure 3. Dose dependent sweat reduction by aluminum chloride hexahydrate in water

Table 1. Mean percent sweat reduction (with 95% confidence interval or 95% CI) in test fields located on the inner and outer region of the back treated with the same concentration of aluminum chloride hexahydrate*

Concentration	Sweat Region	Reduction	95% CI
4%	inner	41%	13
4	outer	46	12
8	inner	60	11
8	outer	61	12
12	inner	70	7
12	outer	73	7
16	inner	81	6
16	outer	79	9

*Formulations: Aluminum chloride hexahydrate 4.0 (or 8.0, 12.0, 16.0), hydroxy ethyl cellulose 400 5.0, aqua purificata ad 100

minutes were not found. Under these standardized treatment conditions fewer outliers occur regardless of the climatic conditions.

Variations between test locations: Treatments are assigned to the test fields in a random manner to balance possible effects due to differences in sweat production in different areas of the back. In fact, analysis of untreated fields in the meta-analysis showed that sweating is higher in the test fields next to the spine (fields 1-2 to 4-3, Figure 1) than the outer test fields (fields 1-1 to 4-1 and 1-4 to 4-4) as well as in the lowest test fields (fields 4-1 to 4-4). As seen in Table 1, the mean percent sweat reduction in treated fields was similar regardless of whether the field was located on the inner or outer region of the back.

Dose-dependent sweat reduction: In order to assess statistical differences between the four doses of an aluminum chloride hexahydrate solution, the mean of the reduction in the inner and outer regions was calculated (based on same data as Table 1). As can be seen in Figure 3, there was a clear dose dependency. The advantage of parallel comparisons of all four concentrations in the same panel is evident in the sensitivity of the statistical test (paired t-test, alpha = 5%). Statistical differences were significant between all concentrations (sequential Bonferroni-Holm correction applied).

Conclusions

The ability to recognize small differences between antiperspirant products is important for the selection of the most promising developmental formulations. In this test model on the back, relative differences between products can be assessed in a one-week design. Testing of up to eight products in parallel allows ranking of products and comparison with a standard of known efficacy. Reliable results can be obtained in a panel of 20-22 women, largely because of the standardized treatment conditions. All applications are performed by study staff, eliminating compliance problems. Since the test is performed on the back, a wash-out period is not necessary. Costly testing in the axillae can be limited to finished formulations.

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