THE THERAPY OF THE COMMON COLD WITH A COMBINATION HOMEOPATHIC PREPARATION, COMPARED WITH TREATMENT WITH ACETYLSALICYLIC ACID:

A CONTROLLED RANDOMIZED, SINGLE-BLIND STUDY

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SUMMARY:

A clinical test was carried out on 170 West German army soldiers suffering from the common cold. The test was conducted on a monocentric, randomized, non-sequential, and inter-individual basis. The research personnel were kept blind on the identity of the medication. The purpose of testing was to compare the effectiveness of a combination homeopathic preparation (Gripp-Heel) with that of acetylsalicylic acid. On the 4th and 10th treatment days, no significant difference was determined with respect to changes in clinical findings, subjectively assessed complaints, or the length of time the patients were unable to work. **Thus it can be concluded that the two preparations possess comparative effectiveness in the treatment of the common cold.**

Acetylsalicylic acid, common cold, Gripp-Heel, homeopathic drugs

1. INTRODUCTION AND OBJECTIVE OF THE STUDY

Conventional, standard medicamentous therapy in symptomatic treatment of the common cold usually includes administration of acetylsalicylic acid.

The often considerable side effects of this preparation, however, have prompted studies to determine medication at least as effective and without these deficiencies. In this study, the therapeutic effectiveness of acetylsalicylic acid for treatment of the common cold, known for decades, is compared with that of a homeopathic preparation. The objective of this study was to determine whether the combination homeopathic preparation Gripp-Heel, made by the company Heel of Baden-Baden, West Germany, influences the progress of a diagnosed common cold in one or more of its characteristics, in a manner similar to that of acetylsalicylic acid.

What the English world calls the common cold is closely associated with the disease called “Grippe” in German. In Germany, the term “Blitzkatarrh” was used earlier to denote the acute and tempestuous beginning of the illness [10, 15, 23]. From the standpoint of its clinical picture, the disease termed in English, the common cold, is a catarrhal disorder of the upper respiratory tract, which may be viral in nature, a mixed infection, or an allergic reaction. Influenza colds can be associated with epidemic or pandemic phenomena which occur in long cycles of approximately every 25 to 30 years [1, 13, 22-24, 31]. Transmission of the disease is by droplet infection.

Undercooking or the action of dampness on the body generally prepares the way for the common cold. A considerable number of viruses have been considered as the agent [12, 22,24, 31]. Bacterial infections, on the other hand, are usually of secondary importance. After an incubation period lasting from several hours to several days, the patient suffers from chills, shivering attacks, and fever above 37°C (98.7°F). Development follows of inflammatory swelling of the naso-pharyngeal mucous membranes, with rhinitis and pharyngitis. The victim complains of earaches, pain in the limbs, headaches, and sore throat - as well as of the familiar abnormal fatigue, loss of appetite, unnatural thirst, insomnia, excessive perspiration, and a runny nose. Further development of the inflammation is associated with laryngotracheobronchitis and with stubborn dry cough. Unless complications develop, a common cold of this nature will normally subside within 5 to 10 days. Depending on the age and resistance of the patient, there is the possibility of the further development of bacterial superinfection - e.g., through pneumococci, streptococci, staphylococci, hemophilus influeruae, or klebsiella pneumonia - including occurence of bronchial pneumonia. Further complications are croup, sinusitis, otitis, encephalitis, and myocarditis [22, 23].

In addition to the clinical symptom complex, definite diagnosis can be performed on the basis of serological antibody titer tests [23]. Such determination is, however, too late to be of practical use to the patient, and is of significance only in an epidemiological context. In most cases without complications, the doctor will administer symptomatic therapy [14, 19]. In addition to traditional chemical pharmaceutical products, however, the modern physician has recourse to a great number of preparations based on phytotherapeutic and homeopathic principles [6, 10, 12, 13, 19, 26, 30].

The effectiveness of these medications can and should be verified by means of the modern methods of clinical research and the techniques of medical statistics.

2. MATERIAL AND METHODOLOGY

2.1 TEST POPULATION

During the spring, autumn, and winter months from January of 1984 to March of 1986, recruits and soldiers serving for longer specified terms in the West German army provided the population for this study. The test covered a total of 170 patients between 17 and 49 years old. The test group included 88 soldiers, and the control group, 82. Three doctors performed the examinations. In advance, test personnel notified the patients of the purpose of the study and of the possible side effects of the medication (as stipulated by German law, § 40, Para. 1, and 41, AMG 76). The physicians applied criteria both of inclusion and of exclusion in their diagnosis of the common cold, as described below:

INCLUSION CRITERION NO. 1 (General subjectively assessed complaints):

At least 3 of the following subjective sensations had to be present: abnormal fatigue, loss of appetite, excessive thirst, insomnia, chills, excessive perspiration, runny nose, or cough.

INCLUSION CRITERION NO. 2 (Pain):

At least 2 symptoms of the following group of pain complaints had to be present: sore throat, earache, aches in limbs, or headache.

INCLUSION CRITERION NO. 3 (Clinical findings):

At least 1 symptom from the following clinical findings needed to be present: nasal secretion, swelling of lymph glands, eardrum retraction, or sounds indicating bronchitis. In addition, the patient's temperature (axillary measurement) needed to be at least 37°C (98.7°F). Satisfaction of all of the above 3 criteria was required for patients to be included in the study.

The following were the criteria of exclusion:

1. Beginning of the illness more than 2 days before possible inclusion in the study
2. A history of chronic bronchitis or suppurative angina tonsillaris
3. Fever over 39°C (axillary measurement)
4. The necessity of long-term therapy with similarly acting preparations which could influence the study (e.g., anti-rheumatics)
5. Administration of medication immediately prior to the study
6. Contraindications for acetylsalicylic acid
7. Weight in excess of 10% of normal (i.e., height in cm less 100, expressed in kg)
8. Alcohol consumption of more than 500 ml per day of wine or its equivalent

On the day that the patients reported sick, the test staff examined and questioned them and made the decision - on the basis of the above criteria - for or against inclusion into the study. The staff additionally collected the following data: date of examination, birthdate, height, weight, previous term of illness in days, suspicion of intolerance to acetylsalicylic acid, medication currently being taken, other current illnesses, consumption of alcohol per day, and record of vaccination against flu. The staff additionally reported the following as part of the clinical examination: blood pressure, pulse, and temperature (axillary measurement). The symptoms of the subjective complex of complaints (see Inclusion Criterion No. 3 above) were evaluated on the basis of the following 3-point scale:

0= no complaints
1= slight complaints
2= severe complaints

Subsequent examination for the following took place on the fourth and tenth days after inclusion in the study, in the form of supervision of clinical findings: temperature, pulse, blood pressure, nasal secretion, lymph-gland swelling, eardrum retraction, and sounds indicating bronchitis. Changes in subjectively assessed complaints and in pain were also registered by questioning and by use of the 3-point scale. Important data on the following were also noted: lengthy exposure to the elements, side effects of the medication (e.g., gastro-intestinal disturbances, hypersensitive reactions, or arrhythmia). On the 20th day, subsequent examination took place, with documentation of the term of inability to work and of any other symptoms which may have appeared in the meantime. The staff took blood samples from every second patient from test and control groups, on the 1st, 4th, 10th, and 20th days. Data involving parameters on the following were obtained: blood sedimentation rate, differential blood-count, Quick's test, thrombocytes, gamma-glutamyl transpeptidase, antistreptolysin, antistaphylolysin, influenza mycoplasmas (only upon suspicion), and mumps titer (only upon suspicion).

2.2 MEDICATION

Treatment took place on an out-patient basis, with administration of the homeopathic combination preparation from the 1st to the 10th day, in the form of 3 x 3 tablets per day. Treatment of the control group with acetylsalicylic acid took place as follows: 3 x 500 mg of acetylsalicylic acid daily from the 1st to the 4th days, followed by 1 x 500 mg from the 5th to the 10th days. The homeopathic combination preparation Gripp-Heel has the following composition for a 300-mg tablet:

- 20 mg of Aconitum 4X (monkshood)
- 60 mg of Bryonia 4X (bryonia)
- 60 mg of Lachesis 12X (bushmaster snake venom)
- 30 mg of Eupatorium perfoliatum 3X (water hemp)
- 30 mg of Phosphorus 5X.

Preparation of the mother tinctures, the potentizations, and the final drug takes place in accordance with the legally recognized stipulations contained in the German Homeopathic Pharmacopoeia.

Breakdown of patients into test and control groups was performed by flipping a coin (heads: control, and tails: test group) and preparing a randomized list. Staff noted the group assignment on cards issued to all the patients, which were sealed into consecutively numbered envelopes and provided to the test center.

Due to difficulties involved in double-blind studies with the dosing and administering of preparations being compared - especially in view of the fact that only lactose as a medium was possible for the homeopathic test preparation in tablet form - the decision was made to conduct single-blind testing. As a result, the patients were aware of the identity of the medication being administered to them by the head of the clinic, after opening of the randomization envelope. The examining test physician (military doctor), however, was not aware of the nature of the medication administered to each patient. This arrangement was intended to prevent influencing the test doctor by knowledge of the type of medication. This procedure also avoided tempting the physicians to formulate suggestive questions during their surveying of the subjectively assessed complaints. During initial briefing, the test staff instructed the patients not to reveal the identity of their medication before conclusion of the study.

2.3 METHODOLOGY

The main criterion was defined as follows to determine whether therapy had in fact been successfully conducted on an individual basis:

* The score total of evaluated points for subjectively assessed complaints, pain, and clinical findings - as determined on the 3-point scale - is reduced by half between the initial examination and the 4th day. * The patient's temperature is not above 37°C.

The quotient expressing the fraction of successfully treated patients was used as primary means of comparing the effectiveness experienced in the two groups. Secondary criterion no. 1 was defined as the share of successfully treated patients during the period of 10 days following the initial examination. Secondary criterion no. 2 was defined as the length of time the patients were unable to work. It was expected that a

success quotient of 0.70 (70% successful) would be obtained for the control group. In view of the well-known side effects of acetylsalicylic acid, a success quotient for the test group was in advance defined to be "clinically relevantly less successful" only if it were 20% (0.20) or more less effective than the success quotient for the control group (delta = 0.20).

The chi-square (4-field) test was utilized for qualitative data, and the test was applied for quantitative data. The number of successfully treated patients was considered within each treatment group to be a binomially distributed stochastic variable with parameters of nl, pl (control group), and n2, p2 (test group). It was assumed as null hypothesis that both of the medications were equally effective (p1 = p2, with a significance level of alpha = 0.05). For the doublet test, a stipulation of 1- beta = 0.80 was set to establish the power of testing. A total of n = 72 cases capable of evaluation was required per group in accordance with the procedure of Casagrande, Pike, and Smith. After registration of data and application of the exclusion criteria, only 33 patients remained for purposes of statistical analysis and plausibility testing (see Table 2). As a result, the exclusion criteria had to be modified as follows:

1. Patients with other diseases were no longer excluded, unless these other illnesses were angina tonsillaris or chronic bronchitis (which remained as grounds for exclusion).
2. The patient's weight was no longer considered.
3. The interval between examination days was selected on a more flexible basis: 1st subsequent examination on 4th or 5th day, and 2nd subsequent examination on 10th or 11th day.
4. The originally stipulated interval between pre-treatment and post-treatment examinations (20 days) was no longer taken into account, since the point in time of the post-treatment examination is not relevant for the main criterion.
5. The permissible number of sick days before acceptance into the study was increased to 4.
6. The question concerning alcohol consumption was deleted, since only 2 patients indicated consumption above the original limit.
7. Patients who interrupted treatment after only the third examination (on the 10th or 11th days) were not excluded from statistical analysis.

All statistical evaluations were performed by the programs Statistical Analysis System Release 82.3 and Release 5.08. Monitoring of compliance is basically difficult with orally administered medication. Additional difficulty is involved with medication of the type used here, moreover, since the use of a tracer proved to be unfeasible. The fact, however, that all patients lived in the relatively well supervised environment of troop bar-racks, speaks per se for higher compliance levels than can be expected under conventional studies of this nature.

3. RESULTS OF THE STUDY

Approximately equal distribution resulted in both groups regarding the following influencing factors: age, weight, alcohol consumption, lengthy exposure to the elements, influenza vaccination, influencing medication taken at the same time (Table 1), and deviations from the test plan (Table 2).

3.1 MAIN CRITERION

A total of 115 cases were able to be analyzed for assessment under the main criterion: i.e., therapeutic success within four days (see Table 3). A total of 18 out of 62 patients in the test group were successfully treated, and a total of 12 of 53 from the control group (see Table 4).

3.2 SECONDARY CRITERION NO. 1

In order to enable assessment of the effectiveness of the medication over a longer period of time, the quota of successfully treated patients was also studied from the time of the intial examination until the 10th (or 11th) day. For these analysis, the patients were no longer available who had interrupted therapy after the first subsequent examination, nor were those available for whom the interval between the initial examination and the second subsequent examination did not amount to 9 or 10 days. A total of 82 cases were analyzed (see Table 6). In this instance, there was a reversal in the ratio of successfully and unsuccessfully treated patients: in the first instance, there were more unsuccessful than sucessful results; in the second, however, there were more successes. In the test group here, the total quota of successfully treated patients amounted to 30 out of 42 (71%); in the control group, the figures were 25 out of 40 (60%). See Tables 7 and 8. From the fourth day onward, 12 patients were simultaneously taking an additional medication which could have influenced study findings. Since 6 patients from the acetylsalicylic acid control group had been

TABLE 1: Possible influencing factors

Number of patients	Test group (n=88)	Control group (n=82)	Total
Age: 17-25 years old	75	74	149
Age: 26-49 years old	13	8	21
Weight within normal range	50	51	101
Weight outside normal range	38	31	69
Alcohol comsumption (wine)			
Up to 0.5 liter per day	86	82	168
0.5-1.0 liter per day	2	0	2
Lenghty exposure to elements	2	1	3
Influenza vaccination			
Yes	4	3	7
Unsure	4	1	5
Other medication taken	14	12	26
Other influencing medication beginning on 4th day	5	7	12

TABLE 2: Distribution of the total number of deviations from test plan

	Test group (n=88)	Control group (n=82)	Total
Long-term medication	3	4	7
Interruption after the first examination	14	7	21
Interruption after the second examination	26	16	42
Inclusion criterion 2 not fulfilled	1	3	4
Inclusion criterion 3 not fulfilled	8	14	22
Interval of 4 days between 1st examination and first subsequent examination not maintained	3	6	9
Interval of 10 days between 1st examination and 2nd subsequent examination not maintained	16	16	32
	71	66	137

successfully treated for the common cold by the tenth day - in contrast to only 3 patients from the test group - it can be concluded that the apparent effectiveness of the homeopathic medication had not been favorably falsified by this additional medication. As a result, these patients who had simultaneously taken additional medication were not deleted from the analysis in the study. The varying data on frequency of successfully treated patients - as verified by the chi-square test (with one degree of freedom) and by the exact Fischer test (double) - provialed an observed significance level of p = 0.437 for the main criterion and p = 0.390 for secondary criterion no. 1.

3.3 ADDITIONAL SECONDARY CRITERIA

Results with regards to the other secondary criteria were as follows: the mean value for length of inability to work for the test group was 11.72 days (standard deviation = 3.93), and 12.95 for the control group (with standard deviation = 4.87). The observed difference between these mean values is not significant.

3.4 RESULTS WITH REGARDS TO ILLNESS SYMPTOMS AND LABORATORY PARAMETERS

a. In the case of all individual symptoms in the two groups, a continuous decrease in the mean values - calculated according to the 3-point scale - was observed between the 1st and 10th (or 11th) days. Only the symptoms of nasal secretion, catarrhal rhinitis, and coughing exhibited a slowed tendency toward improvement.

b. The laboratory parameters provide relatively uniform descriptions, without showing particular tendencies or enabling particular conclusions. In titer tests for Influenza A and B, only endemic-infection titers were determined: i.e., there was no evidence for fresh infection.

c. The initial values and progress of change for the circulation parameters for blood pressure and pulse also revealed no differences between the test and control groups.

3.5 RESULTS OF OVERALL STATISTICAL ANALYSIS

The relative shares of successfully treated patients up to the 4th (or 5th) and up to the 10th (or 11th) days of treatment were greater in the test group (with the homeopathic remedy) - or were lesser there to only an insignificant degree - than those in the control group (with acetylsalicylic acid). This result held true both on an overall basis, as well as for the various individual sections of the study. The differences were not sufficiently pronounced to be considered statistically significant up to a level of alpha = 0.05 for the small number of cases involved in some parts of the study. Since the number of patients provided was not large enough for a statistical power of 0.80, the observed confidence was computed for the case that the absolute difference between the success probability in the test group and in the control group was equal to or less than 0.2 (- 0.2 c delta e + 0.2). The confidence figure quantifies the strength of evidence for an area of clinically equivalent success probabilities on a scale between 0 and 1. It amounts to 0.95 for the main criterion in the overall study conducted here (cf. [16] for the details of this procedure).

TABLE 3: Distribution of patients eliminated from analysis for main criterion of "therapeutic success within 4 days"

	Test group (n=88)	Control group (n=82)	Total
Long-term medication	2	1	3
Interruption after the 1st examination	14	7	21
Inclusion criterion 2 not fulfilled	0	3	3
Inclusion criterion 3 not fulfilled	7	12	19
Interval of 4 days between 1st examination and first subsequent examination not maintained	3	6	9
Eliminated from analysis	26	29	55
Included in analysis	62	53	115

TABLE 4: Results for the main criterion "therapeutic success within 4 days"

	Test group successful	Control group successful	Total successful
Total	18/62	12/53	30/115
Jan-Mar 1984	11/30	4/21	15/51
Jan-Mar 1985	2/5	2/7	4/12
Jul '85-Mar '86	5/27	6/25	11/52

TABLE 5: Results for the main criterion "therapeutic success within 4 days" (in percent, with 95% confidence interval)

	Test group successful	Control group successful	Total successful
Total	30% (17-42%)	20% (12-36%)	26% (18-35%)
Jan-Mar 1984	40% (20-56%)	20% (5-42%)	30% (17-44%)
Jan-Mar 1985	40% (5-85%)	30% (4-71%)	30% (10-65%)
Jul '85-Mar '86	20% (6-38%)	25% (9-45%)	20% (11-35%)

Expressed in percent with a 95% confidence interval, the homeopathic combination preparation was successful with 30% (17-42%), and acetylsalicylic acid was successful with 20% (12-36%). The success quota with acetylsalicylic acid treatment (0.20) was considerably lower than had been initially assumed (0.70).

TABLE 6: Distribution of patients eliminated from analysis on the basis of secondary criterion no. 1: "therapeutic success within 10 days"

	Test group (n=88)	Control group (n=82)	Total
Long-term medication	2	1	3
Interruption after the first examination	14	7	21
Interruption after the second subsequent examination	12	10	22
Inclusion criterion 2 not fulfilled	0	2	2
Inclusion criterion 3 not fulfilled	6	11	17
Interval of 4 days between 1st examination and first subsequent examination not maintained	3	6	9
Interval of 10 days between 1st examination and 2nd subsequent examination not maintained	12	11	33
Eliminated from analysis	46	42	88
Included in analysis	42	40	82

4. DISCUSSION OF THE STUDY

The effectiveness of the homeopathic combination preparation tested here [Gripp-Heel®] is comparable to that of acetylsalicylic acid with respect to the beneficial changes brought about in clinical findings up to the 4th and 10th days of treatment, as well as with regards to the length of time that patients were unable to work. The determined success quota of acetylsalicylic acid (0.20) was considerably lower than the assumption made before testing (0.70). We interpret this to signify that our criteria for success had been strictly formulated. These findings can, however, also signify that effectiveness of acetylsalicylic acid cannot be demonstrated under the test conditions as they were applied here - and that the homeopathic combination preparation was as equally ineffective as acetylsalicylic acid. As had been expected, the quota of side effects for the test group was very low: only 3 cases. Fortunately, only 7 patients treated with acetylsalicylic acid registered slight to moderate abdominal side-effect complaints.

With regards to age, daily routine, and social surroundings, the population - all soldiers on a military base - in the test and control groups was composed of persons with relatively highly similar individual characteristics. The military medical service provided by the German army even enabled in-patient care and monitoring of the more seriously ill test persons. Unfortunately, nevertheless, the unsatisfactory conformance to the selection criteria of the test plan gave occasion for concern regarding observance of the remaining study stipulations designed to ensure an undistorted process of subsequent patient examination. The course of the illness for patients with a previous influenza vaccination was not milder than for patients without this prophylaxis. This finding was not surprising, in light of the great number of possibly participating causative agents, and the difficulties of providing effective measures against them [11, 12, 31]. Gassinger *et al* [5] came to similar conclusions in a clinical study of 53 patients suffering from common colds, with comparison of therapy by acetylsalicylic acid and treatment by the preparation Eupatorium Perfoliatum 2X (water hemp). In our study, we attempted to avoid subjective influence on results by the medical staff through the single-blind organization (concealing the identity of the medication from the staff). The question remains open, however, as to how effective the homeopathic preparation actually is in comparison to placebos and to acetylsalicylic acid under test conditions in which the success quota of acetylsalicylic acid therapy is significantly higher than in our study (i.e., closer to the 0.70 expected at the beginning of testing). We decided not to conduct a placebo-controlled study, "which would have also included any occurring cases of spontaneous remission. A double-blind study, however, has in fact been conducted by Vorberg [28] on this problem area. He studied a phytotherapeutic medication similar to the combination preparation tested by us here, in comparison with a placebo (vitamin C). Significant alleviation of the symptom picture of the common cold was obtained for the phytotherapeutic medication. We can justify our recommendation for employing a homeopathic medication of this nature for therapy of the common cold on the basis of the following: the effectiveness of acetylsalicylic acid is based on a symptomatically analgesic, antipyretic, as well as unspecific inhibitory effect on the inflammation through blocking of prostaglandin synthesis [9]. The

TABLE 7: Results for secondary criterion no. 1: "therapeutic success within 10 days"

	Test group successful	Control group successful	Total successful
Total	30/42	25/40	55/82
Jan-Mar 1984	21/28	14/20	35/48
Jan-Mar 1985	1/ 4	4/6	5/10
Jul '85-Mar '86	8/10	7/14	15/24

TABLE 8: Results for secondary criterion no. 1: "therapeutic success within 10 days" (in percent, with 95% confidence interval)

	Test group successful	Control group successful	Total successful
Total	70% (55-84%)	60% (46-77%	70% (56-77%)
Jan-Mar 1984	75% (55-89%)	70% (46-88%)	75% (58-85%)
Jan-Mar 1985	25% (0-81%)	70% (22-96%)	50% (19-81%)
Jul '85-Mar '86	80% (44-97%)	50% (23-77%)	65% (41-81%)

administration of an antipyretic in cases of the common cold can therefore have negative consequences under certain conditions, since elevation of body temperature acts to inhibit virus reproduction [12]. The antagonistic or suppressive approach to therapy as represented by administration of acetylsalicylic acid must therefore be interpreted in contrast to regulative therapy with a homeopathic preparation. The latter, homeopathic approach attempts to motivate the body's regulation mechanisms and to normalize its dysfunctions. A critical prerequisite to this approach, however, is that the organism be capable of reaction. The therapeutic effects of regulation therapy include inducing paramunity [see 17 for unspecific mechanisms of infection resistance]: i.e., the attempt is made to achieve unspecific enhancement (one not related to causative agents or antigens) of the body's resistance, which becomes effective within several hours and which lasts up to several weeks [8, 11,20, 21]. The phagocytosis rate is increased [2, 3, 18, 29] and stimulation of the following is observed:

- Humoral factors
- Cellular enzymes
- The lymphopoietic system (especially, T lymphocytes)
- Cell-mediated cytotoxicity
- Lysis activity of the monocytes
- Production and/or release of interferon

After subsidence of the stimulated body functions, specific memory reactions do not develop [17, 25]. This broad effectiveness of homeopathic agents upon employment of extremely small amounts of active substances can unquestionably be preferred to the administration of an antipyretic with its inhibitory action: especially if both therapeutic agents - the homeopathic and the chemotherapeutic - have proven to be of comparable effectiveness in treatment of the common cold.

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