



Effectiveness and tolerability of a homoeopathic remedy compared with conventional therapy for mild viral infections

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SUMMARY

Treatments for mild viral infections are usually directed at providing symptomatic relief. The effectiveness of the homoeopathic remedy Gripp-Heel[®] was compared with that of conventional treatments in a prospective, observational cohort study in 485 patients with mild viral infections and symptoms such as fever, headache, muscle pain, cough or sore throat. Practitioners specialised in homoeopathy or conventional treatment, or practised both to similar extents. As evaluated by the practitioners, the homoeopathic therapy was effective to similar or greater degree than the conventional therapies: 67.9% of patients

were considered asymptomatic at the end of Gripp-Heel[®] therapy vs. 47.9% of patients in the control group. Practitioners judged homoeopathic treatments as 'successful' in 78.1% of cases vs. 52.2% for conventional therapies. Tolerability and compliance were good in both treatment groups, with the verdict 'very good' given for 88.9% of patients in the homoeopathic group vs. 38.8% in the conventional treatment group.

Keywords: Gripp-Heel; anti-tussive; NSAID; cohort study; compliance

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INTRODUCTION

Mild viral infections, such as the common cold or milder versions of influenza, are benign illnesses which nevertheless burden individuals and society. It has been estimated that the common cold syndrome is responsible for 20 million days of loss of productivity and 22 million days of absence from school in the United States every year (1). About 25 million yearly practitioner visits in the United States are due to uncomplicated upper respiratory infections (2).

There is no effective treatment for the disease underlying mild viral infections, mainly because of the multitude of different viruses with different mechanisms of pathogenicity responsible for these illnesses. Among the most popular, self-administered medications are large doses of Vitamin C, which have been used for some 30 years (3), both to treat acute symptoms and as a long-term preventive therapy. A large number of studies on Vitamin C for the common cold have been conducted, but the evidence of benefits from therapy is weak at best, both for prevention (4) and for acute symptomatic therapy (5,6).

Most of mild infections such as the common cold are self-healing within a couple of weeks, and a number of remedies are available to achieve symptomatic relief (7,8). The majority are directed at reducing nasal congestion, cough, sore throat, fever and other similar symptoms and consist of anti-histamines, anti-tussives (although their efficacy is debated) (9), mucolytic agents and non-steroidal anti-inflammatory drugs (10,11). In addition, remedies such as zinc are frequently used, although their effectiveness is disputed (12).

Complementary medicine, particularly homoeopathy, has a long history of use in Germany and is publicly well recognised by many practitioners practising both conventional and complementary medicine. We report here on the effectiveness and tolerability of the homoeopathic medication Gripp-Heel[®] (Gripp-Heel) compared to conventional treatments in patients with mild-to-moderate symptoms of viral infections. The preparation is based on highly diluted plant extracts and phosphorus (listed in Table 1). Gripp-Heel is used in complex homoeopathic practice, which employs fixed combinations of a number of homoeopathic agents. All constituents of Gripp-Heel are listed in the Homoeopathic Pharmacopoeia of the United States (13) and the formulation has been used for many decades in Europe and the United States in the treatment of various types of influenza, the common cold and other viral infections.

The study was a non-interventional, observational cohort study in 485 German patients. This choice of study design was governed by the wish to capture actual clinical practices across a large spectrum of patient types and indications.

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Table 1 Constituents and indications of Gripp-Heel®

<i>Constituent</i>	<i>Indications</i>
Aconitum (monkshood)	Inflammatory diseases; neural disorders; cardiac disorders
Bryonia (bryony)	Inflammations of respiratory organs, pleura, peritoneum and liver; acute and chronic rheumatic disorders
Eupatorium perfoliatum (water hemp)	Influenza and fever; rheumatic ailments
Lachesis (bushmaster snake venom)	Dermal inflammations; infectious diseases; fatigue
Phosphorus	Inflammations, infectious diseases, cardiac insufficiency; neuralgia and headaches; vascular disorders

METHODS

This was a multicentre, prospective, parallel group, non-interventional, observational cohort study. Included were 182 practitioners and a total of 485 patients. Practitioners could be from practices with emphasis on conventional medicine, from practices emphasising homoeopathic practises or from practices offering both kinds of therapies to a similar degree. The choice of study medication laid with the practitioner or with practitioner and patient in dialogue. Patients were not randomised and there was no selection of patients at the time of inclusion.

Included were patients with acute respiratory viral infections (not otherwise specified) and symptoms such as fever, headache, muscle pain, cough, nasal congestion or sore throat. Symptoms were characterised as mild, of medium intensity or severe. If patients presented with more than one symptom, the secondary symptoms were graded on the same scale. The hypothesis was that treatment with Gripp-Heel would be as effective and better tolerated ($\geq 10\%$) than conventional therapies.

Patients were excluded if they were currently undergoing treatment for viral infections and if they were taking medications that were not included in the German drug directory ('Rote Liste'). Additional therapies (both homoeopathic and conventional medications) were allowed in both treatment groups. The study was conducted according to good clinical practice and according to the declaration of Helsinki. Full confidentiality of the data was ensured. As the study was non-blinded, patients had full information as to the kind of medication they were receiving. Data were gathered on patient characteristics (sex, age group, indications, severity and duration of symptoms, accompanying illnesses, the use of other medications besides those prescribed, etc.) and on prescription patterns.

Patients were followed-up for a maximum of 3 months. Treatments were evaluated for effectiveness as graded by the respective practitioner on three grades: asymptomatic, marked symptom improvement or minor improvement. In addition, effectiveness was evaluated as the time to symptomatic improvement: less than 4 days, 4–7 days, 2–4 weeks and longer than 4 weeks. Analyses of effectiveness were done on primary and secondary symptoms separately.

Treatment satisfaction was evaluated as practitioner-assessed patient compliance, graded on four scores: very good, good, satisfactory or unsatisfactory. Safety of medications was assessed by the respective practitioners on the same four scores. Adverse events were recorded by severity, kind of event, duration, actions taken and outcome, relation to treatment and whether the event led to interruption of therapy.

Data were analysed in multivariate fashion, with separate analyses for primary and secondary symptoms, using Fisher's exact tests, Wilcoxon–Mann–Whitney tests and Cox proportional hazard regression model as appropriate. For the safety analysis, the entire study population was used. For the evaluation of compliance and tolerability and effectiveness of treatments, patients were stratified according to propensity score as described by Rosenbaum et al. (14,15) to construct matched strata that balance observed covariates for the treatment groups. Statistical analyses were conducted using SPSS 11.

RESULTS

Patients

The study enrolled 485 patients, 196 of which received Gripp-Heel and 289 receiving conventional therapies. The majority of participating practices offered homoeopathic and conventional therapies to a similar degree (67.6% of practices). Practices with emphasis on conventional treatments were slightly more frequent than practices emphasising homoeopathic medicine (18.2 and 14.2%, respectively).

Patient characteristics are summarised in Table 2. The two groups were not completely balanced at baseline for all baseline variables: Gripp-Heel patients tended to be older, with 58.7% <40 years compared with 70.9% of patients in the conventionally treated group. However, the proportion of men and women was highly similar in both groups, as was the duration of symptoms. There were more women than men in both treatment groups, and the overwhelming majority of patients (>80% in both groups) presented with symptoms within 1 week of the onset of illness. The severity of symptoms at first presentation likewise did not differ between the treatment groups, with most symptoms judged by practitioners as moderate-to-severe.

Table 2 Population characteristics at baseline

Patient characteristic	Gripp-Heel, n (%)	Conventional therapy, n (%)
Age (years)		
<18	45 (23.0)	104 (36.0)
18–40	70 (35.7)	101 (34.9)
41–65	67 (34.2)	69 (23.9)
>65	14 (7.1)	15 (5.2)
Men	80 (40.8)	129 (44.7)
Women	115 (58.7)	159 (55.0)
No data	1 (0.5)	1 (0.3)
Duration of illness		
<1 week	173 (88.3)	246 (85.1)
1–4 weeks	20 (10.2)	37 (12.8)
1–6 months	1 (0.5)	2 (0.7)
>6 months	1 (0.5)	4 (1.4)
No data	1 (0.5)	0 (0.0)
Indications [#]		
Total	229 (100.0)	394 (100.0)
Otorhinolaryngological	187 (81.7)	313 (79.4)
Infections	25 (10.9)	30 (7.6)
Eye, ear	4 (1.7)	28 (7.1)
Other symptoms	4 (1.7)	23 (5.9)
Severity of primary symptom		
Mild	11 (5.6)	8 (2.8)
Moderate	81 (41.3)	122 (42.2)
Severe	114 (53.1)	159 (55.0)

[#]Patients may present with more than one indication.

Most patients presented with otorhinolaryngological symptoms. The most notable difference in symptoms between patient groups was that fewer patients in the Gripp-Heel group presented with eye and ear infections than in the conventional-therapy group.

The proportions of patients receiving more than one therapy were similar between groups (54% in the homoeopathy group vs. 59% in the control group). In the conventional-therapy group, the most common treatments were cough remedies (anti-tussives/expectorants) (32.4%), analgesics (21.6%) and antibiotics (20.3%). In the Gripp-Heel group, 24.0% of patients received one additional treatment, 14.3% received two and 29.6% received three or more treatments. The additional treatments in this group were homoeopathic remedies, most commonly the herbal-based preparations Engystol[®] (20.4% of patients), Euphorbium compositum[®] (7.7%), Traumeel S[®] (16.8%) and Lymphomyosot[®] (10.7%) in different combinations.

Effectiveness

The effectiveness of Gripp-Heel appeared superior to or equal to that of the conventional comparator therapies on all variables measured. A greater percentage of patients reported no symptoms at the end of the therapy with Gripp-Heel than other therapies (67.9% on Gripp-Heel vs. 47.8% for the conventionally treated group) (Figure 1a), and the practitioner-assessed success rate of

treatment was greater in patients receiving Gripp-Heel than other treatments (78.1% on Gripp-Heel vs. 52.2% for the conventionally treated group) (Figure 1b). Measured as percentage of patients with improved symptoms at different time points, about twice as many patients (64.6 vs. 31.5%) needed less than 4 days to show symptom improvement with Gripp-Heel therapy than with other remedies (Figure 2). Less than 10% of patients (9.4%) in the Gripp-Heel group needed more than 7 days to show improved symptoms, compared with 20.4% of patients on conventional therapies (Figure 2).

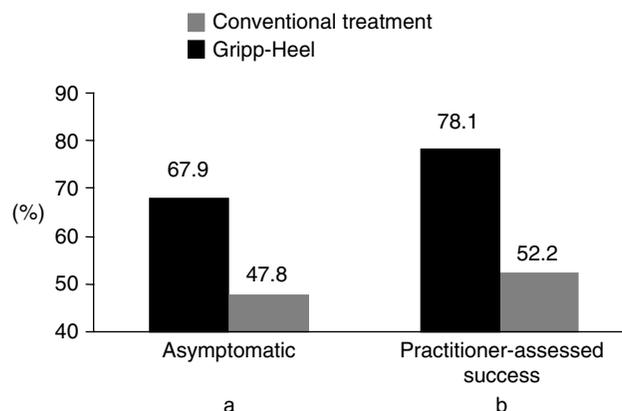


Figure 1 Effectiveness of Gripp-Heel compared with conventional therapies. Percentages of asymptomatic patients at the end of therapy (a); percentage of patients in which successful treatment was achieved as assessed by the practitioner (b)

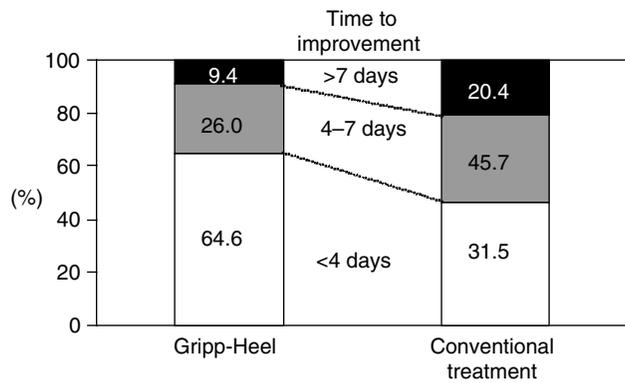


Figure 2 Percentages of patients with improved symptoms at different time points after treatment with Gripp-Heel and conventional therapies

Tolerability

Tolerability was very good in both treatment groups. No treatment-related adverse events (AEs) were reported on Gripp-Heel. In the group receiving conventional treatments, 24 AEs (8.3%) were reported. The majority of AEs were gastrointestinal disorders (58.3%) and allergic reactions (25.0%). Practitioners related AEs to study treatment in 79.2% of cases. Although the events were rated as mild to moderate, AEs led to discontinuation of therapy in 41.7% of cases.

Practitioner-assessed tolerability appeared better in the Gripp-Heel group than in the group receiving conventional treatments; for 89.8% of patients in the Gripp-Heel group, tolerability was reported as 'very good', and this verdict on treatment tolerability was given for only 38.8% of patients in the comparator group (Figure 3a).

Patient compliance rates were also greater with Gripp-Heel than with other treatments; practitioner-assessed compliance rates were 76.7% with Gripp-Heel compared with 49.1% with conventional treatments (Figure 3b).

DISCUSSION

This study showed that the herbal-based homoeopathic preparation Gripp-Heel had beneficial effects in patients with mild such symptoms of viral infections as fever, headache, muscle pain, cough, nasal congestion or sore throat. Compared with conventional anti-tussives, non-steroidal anti-inflammatory drugs (NSAIDs), etc., the proportion of patients who became asymptomatic or for whom the practitioner rated treatment as a success was markedly higher with Gripp-Heel than with conventional treatments. Given the heterogeneity of treatments and the presence of minor differences between the treatment groups in this non-interventional, observational cohort study, the data cannot be taken as proof of significant superiority of the homoeopathic therapy, but the consistency of the results measured on different variables is highly suggestive.

As this was an open-label study and there was no randomisation of patients, the baseline characteristics differed slightly between treatment groups, with more symptoms reported on the patients in the conventionally treated group. This group presented with more number of eye and ear infections than the homoeopathic group. Such differences may have affected the outcome, although we consider it unlikely that the very large differences between the groups in effectiveness and tolerability can be attributed solely to differences in patient group composition. A multivariate analysis would possibly be able to validate our findings. Such a study would be highly welcome but would differ in design from the current investigation.

The possible mechanisms behind the observed effects are still in the realm of speculation. There are reports of increased phagocytotic index and increased phagocytic activity of neutrophils with Gripp-Heel (16) and also of increased humoral response to challenges with influenza virus (17). The use of Gripp-Heel during an influenza epidemic has been evaluated over a 6-month period, which reported increased anti-influenza (H1N1, H3N2, HB) haemagglutinin and neuraminidase antibody titres in Gripp-Heel-treated patients compared with untreated controls (18). However, as for most homoeopathic preparations, there are few scientifically rigorous studies available.

As is common with mild viral infections such as the common cold, many patients in both treatment groups received more than one therapy, and thus, the study can be seen as a comparison of a homoeopathy-based treatment regimen and a conventional regimen. The majority of symptoms in both groups were otorhinolaryngological, which are reflected in the high use of anti-tussives and expectorants in the conventionally treated group. The effectiveness of some cough remedies has been questioned (19) and may be indicated in the current study as well, although the differences in tolerability between the groups cannot be attributed to cough medications which are generally well tolerated.

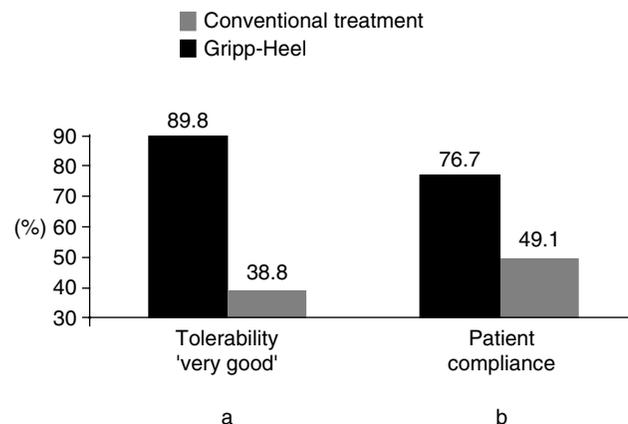


Figure 3 Practitioner-assessed tolerability of treatments as percentage of patients in which tolerability was considered 'very good' (a) and in terms of patient compliance (b)

In the homoeopathy group, the most frequently used additional remedies were Engystol, Euphorbium compositum, Traumeel S and Lymphomyosot in different combinations. All these preparations are herbal-based. Traumeel S is a preparation of highly diluted herbal and mineral extracts with recorded anti-inflammatory and analgesic effects (20). Euphorbium compositum is one of the oldest medicinal herbs known, and the active ingredient, the vanilloid resiniferatoxin, has analgesic and anti-inflammatory properties (21). Engystol is used to treat vague feverish infections and influenza, and Lymphomyosot is indicated to be beneficial on glandular swelling and tonsillar hypertrophy and to have generally strengthening effects (22). The extent to which these therapies have influenced is unclear, but subanalyses of patient groups indicate that benefits from Gripp-Heel monotherapy do not differ widely from those seen in the entire sample (unpublished data). It is interesting to note that *Echinacea* was only used by five patients (2.6%) despite the widespread use of extracts from this plant to treat the common cold, particularly in Germany and recently the United States (1,23).

Homoeopathic medications are as a rule very well tolerated, and this record was confirmed by the lack of AEs in the Gripp-Heel treatment group in the current study. The issue of potential harmful effects of certain herbal remedies has been discussed recently (24–27), but our results indicate that in the case of the treatment used in the homoeopathic group, safety is excellent. Both in terms of tolerability and in terms of patient compliance, rates in this group were twice as high as in the group receiving conventional therapies and all AEs were observed in the conventionally treated group.

In summary, for patients opting for a homoeopathic remedy rather than conventional treatment, Gripp-Heel appears to be an appealing alternative to current therapies directed at providing symptomatic relief for mild viral infections. The homoeopathic treatment was at least equivalent to conventional medications in providing symptomatic relief and shortening the time to improvement. Tolerability, both in terms of AEs and in terms of patient compliance, was generally good but appeared to be better in the group receiving Gripp-Heel.

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