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Randomized trial of a fixed combination (KanJang®) of herbal extracts containing *Adhatoda vasica*, *Echinacea purpurea* and *Eleutherococcus senticosus* in patients with upper respiratory tract infections

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Abstract

The clinical efficacy of KanJang® oral solution, a fixed combination of standardised extracts of *Echinacea purpurea, Adhatoda vasica* and *Eleutherococcus senticosus*, was compared with the combined extracts of *Echinacea purpurea* and *Eleutherococcus senticosus* alone (Echinacea mixture) in a controlled, double blind, randomized trial, and with Bromhexine (a standard treatment) in a controlled, open, randomized clinical trial on patients with non-complicated acute respiratory tract infections. Many of the parameters evaluated, such as severity of coughing, frequency of coughing, efficacy of mucus discharge in the respiratory tract, nasal congestion and a general feeling of sickness, showed significantly greater improvement in patients treated with KanJang compared with those receiving the standard treatment. However, no significant differences in the improvement of these symptoms (except in a reduced frequency of coughing) were observed between patients treated with the Echinacea mixture and those receiving the standard treatment. The only explanation is that the lack of extract of *A. vasica* in the Echinacea mixture reduces its efficacy compared with the complete KanJang oral solution even though direct double-blind comparison yielded no significant differences between these two groups of patients. The recovery time of patients being treated with KanJang or Echinacea mixture was 2 days shorter than that of patients receiving the standard treatment. None of the patients completing the study reported adverse reactions to the medication taken. The significance of the results obtained in this study is discussed with respect to the efficacy of KanJang in the treatment of acute respiratory infection and to the concept that multi-drug therapy offers higher efficacy compared with mono-drug treatment of such infections.

Keywords: *Echinacea purpurea*; *Adhatoda vasica*; *Eleutherococcus senticosus*; Fixed combination; KanJang®; Bromhexine; Bronchitis; Controlled parallel group clinical trial

Introduction

The general, and very successful, approach of oriental medicines, such as Ayurveda and Unani in India and

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Kampo in China and Japan, involves treatment with complex combinations of several herbs. In some cases, the medicinal value of the preparation may be due entirely to the combination of constituents and cannot be reproduced by one or two so-called active principles alone. For the treatment of viral diseases, recent research has shown that fixed combinations of plant extracts show greater-than-expected medicinal benefit because of the mix of constituents that have synergistic effects and act upon different molecular targets (Vlietinck and Vanden Berghe, 1991; Nelson and Kursar, 1999; Wagner 1999, 2004).

KanJang® oral solution, a fixed combination of standardised extracts of *Echinacea purpurea, Adhatoda vasica* and *Eleutherococcus senticosus*, has been available in Scandinavia for around 20 years as a herbal medicinal product for the relief of symptoms associated with the common cold (coughing and irritability of the throat) with a well-established medical use comprising over 50 million human daily doses. In a controlled clinical study (Thom and Wollan, 1997), the preparation was demonstrated significantly to ease symptoms related to uncomplicated upper respiratory tract infections (i.e. coughing, quality of sleep, mucus discharge in the respiratory tract, and nasal congestion) compared with placebo.

Extracts of the three plants combined in KanJang oral solution have been used separately, and in combination with other plants, for the treatment of infectious diseases. Mono-preparations and combinations containing *Echinacea purpurea* (coneflower) are widely used in Europe for the prophylaxis and treatment of mild to moderately severe colds and of influenza. In Germany alone, more than 200 different preparations of *E. purpurea* are currently marketed with the major indications for use being immunomodulation and symptom relief in connection with common colds of viral origin. Numerous controlled clinical trials have indicated that preparations containing extracts of *E. purpurea* can be efficacious immunomodulators for the treatment of upper respiratory tract infections (Melchart et al., 2001, 2002).

Leaves of *A. vasica* (Malabar nut) have been used for more than 3000 years in Ayurvedic medicine for the treatment of various kinds of bronchial disorders including coughs, bronchial catarrh, asthma and bronchitis (Bose, 1984; Atta-ur-Rahman et al., 1986; Schneider, 1988; Kapoor, 1990). European pharmacognosy literature also mentions the use of Adhatoda folia as a cold remedy, especially for coughs, and as an expectorant in the treatment of acute and chronic bronchitis (Planchon and Collin, 1995; British Pharmaceutical Codex, 1949; Hagers Handbuch der Phannazeutischen Praxis, 1993; Claeson et al., 2000). Furthermore, an extensive clinical trial in India confirmed that the drug had a definite expectorant action (Chopra et al., 1958) in acute bronchitis: in chronic bronchitis, coughing was relieved, and the viscosity of sputum decreased such that it could be expelled more readily. Clinical observations indicated that a tincture of *A. vasica* produced an expectorant effect in patients with acute or chronic bronchitis. An infusion made from the leaves of the drug was shown to exhibit expectorant and bronchial-dilating activities by virtue of the presence of the quinazoline alkaloid vasicine (Hänsel, 1991).

Several clinical studies have also confirmed that *Eleutherococcus senticosus* (Syn. *Acanthopanax senticosus*; Siberian ginseng) exhibits pronounced effects on the symptoms of common colds and influenza-like diseases (Elkin et al., 1984; Kalashnikov, 1984; Protasova and Zykov, 1984; Shadrin et al., 1984; Kupin et al., 1986; Gagarinova et al., 1995; Savenko and Tsvetkov, 1996). Moreover, extracts of the roots of *E. senticosus* have been shown to possess adaptogenic and anti-stress activities in a number of *in vitro* and *in vivo* models. Such effects might be occasioned partly by an endocrine and partly by an immunomodulatory mechanism of action (Brekhman, 1968; Dardimov, 1976; Farnsworth et al., 1985). In these extracts, the eleutherosides seem to be the main low-molecular weight compounds responsible for modulating the biosynthesis of eicosanoids (LTB_4, 5-, 12- and 15-HETEs) and the release of arachidonic acid from isolated human neutrophils (Sprigin et al., 1988), whilst the polysaccharides show primarily immunologically induced anti-tumour and anti-viral effects. Extracts of *E. senticosus* have been shown to inhibit the productive replication of human rhinovirus, respiratory syncytial virus (RSV) and influenza A virus in cell culture (Glatthaar-Saalmuller et al., 2001).

The primary aim of the controlled clinical trial reported in this study was to evaluate the contribution of the extract of *A. vasica* in the curative effect of KanJang oral solution in order to obtain clinical evidence in support of the concept that multi-drug therapy can offer higher efficacy in comparison with mono-drug treatment (Williamson, 2001; Wagner, 2004). To this end, the clinical efficacies of KanJang and a fixed combination of extracts of *Echinacea purpurea* and *Eleutherococcus senticosus,* were compared with that of Bromhexine, a standard anti-cough drug generally used for the treatment of non-complicated respiratory tract infections (bronchitis).

Materials and methods

Study design

This was a randomized, controlled, two arm study of 90 patients with non-complicated acute respiratory tract

infections carried out at the Department of Family Medicine at the Armenian State Medical Institute during the autumn and winter of 2003. A fixed combination of standardised extracts of *Echinacea purpurea, A. vasica* and *Eleutherococcus senticosus* (KanJang oral solution) was compared with the combined extracts of *Echinacea purpurea* and *Eleutherococcus senticosus* alone (Echinacea mixture) in a controlled, double blind, randomized clinical trial, and with Bromhexine (a standard treatment) in a controlled, open, randomized clinical trial. The protocols of the study were reviewed and approved by the Ethics Committee of the Armenian Drug and Medical Technology Agency of the Ministry of Health of the Republic of Armenia. Study subjects were randomized according to the order of first contact with a doctor on day 0. The identification number of each patient and the drug code number (randomly encoded in a drug-list) were both recorded in a protocol and in the patient's journal to allow subsequent identification. Information concerning the content of extracts became known to the investigators and volunteers only after completion of the study and final statistical analysis of the results.

Study drugs

The test medications were manufactured in liquid form according to Good Manufacturing Practice (GMP) by the Swedish Herbal Institute (Gothenburg, Sweden). KanJang oral solution (batch EX-0307A), was a fixed combination of extracts from leaves of *A. vasica* L. (15–25 mg/ml), from *Echinacea purpurea* L. (14–20 mg/ml) and from *Eleutherococcus senticosus* Maxim (5 mg/ml) that had been standardised to contain 0.2 mg/ml of the alkaloid vasicine, 0.8 mg/ml of cichoric acid, and 0.03 mg/ml of eleutherosides B and E. Echinacea mixture (batch EX-0307A), was a fixed combination of extracts from *Echinacea purpurea* L. (14–20 mg/ml) and from *Eleutherococcus senticosus* Maxim (5 mg/ml) that had been standardised to contain 0.8 mg/ml of cichoric acid, and 0.03 mg/ml of eleutherosides B and E. The liquid matrix for both test medications contained liquorice, nipagin, nipasol, sorbitol, polysorbate, eucalyptus oil, peppermint oil, coltsfoot leaf aroma, ginger extract and water. The medications were provided in dark glass bottles (500 ml) with a cap, sealing ring and a measuring dosage cup (graduated 5, 10, 15, 20 and 30 ml), and were labelled "KanJang/Echinacea A" (for the verum) or "KanJang/Echinacea B" (for the negative active control) followed by "500 ml, shake before use"; the appearance of the medications and packages were similar such that the placebo and drug could not be distinguished one from another. Patients of the positive active control group received a standard treatment of Bromhexine coated tablets (Berlin-Chemie, Berlin, Germany) containing 8 mg of bromhexine hydrochloride together with inactive excipients. All drugs employed were stored separately at room temperature in a secure location so as to prevent their use for purposes other than the described study.

Patients

Patients of either gender showing symptoms of uncomplicated acute respiratory tract infections (IPCP code 400) were selected to take part in the trial to investigate the efficacy and tolerability of KanJang oral solution versus an Echinacea mixture and Bromhexine standard treatment. For the purposes of diagnosis, prior to consideration for inclusion in the study, volunteers initially underwent the following examinations and analyses: physical examination by a physician (compilation of anamnesis, detailed chest auscultation and percussion, thermometry), chest X-ray, and general blood and urine analysis. An investigator completed a baseline questionnaire for each patient in order to obtain details concerning age, smoking habit and history of illness. Using visual analogue scales (VAS) with marked end points (0 cm = no problems; 10 cm = pronounced problems), the investigator gathered further information concerning the following parameters: degree (severity) of coughing (1), frequency of coughing (2), quality of sleep, (number of times the patient awoke during the night) (3), efficacy of mucus discharge in the respiratory tract (4), degree of nasal congestion (5), soreness of throat (6), hoarseness or disturbance of voice (7), fatigue (8), and general feeling of sickness (malaise) (9). From the recorded VAS scores for each patient, the distance (in mm) from the zero-point to the indicated mark was used for statistical evaluation.

The criteria for patient inclusion were: males or females between 18 and 54 years suffering from cough and acute bronchitis with a positive test for cilia abnormalities. The criteria for exclusion were: patients with an allergic reaction to herbal products or to bitterness, pregnant patients or those attempting to become pregnant, breast-feeding mothers, patients receiving therapy (other than the medications under study) that could affect the course of the infection (e.g. anti-inflammatory drugs, antibiotics, etc.), patients who had suffered from emphysema, bronchiectasis or pneumosclerosis, persons known to have problems with abuse of medications, narcotics, tobacco or alcohol.

Following selection for inclusion in the trial, written informed consent was obtained from each participant in accordance with the revised declaration of Helsinki (World Medical Association Declaration of Helsinki, 2000).

Methods

Selected patients were randomized into one of three treatment groups (30 patients per group) to receive: group A – KanJang oral solution; group B – Echinacea mixture (negative active control); and group C – bromhexine hydrochloride (positive active control). Patients in group C received a standard treatment with Bromhexine tablets. Patients in groups A and B were provided with one bottle of KanJang/Echinacea A or B (as described above) containing 500 ml of liquid, 30 ml of which was to be taken three times a day for 6 days. Each bottle was given a sequential number with the code concealed from the investigator: the sequential numbers were matched with the order of arrival of the patients. Patient identification numbers were noted in a protocol and on the bottles in order to allow subsequent identification after completion of study. The identity of the medication received by an individual became known to the investigators only after completion of the study and after the statistical analysis had been performed.

After being grouped (study day 0), the patients commenced the double-blind treatment. The efficacy of the treatment was evaluated by patients using self-assessment questionnaires completed on a daily basis, from results of examinations by a physician (including assessment of cough relief and reduction of irritation 30 min after drug intake during the first and the final visit to the doctor), and from the duration of clinical manifestations of the acute phase of the disease. Each patient was provided with an individual test-book, analysis log and a health diary for self-assessment by VAS scores of parameters 1–9 as determined in the initial baseline questionnaire (see above). For patient assessment, the VAS end points were marked: 0 cm – no improvement, and 10 cm – pronounced improvement. The distance (in cm) from the zero-point to the indicated mark was used for statistical evaluation. The follow-up period of treatment for the whole study was up to 8 days.

Patient compliance

Compliance was ensured by questioning the patients and by collecting the bottles and their contents during the final visit. The volume of unused liquid was measured and the lower limit for compliance was set at 98%.

Statistical methods

Each patient was identified by a number and by trial identification. The data were entered into the database (Microsoft™ Excel® 2000) patient by patient. The mean, standard error of the mean and standard deviation (SD) values for VAS scores were calculated according to standard methods. In order to conclude whether mean values of parameters determined before and after treatment, and between treatments, were statistically significant, one-way repeated ANOVA, with Tukey's multiple comparison post-test, was applied. Data management and calculations were performed using GraphPad (San Diego, CA, USA) Prism software (version 3.03 for Windows).

Results

The study population consisted of 90 patients, 28 males (31.1%) and 62 females (68.9%), aged between 19 and 54 years (mean 37.1 years). No statistically significant differences were observed with respect to smoking status or severity of illness as measured by degree (severity) of coughing (1), frequency of coughing (2), quality of sleep (number of times the patient awoke during the night) (3), efficacy of mucus discharge in the respiratory tract (4), degree of nasal congestion (5), soreness of throat (6), hoarseness or disturbance of voice (7), fatigue (8), and general feeling of sickness (malaise) (9). The baseline (day 0) VAS scores for some of these parameters are shown in Table 1.

At the end of the trial all subjects had complete health diary records and there were no dropout patients. None of the patients reported adverse reactions to the medication taken during the study. At the conclusion of the study, the volume of medication remaining in the bottle returned by each participant was compared with the anticipated volume as calculated on the basis of the patient's statement of the duration of treatment. The correlation between the amount of unused medication and the information revealed by each patient concerning the number of days that medication had been administered was extremely high, showing that all patients fulfilled the compliance criterion by taking 98% of the recommended dose.

The follow-up VAS scores for parameters 1–9 assessed on days 1–8 of the trial are listed in Table 2 for each of three groups. A significant improvement in scores for all parameters was observed in each treatment group starting from days 2 to 3 of treatment. However, the improvement in scores for degree (severity) of coughing (1), frequency of coughing (2), efficacy of mucus discharge in the respiratory tract (4), degree of nasal congestion (5), and general feeling of sickness (malaise) (9) was significantly greater for the group treated with KanJang oral solution compared with the group receiving the standard treatment as early as 4–6 days after starting the treatment (Fig. 1(a)–(e)). On the other hand, no significant differences in the improvement of these symptoms (except for a reduction in the frequency of coughing) were established between the *Echinacea* mixture group and the standard treatment

Table 1. Baseline characteristics and parameter values of the study groups

Parameter	Group A KanJang oral solution (verum)[a]	Group B Echinacea mixture (negative active control)[a]	Group C Bromhexine standard treatment (positive active control)[a]
Age (years)	36.8 ± 1.9 (10.3)	36.0 ± 2.2 (12.1)	38.6 ± 1.82 (9.5)
Gender (female/male)	27/3	23/7	12/18
Degree (severity) of cough[b]	6.45 ± 0.38 (2.06)	6.31 ± 0.30 (1.67)	6.31 ± 0.29 (1.58)
Frequency of bouts of coughing[b]	6.42 ± 0.37 (2.02)	6.19 ± 0.33 (1.81)	6.17 ± 0.30 (1.66)
Quality of sleep (number of times the patient awoke during the night)[b]	5.55 ± 0.51 (2.8)	5.61 ± 0.49 (2.7)	5.55 ± 0.37 (2.0)
Efficacy of mucus discharge in the respiratory tract[b]	5.68 ± 0.52 (2.8)	6.21 ± 0.39 (2.15)	6.03 ± 0.31 (0.93)
Shortness of breath[b]	5.59 ± 0.47 (2.6)	5.71 ± 0.44 (2.4)	5.61 ± 0.35 (1.9)
Fatigue[b]	6.21 ± 0.39 (2.12)	5.81 ± 0.40 (2.17)	5.51 ± 0.37 (2.0)

[a]Values are means ± standard error (standard deviation).

[b]Parameters determined using visual analogue scales with marked end points "0 cm = no problems" and "10 cm = pronounced problems" (10 cm): the distance (mm) from the zero-point to the indicated mark was used for statistical evaluation.

group. No significant differences were established between the groups receiving KanJang and the standard treatment with respect to quality of sleep (3), soreness of throat (6), hoarseness (7) and fatigue (8). Whilst the standard treatment group clearly knew that their medication (being in tablet form) was different from that provided to the other volunteers (who apparently received identical solutions), any potential bias for or against the tablets should have effected the results with respect to the other two groups in an identical manner. However, a significant difference between the results obtained following treatment with the KangJang solution compared with the standard treatment was established, but not for the Echinacea mixture versus the tablets. Thus it is quite clear that tablet bias played no part in determining the results obtained.

The results presented in Table 2 may be explained on the basis that the lack of components from *A. vasica* in the Echinacea mixture lead to a reduction in efficacy for the treatment of bronchitis compared with the complete KanJang oral solution. Whilst direct comparison of the efficacy of KanJang and Echinacea mixture did not reveal statistically significant differences (there being only 30 patients in each sample group), the tendency towards higher efficacy of the former medication is clearly highlighted in Fig. 1. The duration of treatment required was significantly shorter for the groups treated with KanJang oral solution/Echinacea mixture (6 days) compared with the 8 days of treatment required by the group receiving the standard treatment.

Discussion

In general medical practice, the problems most often encountered, in infant and adult patients alike, relate to respiratory infection. Acute respiratory infections are most dangerous in the first year of life and in the elderly as they can readily give rise to a number of complications including bronchitis, acute pneumonia and even bronchial asthma and chronic obstructive pulmonary disease (COPD). Unfortunately, at the present time, there is no evidence-based approach to the diagnosis, evaluation, prognosis or even treatment of acute respiratory infections. Most clinical guidelines for general practitioners focus on the common cold and, commonly, ignore the problem of early diagnosis and effective treatment of acute non-complicated respiratory infections (Douglas et al., 1999). Typically, the recommended treatment is with anti-inflammatory drugs followed by a course of antibiotics if the duration of the respiratory infection exceeds a week (Arroll and Kenealy, 1999).

However, the basic mechanism for complication in acute respiratory infection involves damage to the local immunity of the respiratory tract and of the mucociliary clearance system (Janeway et al., 1999). Such changes in the immune system are different for each individual thus making it somewhat difficult to take them into specific account during the treatment of respiratory infection. Nonetheless, because of the present lack of unified recommendations for treatment, even the general state of the immune system (especially its local respiratory part) of a patient presenting respiratory infection is often not controlled. Clearly there is a need to enhance the range of drug therapies available for respiratory infections in order to address the immunological problems that can arise.

The efficacy and safety of KanJang oral solution (a fixed combination of standardised extracts of *Echinacea purpurea, A. vasica* and *Eleutherococcus senticosus*) in the treatment of non-complicated respiratory infections has already been demonstrated through clinical

Table 2. Patients' self-assessment of parameter values during the trial

Parameter[a]		Group A: KanJang oral solution (verum)						Group B: Echinacea mixture (negative active control)						Group C: Bromhexine standard treatment (positive active control)							
		Day						Day						Day							
		1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6	7	8
Degree (severity) of coughing (1)	Mean[b]	3.47	4.32	5.67	6.90	**8.08****	**9.01*****	3.42	4.19	5.46	6.62	7.60	8.53	3.63	4.24	5.12	5.99	6.60	7.34	7.99	8.33
	SD[c]	2.22	1.76	1.37	0.87	0.68	0.53	1.68	1.48	1.16	0.92	0.82	0.91	1.79	1.42	1.44	1.39	1.46	1.11	1.11	1.27
Frequency of coughing (2)	Mean	3.41	4.38	5.77	7.13	**8.20*****	**9.15*****	3.36	4.24	5.75	6.73	**7.71***	**8.62****	3.49	4.12	5.21	6.17	6.65	7.36	8.03	8.37
	SD	1.99	1.73	1.28	0.88	0.77	0.54	1.66	1.44	1.10	1.10	0.83	0.95	1.68	1.45	1.46	1.48	1.42	1.32	1.16	1.34
Quality of sleep (3)	Mean	4.36	4.91	6.37	7.49	8.58	9.32	3.95	4.77	6.17	7.41	8.35	9.10	4.45	5.04	5.79	6.76	7.52	8.04	8.42	8.66
	SD	2.44	2.14	1.62	1.04	0.67	0.47	2.25	2.00	1.66	1.28	0.77	0.58	2.54	2.24	2.01	2.06	1.93	1.62	1.43	1.22
Efficacy of mucus discharge (4)	Mean	4.13	5.18	6.59	**7.75***	**8.67*****	**9.46*****	3.29	4.43	5.64	6.83	7.72	8.70	3.40	4.59	5.34	6.23	6.85	7.44	8.20	8.34
	SD	2.79	2.35	1.84	1.28	0.83	0.45	1.78	1.42	1.10	1.06	0.97	0.88	1.67	1.57	1.30	1.39	1.26	1.21	1.17	1.44
Degree of nasal congestion (5)	Mean	3.88	4.85	6.20	7.40	8.50	**9.16***	3.58	4.49	5.86	7.05	8.02	8.84	3.57	4.64	5.59	6.41	7.14	7.83	8.32	8.81
	SD	2.29	1.89	1.51	0.88	0.60	**0.57***	1.80	1.48	1.30	1.23	0.87	0.89	1.76	1.50	1.55	1.51	1.34	1.37	1.31	1.17
Soreness of throat (6)	Mean	3.99	5.08	6.65	7.64	8.74	9.43	3.86	4.84	6.25	7.57	8.23	9.17	3.97	5.01	5.90	6.82	7.62	8.10	8.58	8.84
	SD	2.43	2.08	1.59	1.11	0.75	0.52	2.15	1.78	1.46	1.27	0.96	0.65	1.93	1.70	1.61	1.60	1.51	1.41	1.09	1.13
Hoarseness of voice (7)	Mean	4.77	5.52	6.91	7.66	8.44	9.24	4.79	5.75	7.01	7.97	8.67	9.25	4.52	5.31	6.31	7.05	7.66	8.44	8.96	8.44
	SD	3.08	2.53	2.04	1.59	1.34	1.03	3.18	2.74	2.10	1.64	1.20	0.91	2.68	2.10	1.86	1.69	1.51	1.21	0.90	1.21
Fatigue (8)	Mean	3.87	4.82	5.98	7.09	7.99	8.73	4.04	4.95	6.32	7.54	8.20	8.91	3.63	4.59	5.39	6.16	6.93	7.50	8.08	8.31
	SD	2.21	1.93	1.19	0.92	0.76	0.65	2.43	2.20	1.54	0.99	0.85	0.64	1.81	1.59	1.65	1.56	1.61	1.51	1.58	1.60
General feeling of sickness (9)	Mean	3.59	4.58	5.96	7.11	8.06	**8.89***	4.01	5.03	6.36	7.51	8.34	**8.95***	3.49	4.36	5.36	6.14	6.80	7.43	7.98	8.25
	SD	1.76	1.63	1.23	0.91	0.70	0.63	2.46	1.98	1.48	1.06	0.80	0.65	1.65	1.55	1.46	1.53	1.72	1.42	1.32	1.57

[a]Self-assessments of these parameters were made using visual analogue scales with marked end points "0 cm = no improvement" and "10 cm = pronounced improvement": the distance (mm) from the zero-point to the indicated mark was used for statistical evaluation.

[b]Mean values shown in bold are significantly different (at $p<0.05$, $p<0.01$ or $p<0.001$as indicated by *, **, or ***, respectively) from the corresponding values of the Bromhexine standard treatment group.

[c]SD = standard deviation.

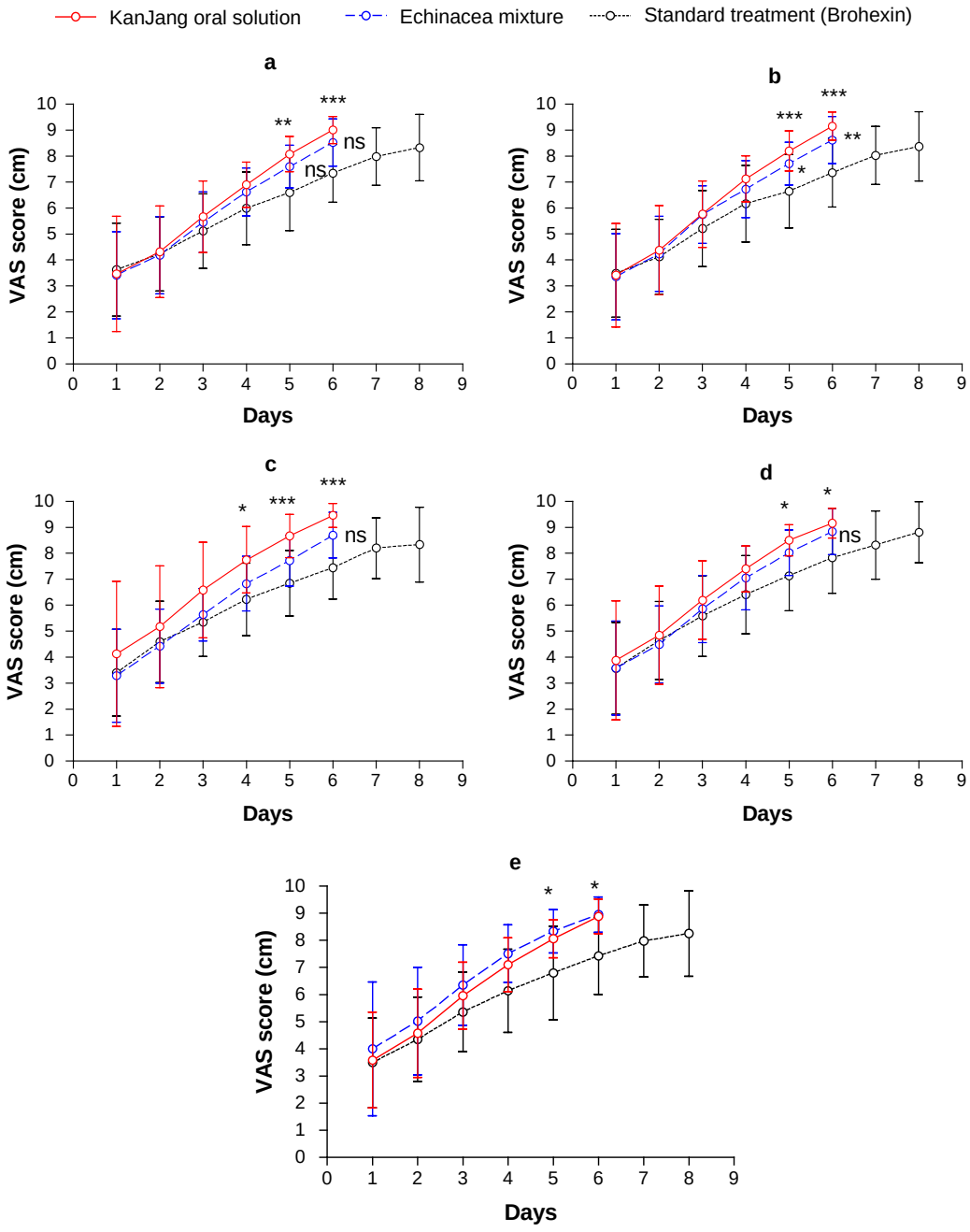

Fig. 1. Patients self-assessment scores showing improvements in (a) degree (severity) of cough (parameter 1), (b) frequency of coughing (2), (c) efficacy of mucus discharge in the respiratory tract (4), (d) degree of nasal congestion (5), and (e) general feeling of sickness (malaise) (9) in patients with bronchitis treated with KanJang oral solution, Echinacea mixture or Bromhexine standard treatment. Parameters were determined using visual analogue scales marked in cm (for details of the protocol see the Methods section): data are expressed as mean ± standard deviation ($n = 30$). The significance of the difference (if appropriate) between a mean score recorded by patients treated with KanJang oral solution and those receiving the Bromhexine standard treatment is given by ***($p < 0.001$), **($p < 0.01$) and *($p < 0.05$). The symbol ^{ns} indicates no significant difference between a mean score recorded by patients treated with Echinacea mixture and those receiving Bromhexine standard treatment.

evaluation (Thom and Wollan, 1997). With this type of mixed herbal therapy, the additional medical benefits are occasioned by virtue of the combination of constituents. In the present clinical study, the contribution of the extract of *A. vasica* to the curative effect of KanJang oral solution was evaluated and the results provide further evidence in support of the concept that multi-drug therapy can offer higher efficacy than mono-drug treatment. Studies involving larger sample sizes will be required, however, in order to

provide unequivocal proof of the validity of this concept.

Traditionally, *A. vasica* has been used for the treatment of bronchial disorders such as acute and chronic cough, bronchitis and asthma, and also as an expectorant in the treatment of acute and chronic bronchial catarrh and bronchopulmonary disease. Other constituents of KanJang have been shown to have anti-stress effects, which might be occasioned partly by an endocrine and partly by an immunomodulatory mechanism of action.

The results of the present study confirm the efficacy of KanJang in the treatment of acute respiratory infection, and also provide an opportunity to enlarge the arsenal of drugs which are currently available for the treatment of one of the most common health problems. However, the parameters monitored in the present study cannot be taken as representative of all of the beneficial changes occasioned by KanJang during treatment of acute respiratory infections. Evaluation of alterations in the immune system following treatment with KanJang will provide new information which may be used for enlarging its indications and for including the preparation in unified standards for the treatment of acute respiratory infections and the prevention of their complications.

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