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Antihomotoxic Treatment of Agitation, with and without Fever, in Children

Results of a Postmarketing Clinical Study

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Abstract

In a drug monitoring data were ascertained on the efficacy and tolerance of the homeopathic remedy Viburcol®. Children and infants were treated, suffering from nervousness with or without fever. Infections (particularly respiratory tract infections), general nervousness, teething complaints and stomach ache were primary underlying diseases.

The efficacy of the treatment was assessed by the participating paediatricians as "very good" or "good" in over 90% of the cases. The mean of the intensity of clinical main symptoms was reduced from 3.2 at treatment start to 1.3 at the end of the treatment (5-point scale). A first global improvement of the diseases was observed in approximately 80% of the cases in the first treatment week for the total patient population. The assessment of the tolerability of the remedy was positive.

Keywords: Children, drug monitoring, fever, homeopathy, nervousness, Viburcol®

Introduction

Agitation, nervousness, difficulty in getting to sleep and sleeping through, and disturbances of general well-being in children are often the manifestation of a diagnosable underlying disease. These symptoms can be produced by infections such as otitis media, bronchitis, pharyngitis, and urinary tract infections in particular. The other main possible causes are odontoneuralgia, tooth-eruption problems, and pain resulting from stomach cramps and colic caused by wind. Since infections are frequently accompanied by fever, one must consider whether or not antipyretic/analgesic therapy is appropriate. The main agents employed for this in conventional medicine are aspirin, paracetamol, and NSAIDs (nonsteroidal antiinflammatory drugs); their use is controversial¹⁾, however, firstly because of the possibility of unwanted side effects and secondly because of the view that fever can fulfil an important function in the body by conditioning and stimulating the immune system – provided that a tolerable range is not exceeded²⁾. Nor should one underestimate the widespread attitude of expectancy on the part of the parents of the sick child, who believe that fever should be reduced and should be treated medicinally and who thus contribute to the high level of use of these substances³⁾.

The primary objective of administering, say, paracetamol as an antipyretic/analgesic is symptomatic therapy to reduce the health problems caused by the infection and thus help the sick child feel better more quickly⁴⁾. However, the possibility of side effects and the impairment of the immune functions raises the question of whether there are not perhaps other treatment options which produce comparable

therapeutic results without the above-mentioned risks.

There is a homeopathic remedy available for this purpose: Viburcol suppositories for children and babies (manufactured by Biologische Heilmittel Heel GmbH, Baden-Baden/Germany), the product's primary use being in the treatment of trivial infections and of agitation with or without fever (Table 1). As an earlier postmarketing clinical study showed, Viburcol is employed predominantly in infectious diseases, nervous agitation and pain⁵⁾. A postmarketing clinical study undertaken in 1999 collected data on the efficacy and tolerability of Viburcol in the treatment of agitation with and without fever under conditions of routine use.

Methods

In line with the objectives of this postmarketing clinical study, no conditions were imposed on the participating doctors as regards diagnosis and the administration of treatment or the nature and extent of monitoring investigations. The maximal duration of observation was set at 4 weeks per patient. Data on the patients and treatments, which were collected in a preliminary examination and a final examination and in one or two optional intermediate examinations, were recorded on individual case report forms. In addition to demographic data/vital parameters, the documented information included the nature of the underlying disease and details of the dosage of Viburcol, any other medicinal or non-medicinal therapies, and the nature of any accompanying illnesses.

The therapeutic efficacy of the treatment was evaluated on the basis of the following parameters:

Constituents/Potency	Characteristics/Symptoms
Chamomilla D1	Inflammation of the respiratory organs. Tooth-eruption problems. Inflammation and spasm of the digestive organs. Intense pain. Irritability.
Belladonna D2	Highly febrile inflammation of the tonsils, respiratory organs, gastrointestinal tract, urogenital organs, meninges, skin, and joints.
Dulcamara D4	Febrile infections. Inflammation of the respiratory organs, gastrointestinal tract, urinary tract, joints, and skin, triggered by cold and damp.
Plantago major D3	Pain in head region. Bed wetting. Diarrhoea. Skin rashes.
Pulsatilla D2	Inflammation of the airways and tendency to colds. Inflammation and disturbances of the digestive organs. Inflammation of the bladder. Inflammation of the middle ear. Measles, mumps, headache. Sleep disturbances, psychological problems. Nervous disturbances, disturbances of mood.
Calcium carbonicum Hahnemanni D8	Disturbances of calcium metabolism. Chronic disorders of the skin and mucous membranes.

Table 1: Composition of Viburcol and homeopathic profiles of the individual constituents.

Diagnosis groups	Basic symptoms				All patients	
	Agitation with fever		Agitation without fever		%	N
	%	N	%	N	%	N
Infection	86.9	119	13.0	24	44.5	143
Tooth-eruption problems	8.0	11	22.3	41	16.2	52
General agitation	2.9	4	34.2	63	20.9	67
Abdominal pain	0.7	1	17.4	32	10.3	33
Other	1.5	2	13.0	24	8.1	26
Total	100.0	137	100.0	184	100.0	321

Table 2: Percentage distribution of patients according to basic symptoms 'agitation with/without fever' and percentage in various diagnosis groups.

Criteria		Basic symptoms			
		Agitation with fever		Agitation without fever	
		%	N	%	N
Severity of the illness	mild	19.0	26	24.5	45
	moderate	66.4	91	57.6	106
	severe	9.5	13	16.3	30
Nature of the illness	acute	87.6	120	54.9	101
	chronic	4.4	6	15.8	29
	relapsing	1.5	2	11.4	21
Duration of illness at the start of the treatment	1-3 days	70.8	97	41.3	76
	4-7 days	20.4	28	19.6	36
	1-2 weeks	3.6	5	25.5	47
	> 2 weeks	0.7	1	6.0	11

Table 3: Severity, nature, and duration of the illness at the start of the treatment, stratified according to the basic symptoms (difference from 100% = missing data).

- The change in the severity of three, individually defined, principal symptoms (scale: absent = 1, mild = 2, moderate = 3, severe = 4, very severe = 5)
- The length of time to the first improvement in the symptoms
- An overall assessment of the outcome of treatment (scale: very good, good, moderate, unsuccessful, worse).

The tolerability of Viburcol was ascertained on the basis of the following parameters:

- Adverse drug reactions
- An overall assessment of tolerability (scale: very good, good, moderate, poor)
- Patient compliance (scale: very good, good, moderate, poor).

The data were subjected to statistical evaluation using exploratory methods; absolute and relative frequencies and the associated 95% confidence intervals were presented. The postmarketing clinical study was carried out in accordance with the "Recommendations for the planning, performance, and evaluation of postmarketing clinical studies" (Bundesanzeiger (Federal Gazette) No. 229 of 04.12.98).

Results

Patients

The 36 paediatricians in this postmarketing clinical study treated a total of 321 children with Viburcol. Analysis of the demographic data shows that the patients included in the study were primarily infants. The patients' mean age was 1.3 years, the range being 11 days to 12 years. The percentages of boys and girls were comparable: 52% girls, 45% boys (no information on 3%). Before the diagnosis was established, a general categorization of the patients was undertaken according to the basic symptom: patients with agitation *with fever* (group A), patients with agitation *without fever* (group B). The specified diagnoses showed that in the febrile group infections predominated, occurring in 87% of cases. In the non-febrile group the commonest diagnosis was general agitation (34%), followed by tooth-eruption problems (22%), abdominal pain (17%), and infections and other diagnoses (both with 13%) (Table 2).

The commonest infections treated with Viburcol were reported as: respiratory tract infections, influenza, otitis media, intestinal infections, and urinary tract infections. The most common problem treated in those with general agitation was difficulty in getting to sleep and sleeping

through, with nocturnal screaming and hyperagility. The product was also used to treat accompanying symptoms (agitation) resulting from dermatological complaints (including atopic dermatitis, exanthem, and eczema).

To characterize the diagnosed illness and as a parameter for ascertaining the therapeutic efficacy of the treatment, three individual principal clinical symptoms were identified for each patient by the doctors at the start of treatment. The identified symptoms, with their numerical frequencies, are as follows: sleep disturbances (27%), pain (19%), fever (14%), agitation (12%), screaming/screaming fits (7%), sweating (7%), eating and drinking problems (4%), gastrointestinal problems (3%), breathing problems (2%), cough (1%), pruritus (1%), rhinitis (1%), elevated temperature (1%), others (2%).

The overall severity and the nature and duration of the illness were to be assessed at the start of the treatment. As regards the severity and the nature of the illness, the biggest categories in both groups of patients (group A: agitation with fever, group B: agitation without fever) were "moderate" (A: 66%, B: 58%) and "acute". (A: 88%, B: 55%). The duration of illness at the start of the study was 1-3 days in most cases (71%) in group A. 1-3 days was also the biggest category in group B, though less markedly so (41%), as durations of 4-7 days and 1-2 weeks were also relatively common (20% and 26% respectively) (Table 3).

Treatment

At the start of treatment 46% of the patients in group A (agitation with fever) were prescribed the regular dosage recommended by the manufacturer of Viburcol (1 x 1-3 suppositories/day) and 12% were prescribed an acute dosage (1 suppository several times daily). A combination of the regular dosage and acute dosage, as required, was reported for 42% of the patients. The corresponding data for patient group B (agitation without fever) were as follows: regular dosage 66%, acute dosage 11%, combined regular and acute dosage

23%. The most common dosage (46% of cases) used in the patients prescribed the regular dosage was 2 x 1 suppository/day (all patients: 1 x 1 suppository/day = 22%, 2 x 1 = 46%, 3 x 1 = 27%, other dosages = 5%). The mean duration of treatment was 19 days (median 16 days). In group A, the dose was changed at the first intermediate examination (median 6 days) in 49% of cases, being reduced in 92% of these cases and increased in the other 8%; in group B the dose was changed in 36%, being reduced in 86% of these cases and increased in 14%.

12% of the patients had an accompanying illness at the start of the treatment; the commonest accompanying illnesses were skin diseases, infections, and gastrointestinal complaints. With regard to the use of additional medicinal agents or other forms of therapy for the treatment of the diagnosed underlying disease at the start of treatment, there were clear differences between the two groups of patients. Whereas, in patient group A (agitation with fever), no additional medicinal or other

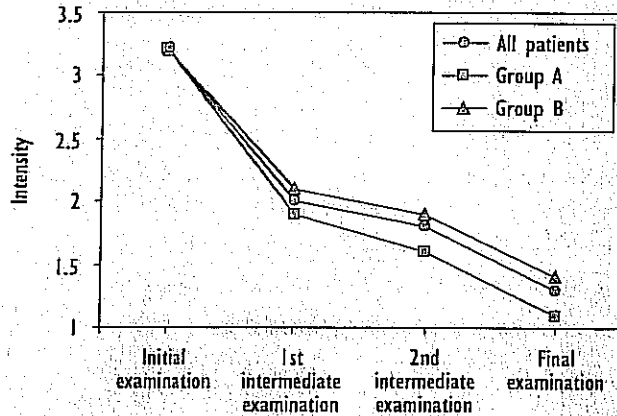


Fig. 1: Course of the mean intensity of the principal clinical symptoms (all symptoms, arithmetic mean, stratified according to total patient population): group A (agitation with fever) and group B (agitation without fever).

Intensity:
 1 = without symptoms
 2 = mild
 3 = moderate
 4 = severe

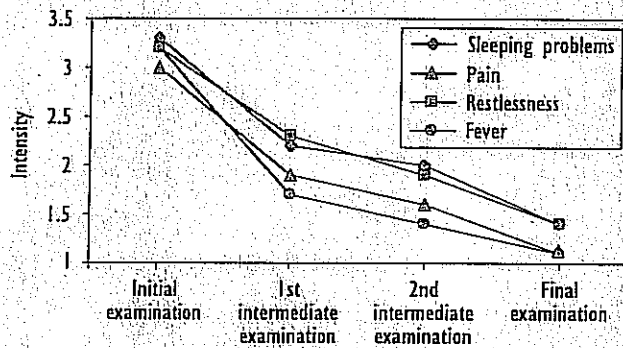


Fig. 2: Course of the intensity of the four most commonly mentioned specific principal clinical symptoms (arithmetic mean, referred to the total patient population).

Intensity:
 1 = without symptoms
 2 = mild
 3 = moderate
 4 = severe

form of therapy was used in 26% of cases, the corresponding figure in patient group B (agitation without fever) was 66%. However, these differences apply primarily to the starting situation at the beginning of treatment. By the 1st intermediate examination 74% of the patients in group A were also being treated solely with Viburcol (group B = 80%). In the cases where patients in group A were prescribed accompanying therapy with a medicinal agent, the predominant products were mucolytics and nasal drops. In group B a wider range of diseases was treated, so no particular categories stood out in this respect.

Therapeutic efficacy

The therapeutic efficacy of the treatment was ascertained, *inter alia*, from the change in the intensity of individually defined principal clinical symptoms; the intensity of these symptoms in the total population decreased from 3.2 at the start of treatment to 1.3 at the end of treatment (arithmetic mean, scale: absent = 1, up to very severe = 5, all symptoms together).

Time	Basic symptoms				All patients	
	Agitation with fever		Agitation without fever		%	N
	%	N	%	N		
After 1st use	5.8	8	14.7	27	10.9	35
After 1 day	11.7	16	8.2	15	9.7	31
After 2 days	20.4	28	11.4	21	15.3	49
After 3 days	24.8	34	16.8	31	20.2	65
After 4-7 days	25.5	35	20.7	38	22.7	73
After more than 1 week	5.1	7	20.1	37	13.7	44
No improvement	1.5	2	0.5	1	0.9	3
Treatment discontinued	4.4	6	6.0	11	5.3	17
No information	0.7	1	1.6	3	1.2	4
Total	100.0	137	100.0	184	100.0	321

Table 4: Length of time to first global improvement in symptoms.

Ratings	Basic symptoms				Adjuvant therapy				All patients	
	Agitation with fever		Agitation without fever		Yes		No		%	N
	%	N	%	N	%	N	%	N		
Very good	62.0	85	44.0	81	50.9	83	52.5	83	51.7	166
Good	29.9	41	46.7	86	40.5	66	38.6	61	39.6	127
Moderate	2.2	3	2.2	4	2.5	4	1.9	3	2.2	7
Unsuccessful	1.5	2	4.9	9	1.2	2	5.7	9	3.4	11
Worse	0.7	1	1.1	2	1.8	3	0.0	0	0.9	3
No information	3.6	5	1.1	2	3.1	5	1.3	2	2.2	7
Total	100.0	137	100.0	184	100.0	163	100.0	158	100.0	321

Table 5: Overall assessment of the therapeutic outcome.

With regard to the intensity of the principal symptoms at the start of treatment, the differences between group A and group B were only slight; there was a tendency to a slightly greater reduction of symptom intensity over the course of treatment in group A (Fig. 1). If the four most commonly mentioned principal symptoms are considered individually, one finds that the biggest decrease in symptom intensity was for "fever" (difference between preliminary examination and final examination = 2.3), followed by "pain" (difference = 2.1), and "sleep disturbances" and "agitation" (difference = 1.9 in each case) (Fig. 2).

The therapeutic efficacy of the treatment was also determined on the basis of the length of time to the first global

improvement in symptoms. Table 4 shows that this occurred within the first 7 days in over 88% of the patients in group A (agitation with fever) and in over 71% of the patients in group B (agitation without fever).

The overall assessments of the therapeutic results by the paediatricians show that, in both groups, the outcome of treatment was "good" or "very good" in over 90% of the cases treated. The prescription of accompanying therapy did not have any decisive influence as far as the assessments of therapeutic outcome are concerned: the outcome of treatment was also rated as "good" or "very good" in over 90% of the patients treated with Viburcol alone (Table 5).

Tolerability

The tolerability of Viburcol was likewise rated favourably in the majority of cases, being evaluated as "very good" in 92% of patients and "good" in 7%. Tolerability was only rated as "poor" in 1 out of the 321 cases; increasing abdominal colic with vomiting was reported in this patient, who had an underlying illness of an allergic nature (allergy to cows' milk); however, since accompanying medicinal therapy was used (Symbioflor 1+2 in the last 2 weeks before the start of the treatment, Pankreaplex and Carbo vegetabilis during the treatment), assignment to a particular product - if, indeed, this was a case of intolerance to a medicinal agent at all - is not possible. Another adverse drug reaction (navel colic and agitation, in a patient whose underlying illness was a febrile infection of the upper respiratory tract) was attributed to overdosage due to a lack of compliance. The treating doctors rated patient compliance as "very good" to "good" in 95% of cases and as "poor" in 0.3% of cases only.

Discussion

The postmarketing clinical study presented here investigated the range of use of Viburcol and also its therapeutic efficacy and tolerability. The patients (children and babies) were divided into an "agitation with fever" group and an "agitation without fever" group, in accordance with the indications of the product. The commonest diagnosis was infection (respiratory tract infections in particular), followed by general agitation, tooth-eruption problems, and abdominal pain. In many instances antipyretic/analgesic therapy, e.g. with paracetamol, is quickly initiated - often at the insistence of the parents⁶. The controversial nature of such treatment (side-effect profile, immunomodulating significance of fever) raises the question of therapeutic alternatives for cases in which there is no compelling indication for antipyresis or analgesia. Mildly sedative, symptomatic treatment is promising here, especially for diseases that are not amenable to causal therapy⁷. A comparative study in children with otitis media, for example, showed that the specific

symptoms improved more quickly with homeopathic treatment than with conventional treatment⁸⁾.

The basic symptoms (agitation with/without fever) in the illnesses treated with Viburcol in this postmarketing clinical study predominantly represented acute problems of "moderate" severity which had been present for only a short time prior to the start of treatment (< 3 days). The nature of the documented principal clinical symptoms was typical of the diagnoses that were made, the commonest symptoms being sleep disturbances, pain, fever, and agitation. The intensity of the principal symptoms decreased significantly in both groups of patients as the treatment progressed. Overall, the mean intensity in the total population fell from 3.2 to 1.3 (scale of 1-5).

In the majority of instances, the first global improvement in symptoms was seen in the first week of treatment. The rapid reduction of the intensity of the symptoms is in line with the global assessments of the therapeutic results, which the treating doctors rated as "very good" or "good" in over 90% of cases. This efficacy, combined with good tolerability and compliance, make Viburcol a reliable remedy for the treatment of children and babies with agitation with or without fever, resulting from things such as infection (especially respiratory tract infections and otitis media), tooth-eruption problems, or other forms of pain.

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For the authors:

Dr. Michael Weiser
Gleißlestraße 34
77815 Bühl
Germany