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Symptomatic Treatment of Acute Feverish Infections with a Modern Homeopathic Medication

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Abstract

This multicenter, prospective cohort study investigated efficacy and tolerability of Viburcol N as compared to paracetamol (acetaminophen) in the symptomatic treatment of acute feverish infections in children. A total of 767 patients were treated with either Viburcol N (n = 361) or paracetamol (n = 406). Main criteria for rating efficacy were: body temperature, general feeling of well-being, severity of the acute feverish infection, severity of clinical symptoms (febrile seizures, general restlessness, disturbed sleep, crying, and eating/drinking problems), onset of efficacy, and scores for overall results of therapy. Criteria for rating tolerability were: adverse effects and overall tolerability scores.

In the course of the study, both treatment groups experienced equivalent and clinically significant improvements in body temperature, general feeling of well-being, severity of the acute feverish infection, and severity of clinical symptoms. Overall efficacy and tolerability of both therapies were rated "very good" or "good" in over 90% of the cases.

This study confirms that the homeopathic medication Viburcol N is a safe, reliably effective medication for treating symptoms of acute feverish infections in children and that its therapeutic potential is comparable to that of paracetamol (acetaminophen).

Keywords: Fever, infections, children, Viburcol N, paracetamol, acetaminophen, cohort study, homeopathy, antihomotoxic medicine.

Introduction

In children, onset of acute feverish infections is often abrupt, and subjectively bothersome symptoms develop rapidly. Although fever is a symptom that may be provoked by any number of factors, it is most frequently caused by uncomplicated infections, 80% of which are viral in origin and thus do not respond to antibiotic therapy.[1] In such cases, symptomatic therapy to relieve infection-induced malaise is both meaningful and indicated.

Antipyretic medication is a frequently considered treatment option, especially when high fever can be expected to cause complications.[2] Fever reducers, however, are often prescribed routinely and unnecessarily for children with relatively mild clinical symptoms. This approach is certainly encouraged by the expectations of many parents, who request fever reducers without understanding either the cause or the physiological purpose of fever.

Several classes of antipyretics are available. Paracetamol (acetaminophen), one of the most frequently prescribed, is also available over-the-counter. It has analgesic and antipyretic effects but is only weakly anti-inflammatory. Its efficacy is based on inhibition of prostaglandin synthesis in the cerebral nervous system.[3] Typical of this medication is the narrow range of dosages at which it is both effective and relatively free of side effects. When dosages exceed the therapeutic range, serious toxicity (especially liver damage) develops quite rapidly due to toxic metabolic products.[4,5]

The value of any therapy whose chief purpose is to reduce fever remains debatable, especially in pediatric cases.[4] Obviously, appropriate intervention is necessary in

cases of very serious symptoms and in patients at risk. In most milder cases, however, it is important to remember that fever is part of the body's complex and purposeful response to infection.[6] The use of drugs to achieve unilateral fever reduction compromises the body's natural defense mechanisms. Sudden reductions in fever also make it difficult for parents and professionals to assess the course of the illness.

Viburcol N suppositories (manufactured by Biologische Heilmittel Heel GmbH, Baden-Baden, Germany) offer an antihomotoxic therapeutic option that does not focus on isolated, short-term fever reduction. This homeopathic medication has been used for years on a daily basis in pediatric practice. Viburcol N's therapeutic potential for treating restlessness with or without fever in pediatric patients has been confirmed by several studies.[7,8]

The present study, conducted under circumstances of routine use in medical practice, compares efficacy and tolerability of Viburcol N and paracetamol (acetaminophen) in the symptomatic treatment of acute feverish infections in children under the age of twelve years.

Methods

Design

This multicenter, prospective cohort study was conducted to investigate modes of application, therapeutic efficacy, and tolerability of Viburcol N in children under age twelve. The study focused on symptomatic treatment of acute feverish infections and especially on the medication's effect on clinical symptoms. To objectively assess the results of the study, analogous data were compiled on the antipyretic paracetamol (acetaminophen), which has served as a reference substance for comparison with other medications and has been the subject of multiple placebo-controlled clinical studies.[3, 9, 10] The objective of the present study was to compile data that reflect usage in actual practice. To minimize the study's impact on the implementation of therapy, no strict criteria for patient inclusion or exclusion were defined (see below). A total of 158 licensed physicians (family practitioners and pediatricians) participated in the study. In addition to mandatory entry and exit examinations, the physicians were required to schedule at least one check-up during the treatment and observation period, which was limited to a maximum of four weeks.

Patients

During the initial examination, the following patient-specific data were compiled:

- demographic data and vital statistics (including age, gender, height/weight, body temperature)
- general risk factors
- cause of the acute feverish infection (underlying illness)
- duration of illness
- frequency and type of any prior treatment (within the last week before commencement of the study)
- frequency, type, and treatment of any concomitant illnesses

Therapy

Therapy-specific data were compiled on:

- dosage of Viburcol N or paracetamol (acetaminophen), including any changes during the course of therapy
- any adjuvant medications or non-drug therapies used in treating the underlying illness (parallel administration of additional antipyretics was not permitted).

Target criteria

Comparative assessment of treatment with Viburcol N and paracetamol (acetaminophen) was based on the following criteria:

Efficacy

- body temperature (taken rectally, in °C).
- patient's general feeling of well-being (as rated by the parents). Scale: 1 = good, 2 = fair, 3 = poor
- overall severity of the acute feverish infection (as rated by the physician). Scale: 0 = no infection present, 1 = mild, 2 = moderate, 3 = severe
- severity of clinical symptoms (febrile seizures, general restlessness, disturbed sleep, crying, eating/drinking problems) as rated by the physician. Scale: 0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe
- onset of efficacy (as rated by the physician). Scale: after first use, after 1 day, after 2 days, after 3 days, after 4-7 days, after 1-2 weeks, after 2-3 weeks, after > 3 weeks, no improvement.
- overall results of therapy (as rated by the physician). Scale: very good (complete freedom from symptoms), good (obvious improvement in symptoms), moderate (slight improvement in symptoms), no success (symptoms remained the same), worsening of symptoms

Tolerability

- incidents of adverse effects (observed by physicians or reported by parents)
- overall rating of tolerability (by the physician). Scale: very good (no intolerance reactions), good (occasional intolerance reactions), moderate (frequent intolerance reactions), poor (intolerance reactions after every use)

Compliance (as rated by the physician): Scale: very good (parents complied strictly with the therapeutic protocol), good (parents complied for the most part with the therapeutic protocol), moderate (inadequate parental compliance), poor (parents did not comply at all with the therapeutic protocol)

Criteria for termination of therapy: Termination of Viburcol N or paracetamol therapy was possible at any time. Possible reasons for termination were:

- freedom from symptoms (underlying illness cured)
- adverse effects
- inadequate efficacy of treatment

Statistical analysis

Exploratory statistical procedures (calculation and graphing of absolute and relative frequencies) were used to analyze data compiled on patients and treatments. The results were tabulated and the differences between the two treatment groups (Viburcol N and paracetamol/acetaminophen) were calculated with 95% confidence intervals. To quantify the severity of each clinical symptom over the course of treatment,

Criterion	Treatment group	
	Viburcol N	paracetamol (acetaminophen)
Patients (n)	361	406
Demographic data (n / %)		
· Age groups:		
– Infants (< 1 year)	142 / 39.3	30 / 7.4
– toddlers (1–5 years)	192 / 53.2	214 / 52.7
– children of school age (6–11 years)	20 / 5.5	146 / 36.0
– not given	7 / 2.0	16 / 3.9
· Gender:		
– female	175 / 48.5	203 / 50.0
– male	174 / 48.2	194 / 47.8
Primary cause of the acute feverish condition (n / %)*		
· common cold	146 / 40.4	96 / 23.6
· rhinitis	138 / 38.2	60 / 14.8
· sore throat	98 / 27.1	124 / 30.5
· bronchitis	82 / 22.7	96 / 23.6
· otitis media	63 / 17.5	76 / 18.7
Symptom severity (mean / SD)		
· febrile seizures	0.1 / 0.47	0.1 / 0.39
· general restlessness	1.6 / 0.89	1.2 / 0.86
· disturbed sleep	1.5 / 0.90	1.3 / 0.86
· eating/drinking problems	1.3 / 0.90	1.4 / 0.96
· crying	1.4 / 1.00	1.0 / 0.98
Scale: 0 = no symptoms, 1 = mild, 2 = moderate		
Body temperature in °C (mean / SD)	38.8 / 0.73	39.3 / 0.66
Patient's general feeling of well-being (mean / SD)	2.4 / 0.66	2.8 / 0.67
Scale: 1 = good, 2 = fair, 3 = poor		
Severity of the acute feverish infection (mean / SD)	2.0 / 0.64	2.4 / 0.65
Scale: 0 = no infection present, 1 = mild, 2 = moderate, 3 = severe		
Duration of illness prior to treatment (n / %)		
· < 1 day	82 / 22.7	128 / 31.5
· 2 days	166 / 46.0	168 / 41.4
· 3 days	71 / 19.7	54 / 13.3
· 4–7 days	25 / 6.9	33 / 8.1
· 1–2 weeks	10 / 2.8	19 / 4.7
· > 2 weeks	5 / 1.4	4 / 1.0

Tab. 1: Demographic and anamnestic patient data at commencement of treatment (*multiple listings were possible, SD = standard deviation).

that symptom's scores for all patients in a group were totaled and averaged.

At the beginning of the study, the equivalence of the two treatment groups was established using ANOVA/Fisher's exact test to compare the following parameters: demographic data, the cause of the acute feverish infection (underlying illness), the severity of selected clinical symptoms (see above), body temperature, general feeling of well-being, and the overall severity of the acute feverish infection. The distribution of baseline criteria across the two treatment groups was described in terms of statistical parameters and absolute and relative frequencies. Influence of baseline criteria on inclusion in the respective treatment group was estimated using a logistic regression model (propensity score method). Because patients with similar scores exhibit similar distributions of baseline criteria, comparison within suitable propensity-score classes can reduce the impact of unequal distribution of baseline criteria on the treatment effect.[11, 12]

Note: Checking the distribution of the above-mentioned baseline criteria within equivalent propensity-score classes resulted in only nine significant p-values. This means that the number of inhomogeneous distributions was only slightly greater than it would have been if patients had been assigned randomly to treatment groups, as is the rule in clinical trials.

Results

Patients

A total of 767 patients with acute feverish infections were included in the study (Viburcol N, n = 361; paracetamol/acetaminophen, n = 406). Over 50% of the patients in both treatment groups were between one and five years old, but there was a significant secondary concentration of infants (age < 1 year) in the Viburcol N group and of school-age children (ages 6-11 years) in the paracetamol group. In both treatment groups, the most commonly listed underlying illnesses were: common colds, rhinitis, sore throat, bronchitis, and otitis (Table 1).

Note: This article presents findings for the total patient population. A subsequent article will evaluate age-stratified results.

Concomitant illnesses

Due to the age of this particular patient population (children < 12 years), concomitant illnesses and risk factors were uncommon. The frequency of general risk factors (e.g., allergies, susceptibility to recurrent infections) was approximately 5% in both treatment groups. Concomitant illnesses (e.g., neurodermatitis, eczema) were higher in the Viburcol N group (9%) than in the paracetamol/acetaminophen group (4%).

Treatment

60% of the Viburcol N patients (average age 2.02 years) received the standard dosage of one suppository two to three times a day. 29% received a combination of the standard dosage and the acute dosage (one suppository several times a day, as needed), and 11% were treated exclusively with the acute dosage.

The preferred treatment regimen in the paracetamol/acetaminophen group (average age 5.23 years) was 125 or 250 mg (for infants and toddlers, respectively) admin-

istered two or three times a day or 500 mg twice a day (for school-aged children). In approximately half of the cases in both groups, dosages were reduced during the course of treatment.

Use of both pharmaceutical adjuvant therapies (including various antibiotics, cough syrups, and decongestant nasal sprays) and non-drug treatments (including compresses and increased fluid intake) for the underlying illness was comparable in the two treatment groups (Viburcol N 66%, paracetamol 63%). Median duration of treatment was nine days for the Viburcol N group and eight days for the paracetamol group.

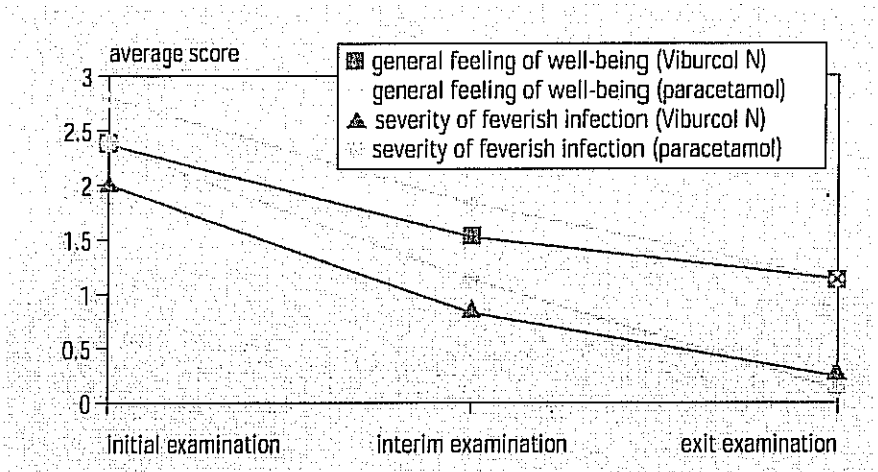

Fig. 1: Changes in the criteria "patient's general feeling of well-being" (Scale: 1 = good, 2 = fair, 3 = poor) and "severity of the acute feverish infection" (Scale: 0 = no infection present, 1 = slight, 2 = moderate, 3 = severe). Median date of interim examination (days after beginning treatment): Viburcol N 5 days, paracetamol 4 days. Median date of exit examination: Viburcol N 9 days, paracetamol 8 days.

Target criteria

Severity of the acute feverish infection: Average severity of the acute feverish infection at commencement of therapy was rated "moderate" (score 2.0 ± 0.64) in the Viburcol N group and "moderate to severe" (score 2.4 ± 0.65) in the paracetamol/acetaminophen group. In both groups, clinically relevant decreases in severity occurred over the course of treatment (to a score of 0.2 ± 0.47 for Viburcol N and 0.1 ± 0.36 for paracetamol). Most patients in both groups were symptom-free on conclusion of treatment (Figure 1, Table 2).

General feeling of well-being: Initial scores (2.4 ± 0.66 for Viburcol N, 2.8 ± 0.67 for paracetamol) reflect "fair" to "poor" subjective states of health at commencement of therapy. On conclusion of treatment, the score for both groups was reduced to 1.1, indicating that patients felt nearly normal (Figure 1, Table 2).

Body temperature: At the beginning of the study, the average body temperature in the Viburcol N group was 38.8 °C, somewhat lower than in the paracetamol/acetaminophen group (39.3 °C). During the course of treatment, temperature readings decreased to normal in both groups (37.0 °C and 36.9 °C, respectively). As expected, paracetamol tended to be somewhat more effective than Viburcol N in reducing fever (Table 2).

Clinical symptoms: At the beginning of the study, the average severity score for all symptoms was 1.74 ± 0.53 for the Viburcol N group and 1.75 ± 0.44 for the paracetamol (acetaminophen) group, corresponding to "mild" to "moderate" symptoms. By the end of the observation periods (different for each patient), the average score dropped to 0.2 ± 0.36 (Viburcol N) and 0.1 ± 0.23 (paracetamol); in other words, the patients were nearly symptom-free (Figure 2). Adjusting the difference between the treatment groups using propensity-score strata resulted in an adjustment of 0.05 points in favor of Viburcol N. Thus the right boundary of the 95% confidence interval fell at 0.05, below the

Target criteria	initial examination		exit examination		AM ± SD of the difference
	Viburcol N	paracetamol	Viburcol N	paracetamol	Viburcol N minus paracetamol
Clinical symptoms:					
· febrile seizures	0.1	0.1	0	0	– 0.02 ± 0.40
· general restlessness	1.6	1.2	0.2	0.1	– 0.09 ± 0.85
· disturbed sleep	1.5	1.3	0.2	0.1	– 0.04 ± 0.85
· eating/drinking problems	1.3	1.4	0.2	0.1	– 0.02 ± 0.90
· crying	1.4	1.0	0.1	0	+ 0.04 ± 0.95
body temperature (°C)	38.8	39.3	37.0	36.9	+ 0.23 ± 0.75
severity of the infection	2.0	2.4	0.2	0.1	+ 0.07 ± 0.75
patient's general feeling of well-being	2.4	2.8	1.1	1.1	+ 0.03 ± 0.65

Tab. 2: Differences in reduction in criteria investigated. Numbers represent average scores (for scales see Table 1). Negative differences correspond to greater reduction under treatment with Viburcol N; positive differences correspond to greater reduction under treatment with paracetamol. AM = arithmetic mean, SD = standard deviation.

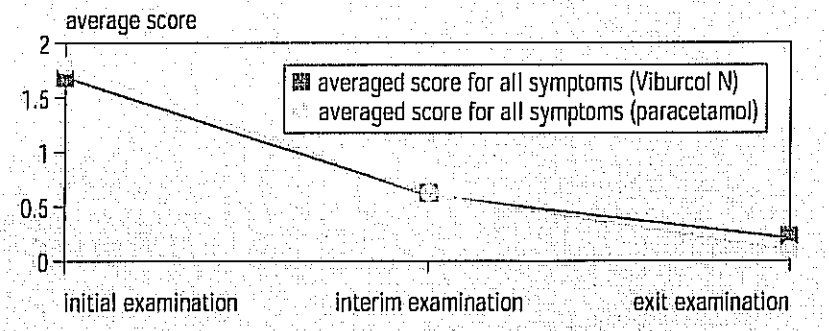

Fig. 2: Changes in the criterion "clinical symptoms" (Scale: 0 = no symptoms, 1 = mild, 2 = moderate). Median date of interim examination (days after beginning treatment): Viburcol N 5 days, paracetamol 4 days. Median date of exit examination: Viburcol N 9 days, paracetamol 8 days.

limits of "slight" inferiority. In other words, Viburcol N was not statistically inferior to paracetamol.

At commencement of therapy, severity scores for the individual symptoms general restlessness, disturbed sleep, crying, and eating/drinking problems ranged from 1.0 to 1.6 ("mild" to "moderate"). During the observation period, severity scores for these symptoms dropped to between 0.0 and 0.2 for both groups, indicating that the patients were virtually symptom-free.

Adjusting the difference between treatment groups using propensity-score strata produced an adjustment of 0.04 points in favor of paracetamol for the symptom "crying" and adjustments of 0.02 (febrile seizures), 0.09 (general restlessness), 0.04 (disturbed sleep), and 0.02 (eating/drinking problems) in favor of Viburcol N (Table 2).

Onset of efficacy: There was no statistical connection between the type of treatment and the onset of efficacy ($p = 0.302$, Cochran-Mantel-Haenszel test). As expected, the immediate effects of paracetamol (acetaminophen) tended to be more pronounced than those of Viburcol N. After three days of therapy, however, fever was significantly reduced in both treatment groups in a high percentage of patients (Viburcol N 87%, paracetamol 92%). After four to seven days, significant fever reduction had occurred in 96% and 99%, respectively.

Results of therapy: No connection was found between the type of treatment and the overall results achieved. "Very good" or "good" results were reported for 93% of the Viburcol N patients and 99% of the paracetamol patients (Figure 3).

Patient compliance: Compliance is a measure of the patients' (or in this case the parents') satisfaction with treatment. Compliance was rated either "very good" or "good" for 96% of the Viburcol N group and 97% of the paracetamol group.

Tolerability: During treatment with Viburcol N, a rash (presumably caused by a virus) appeared on the face of one five-year-old female patient with bronchitis/otalgia but disappeared spontaneously after about six hours. In spite of this single incident, participating physicians rated the tolerability of both forms of therapy as either "very good" or "good" in over 96% of cases.

Discussion

Especially in infectious illnesses, fever is the body's natural response to exogenous pyrogens. It is a complex physiological event involving activation of prostaglandin synthesis and changes in the thermoregulatory system in the hypothalamus. These endogenous processes activate or modulate a number of different components of the immune system. Except in extremely high fevers or patients at risk, fever should be seen as serving the legitimate purpose of activating self-healing. Independent of its physiological function, fever is always an easily measured criterion for assessing the course of an infectious illness. Under certain circumstances, therefore, generalized suppression of fever (and hence of associated symptoms) can mask the need for additional therapeutic or diagnostic measures.[2]

Several different classes of antipyretics are available. Paracetamol (acetaminophen) is used worldwide for reducing fever and is readily available without prescription. Paracetamol's antipyretic effect has been thoroughly confirmed by clinical studies,[3, 4, 9, 10] but its relatively narrow effective therapeutic range remains problematic. In other words, there is relatively little difference between the effective dose and dosages that cause toxic changes in the body. Because the breakdown products of paracetamol are hepatotoxic, overdosing entails risk of serious side effects, including (in extreme cases) necrotic processes with lethal outcomes. Kidney damage due to tubule necrosis has also been described.[3, 5] In view of the fact that paracetamol is so readily available, self-medication and prescriptions that allow "as needed" use involve significant potential risks. Dosage errors on the part of parents have been identified as the primary reason for serious side effects in children.[4]

Antihomotoxic Viburcol N suppositories offer an alternative for treating feverish infections in children. This medication specifically targets the restlessness that often accompanies infectious illnesses in very young patients. Viburcol N, rather than aggressively and one-sidedly reducing fever, reduces associated symptoms by supporting the body's capacity for self-healing.

The purpose of the prospective, multicenter cohort study reported in this article was to compare these two different approaches to treating symptoms of acute feverish infections in children under the age of twelve years. Direct comparison was made possible by selecting identical criteria and appropriate statistical methods.[11] On the whole, the two treatment groups

were comparable with regard to basic anamnestic data and severity of both existing symptoms and the illnesses underlying the clinical symptomatology.

The design of this study, as described above, offered a suitable instrument for comparing two therapeutic approaches under realistic treatment conditions in daily practice. It is important to note that meta-analyses comparing the results of clinical trials and observational cohort studies have proved that studies of this type yield results comparable to those of controlled clinical studies.[15]

Rapid onset of efficacy and lasting improvement in multiple symptoms are decisive criteria in assessing the success of therapy for acute feverish infections. This study demonstrates the equivalence of the two therapies in this regard. Already after three days, statistically significant and clinically relevant improvements in the symptoms of the feverish illness were noted in both groups. Significant improvements (roughly similar for both medications) were achieved with regard to all individual clinical symptoms as well as in ratings of the severity of the illness and the patients' general feeling of well-being. In both treatment groups, body temperatures had been reduced to normal ranges by the end of the observation period.

Statistical analysis confirms that Viburcol N's therapeutic potential for treating symptoms of acute feverish infections is comparable to that of paracetamol (acetaminophen) with regard to all criteria investigated by this study (Table 2). As expected, fevers dropped somewhat less rapidly under treatment with Viburcol N than with paracetamol, but the difference (0.23 points at confidence limits of 0.08 to 0.38) remained below medically relevant limits.

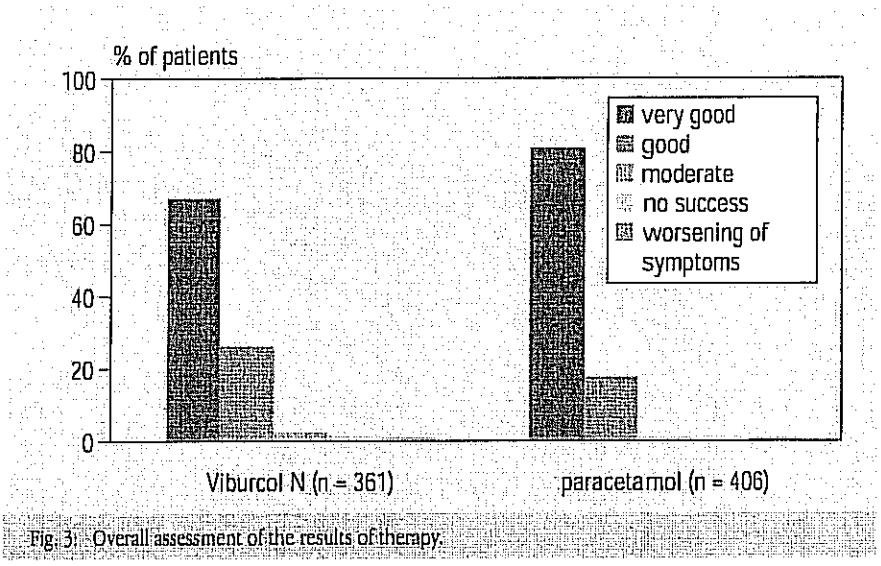

Fig. 3: Overall assessment of the results of therapy.

In conclusion, this study demonstrates that the homeopathic medication Viburcol N is a safe and reliably effective treatment for symptoms of acute feverish infections in children and eliminates the risks associated with chemical therapies.

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