Efficacy of Intranasally Applied Dimethindene Maleate 0.1% Solution (Fenistil® Nasal Dosierspray) versus Placebo in Adults Suffering from Seasonal Allergic Rhinitis

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Summary

There is no doubt that the allergic rhinitis is an increasing problem not only for the patient but also for the health care system. Approximately 15% of the German population is suffering from allergic rhinitis. Most Recent epidemiological studies clearly support the importance with data of a twofold or sometimes even threefold increase in prevalence within the last decade. And especially more and more children are affected by this disease. The reasons for this significant increase in prevalence are unclear but there is no doubt that the allergic rhinitis is a local inflammatory disease causing several secondary diseases like relapsing hydrotypannum in infancy, chronic sinusitis and bronchial asthma following [Etagenwechsel] [?] in adolescence and adulthood. The topical application of H₁-receptor antagonists is a modern and very promising approach for the symptomatic treatment of seasonal allergic rhinitis (SAR). As to the latest international conferences on the treatment of allergic rhinitis in infancy and adulthood especially the topical treatment with antihistamines is getting more into focus regarding initial therapy.

We randomly assigned 36 asymptomatic patients (17 female, 19 male), being allergic to grass pollen to treatment with topical nasal sprays with either dimethindene maleate 0.1% or placebo as negative control in a double-blind, randomised, cross-over- design, with 2 weeks wash-out periods between. The trial period was chosen in a pollen-free time from 20th October to 5th November 1998 to guarantee asymptomatic patients in the beginning. The patients being allergic to grass pollen proved by positive anamnnesis, positive Prick-test and positive nasal provocation test, were challenged under controlled conditions with purified airborne grass pollen of Daetlilis glomerata in the Vienna Challenge Chamber (VCC), located at the Universitätsklinik für Hals-Nasen-Ohrenheilkunde, Allgemeines Krankenhaus (AKH), der Stadt Wien, Vienna (Austria). The tested nasal sprays were applied as single doses (1 puff = 0.14 ml of the respective solution or 0.14 mg DMM) in the evening at 7.30 p.m. and in the morning at about 7.30 a.m. to each nostril 15 min before the start of the 4 h lasting provocation procedure in the VCC, thus simulating the recommended dosage regimen and representing a total daily dose of 0.56 mg DMM or Placebo.

The a-priori sequentially ordered and analysed objective variable total nasal symptom complex (TNSC) (p<0.0001) and the associated single subjective variables rhinorhoea (p=0.0032), sneezing stimulus (p<0.0001), nasal itching (p<0.0001) were rated by the patient by means of a conventional 4-point scale, respectively. Additionally, nasal secretion was measured gravimetrically (p=0.0031). No systemic or topical adverse events were reported.

The sequentially proven primary and also secondary variables “sneezing frequency” and “global assessment of efficacy” showed consistently statistically significant and clinically relevant superiority of 0.1% DMM vs. placebo. It is concluded from this study that 0.1% DMM as nasal spray, is efficient and safe in patients suffering from seasonal allergic rhinitis (SAR).
Zusammenfassung

*Wirksamkeit intranasal angewendeter 0,1%iger Dimetindenmaleat-Lösung (Fenistil® Nasal Dosiesspray) versus Placebo als Nasenspray bei Erwachsenen mit saisonaler allergischer Rhinitis*


Wir teilten dem Zufall folgend 36 asymptomatische Patienten (17 Frauen, 19 Männer) mit Heuschnupfen einer Behandlung mit Dimetindinmaleat 0,1% oder Placebo als Negativkontrolle in einem randomisierten, doppelblinden Cross-over-Design mit 2wöchigen Wash-out-Periode zu. Der Untersuchungszeitraum wurde vom 20. Oktober bis zum 5. November 1998 gewählt, so daß zu Studienbeginn von asymptomatischen Patienten ausgegangen werden konnte. Die Patienten mit Heuschnupfen, nachgewiesen durch positive Anamnese, positiven Prick- und positiven nasalen Provokationstest wurden unter kontrollierten Bedingungen mit nativen Grassporen von Dactylis glomerata in der "Wiener Provokationskammer" belastet. Die untersuchten Nasensprays wurden jeweils als Einzeldosis (1 Sprühstopp = 0,14 ml der jeweiligen Testlösung) am Abend um 19:30 Uhr und am Morgen um ca. 7:30 Uhr 15 Minuten vor der 4 h andauernden Provokation in der VCC verabreicht. Die tägliche Gesamtdosis lag demnach bei 0,56 mg DMM oder Placebo und simuliert damit die empfohlene tägliche Anwendung.

Die a-priori sequentiell geordneten und analysierten Hauptzielkriterien Totaler Nasaler Symptomen Komplex (TNSC) und dessen Einzelsymptome Rhinorhoe (p=0,0032), Niesreiz (p=0,0001), Nasenjucken (p=0,0001) wurden jeweils vom Patienten mit Hilfe einer üblichen 4-Punkt-Skala bewertet. Zusätzlich wurde das Hauptzielkriterium die Nasensekretion gravimetrisch (p=0,0031) gemessen. Er wurden keine systemischen oder topischen Nebenwirkungen berichtet.

Die sequentiell ausgewerteten primären und auch die sekundären Zielkriterien Nieszfrequenz und die „Bewertung der globalen Wirksamkeit" zeigten eine statistisch signifikante und klinisch relevante Überlegenheit von 0,1% DMM versus Placebo. Als Ergebnis der Studie resultiert, daß 0,1% DMM bei Patienten mit allergischer Rhinitis wirksam und sicher eingesetzt werden kann.

Key Words Antihistaminics - Dimetindine - Fenistil® - Foristol™ - Rhinitis, Seasonal Allergic Rhinitis - Topical Treatment

Arzneim.-Forsch./Drug Res. [??] ..............

1. Introduction

The topical application of H1-receptor antagonists is a modern and very promising approach for the symptomatic treatment of seasonal allergic rhinitis (SAR) [1, 2]. As to the latest international conferences on the treatment of allergic rhinitis especially the topical treatment with antihistamines is getting more into focus regarding initial therapy of the nasal symptoms in allergic rhinitis [5, 7]. For the topical treatment the systemic absorption is not necessary, and therefore unwanted CNS-effects do not occur. Furthermore due to the direct contact to the mucosa smaller amounts of the drug are necessary and therefore the onset-of-action is much faster and the therapeutical area is broader.

Dimetindine (Dimetindine maleate, DMM, CAS 3614-69-5, Fenistil® resp. Foristol®) is a very potent and well-established H1-receptor antagonist was tested earlier following oral and also topical nasal application of a gel in patients suffering from pollen-associated rhinitis, and has demonstrated that it exerts the typical antihistaminic effects on general nasal and ocular symptoms in a clinically relevant extent [3, 6]. As a well accepted and validated clinical model in allergic rhinitis the Vienna Challenge chamber (VCC) is a closed exposition chamber with windows, chairs, a ventilation system and with acustic equipment allowing communication and a continuous exposition of 12 volunteers per test sequence with well defined aeroallergens like grass pollens under reproducible, controlled conditions.

1 Manufacturer: Novartis Consumer Health GmbH, Munich (Germany). Fenistil is the trademark used in Germany; registered trademark in the USA is Foristol.
During the provocation over a period of 4 h standard measurements consisted of active anterior rhinomanometry, lung function testing and on-line pollen measurements, mimicking everyday life conditions of patients during normal pollen season. Subjective measurements were done on-line, measuring the seasonal allergic rhinitis-related "Total Symptom Complex" and the general "well being" by Visual Analog Scale (VAS). The aim of this study was to reproduce the efficacy and safety of 0.1 % DMM (Fenistil® Nasal Dosierspray) versus placebo demonstrated in a pharmacodynamic dose-finding [4], an active (DNCG) and placebo-controlled trial using the VCC [2] and a clinical trial in children with levocabastine as active control [1].

2. Materials and methods

2.1 Study design

The study protocol was approved by the Ethics Committee of the University of Vienna and was performed according to the GCP Guidelines. The study was carried out using a double-blind, placebo-controlled, randomised, cross-over study design. Thirty-six Caucasian male and female asymptomatic patients, aged between 19 and 39 years, suffering from SAR induced by grass pollen were assigned either to DMM or to Placebo. The trial period was from 20th October to 5th November 1998 securing that the patient were asymptomatic at baseline.

The positive anamnesis of SAR was confirmed by positive allergic history, positive skin tests, positive Radio Allergo Sorbent Test (RAST) and positive nasal provocation tests to grass pollen. Female patients had to be in the postmenopausal phase or sterile or had to practise adequate birth control for general safety reasons. Excluded were patients with non-allergic rhinitis, chronic sinusitis or severe asthma bronchiale, risk of glaucoma, urine retention, severe infection of the respiratory tract, hypersensitivity against any of the tested compounds, pregnant and lactating women, participation in a clinical trial during the last 4 weeks, treatment with H1 and H2 antagonists within the last 4 weeks and other drugs potentially influencing the allergic status. Professional car drivers and operators of potentially dangerous machines were excluded, too.

The study medication (1 spray puffs = 0.14 ml into each of the two clean nostrils) 0.1 % DMM vs. placebo was applied at 7:30 p.m. and at about 7:30 a.m. exactly 15 min before the onset of VCC provocation. The rescue medication consisted of an inhalational B2-sympathomimetic drug.

The controlled allergen provocation was performed in the "Vienna Challenge Chamber (VCC)" located at Universitätsklinik für Hals-Nasen-Ohrenheilkunde, Allgemeines Krankenhaus (AKH) der Stadt Wien, Vienna (Austria), which had proved already earlier the reproducibility of physiologic longterm provocation with pollen allergens. Due to the limited capacity of the VCC, which is able to monitor 12 subjects in parallel, and according to the cross-over design the tests were divided into six provocation sequences. In order to restore the histamine levels after the respective pollen challenges 2-week washout periods were set between the evaluation days. The allergen provocation with "Dactylis glomerata"-pollen was limited to 4 hours per day.

Table 1: Log of the conditions in the VCC during the test sequences.

<table>
<thead>
<tr>
<th>Sequence</th>
<th>1A</th>
<th>1B</th>
<th>1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td>20.10.98</td>
<td>21.10.98</td>
<td>22.10.98</td>
</tr>
<tr>
<td>Pollen/m3</td>
<td>1,503</td>
<td>1,497</td>
<td>1,501</td>
</tr>
<tr>
<td>SD</td>
<td>121</td>
<td>103</td>
<td>94</td>
</tr>
<tr>
<td>°C</td>
<td>23.9</td>
<td>24.2</td>
<td>23.8</td>
</tr>
<tr>
<td>Humidity</td>
<td>24.2</td>
<td>24.7</td>
<td>24.6</td>
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</table>

<table>
<thead>
<tr>
<th>Sequence</th>
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<th>2B</th>
<th>2C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
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<td>04.11.98</td>
<td>05.11.98</td>
</tr>
<tr>
<td>Pollen/m3</td>
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<td>1,504</td>
<td>1,502</td>
</tr>
<tr>
<td>SD</td>
<td>131</td>
<td>128</td>
<td>128</td>
</tr>
<tr>
<td>°C</td>
<td>23.2</td>
<td>23.5</td>
<td>23.9</td>
</tr>
<tr>
<td>Humidity</td>
<td>24.4</td>
<td>24.0</td>
<td>23.3</td>
</tr>
</tbody>
</table>

As a result all specific conditions of the VCC were comparable regarding the six provocation sequences.

2.2. Evaluations

During the course of the 4 h lasting allergen provocation, in time intervals of 30 min, the primary, secondary and further criteria for evaluation were recorded on-line in the VCC.

As primary criteria the Total Nasal Symptom Score (TNSS), the nasal secretion and the single symptoms of the TSC: running of the nose, sneezing stimulus and itching of the nose were measured. The single subjective nasal variables were rated by a 4-point scale (0 = none; 1 = mild; 2 = moderate; 3 = severe). Thus, the total sum of 3 items for the TNSS ranged from 0 to 9. The nasal secretion was objectivated by gravimetry.

Additionally the following secondary criteria were measured: Sneezing frequency measured as sneezing attacks per hour, global assessment of efficacy rated by a 4-point scale (0 = none; 1 = mild; 2 = moderate;
3 = severe) and the nasal flow reduction evaluated by active anterior rhinomanometry at constant pressure of 150 Pa (sum of left and right nostril values). The nasal flow reduction was expressed as area under baseline (AUB_Ba) of the baseline-adjusted values using the linear trapezoidal rule.

The following further criteria of interest were measured to compare the result with earlier trials:
Total ocular symptom complex consisting of the single symptoms ocular tearing and ocular itching rated by a four-point scale (0 = none; 1 = mild; 2 = moderate; 3 = severe), respectively, an overall severity assessment of the symptoms by means of a 100-mm-VAS Scale and the FEV.

All statistical analyses of the primary criteria were carried out with error levels of $\alpha = 0.05$; $\beta = 0.2$. The tests were carried out as "two-sided". For the primary and secondary criteria the Wilcoxon rank sum test for [?] verbundene Stichproben [?] was used. The primary and secondary criteria were analysed sequentially in accordance with the a-priori defined sequence. The listed further criteria were analysed descriptively.

3. Results

Thirtysix healthy subjects (17 female, 19 male) with a mean age of 25.1 years (±3.5), mean weight of 67.92 kg (±12.90 kg) and a mean height of 173.67 cm (±9.09 cm) were enrolled, randomised and completed the trial according to protocol without protocol violations. All could be evaluated for efficacy variables and safety. Therefore there is no need for a separation into an intention-to-treat and into a per-protocol-analysis in the following description of the results.

<table>
<thead>
<tr>
<th>Demography</th>
<th>Age</th>
<th>Height</th>
<th>Weight</th>
</tr>
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<tr>
<td>Mean</td>
<td>25.1</td>
<td>173.67</td>
<td>67.92</td>
</tr>
<tr>
<td>SD</td>
<td>3.5</td>
<td>9.09</td>
<td>12.90</td>
</tr>
<tr>
<td>Min</td>
<td>19</td>
<td>160.00</td>
<td>50.00</td>
</tr>
<tr>
<td>Max</td>
<td>35</td>
<td>188.00</td>
<td>100.00</td>
</tr>
<tr>
<td>Unit</td>
<td>years</td>
<td>cm</td>
<td>kg</td>
</tr>
</tbody>
</table>

3.1. Subjects

3.1.1. Efficacy

3.1.1.1. Primary efficacy variables

TNSC
The treatment with 0.1 % DMM led to a reduction in the symptomatic nasal sum score TNSC compared to placebo. As can be seen from Table 3 and Fig. 1, for 0.1 % DMM a low peak reaction with scores of 2.2222 after 60 min and a decrease of score values down to 1.8333 at the end was seen. In contrast, for placebo a strong increase in the first 30 min and a higher plateau reaction with increasing values until the end of the provocation and a peak value of 4.0278 could be seen.

The statistical analysis resulted in a p-value of 0.0001 between the 2 treatments. Thus, the level of significance was reached.

Nasal Secretion
As can be seen from Table 3 and Fig. 2, the treatment with 0.1 % DMM led to a weaker increase of the objective variable nasal secretion measured gravimetrically to a peak level of 1.0894 mg in the first hour. From time point 60 min to 150 min a relevant decrease could be detected to 0.63944 mg, followed by slight increasing amounts of nasal secretion of 0.73889 mg to 0.72500 mg from 150-180 min and reached the lowest level of 0.64722 mg at the end of the provocation. The curve for placebo showed a nearly parallel course but at a significant higher level reaching a peak level of 1.7022 mg in the first hour and also a significant higher plateau level of 1.2839 mg from 180 min to 210 min. The sequentially statistical analysis for the 2nd primary criterion resulted in a p-value of 0.0031 between the 2 treatments. Thus, also for nasal secretion the level of significance was reached.

Running of the Nose (Rhinorrhoe)
In the active treatment group with 0.1 % DMM the rating of the single symptom Rhinorrhoe showed an increase of the severity in the first 60 min under provocation up to 1.0000 score point. In the following 2 hours the severity did not reach the peak value and decreased to a score value of 0.8333 in the end of the provocation. In contrast, placebo showed a higher peak reaction with scores of 1.3889 after 60 min. The following plateau reaction kept nearly constant with a final value of 1.3889 score points at the end of challenge.

The sequentially statistical analysis for the 3rd primary variable resulted in a p-value of 0.0052 between the 2 treatments. Thus, also for rhinorrhoe the level of significance was reached.

Sneezing Stimulus
For the symptom sneezing stimulus a low peak reaction with scores of 0.61111 after 60 min and a decrease of score values down to 0.47222 at the end was seen for 0.1 % DMM. In contrast, for placebo a strong increase in the first 30 min and a higher plateau reaction with increasing values until the end of the provocation and a peak value of 1.2222 could be seen. The sequentially statistical analysis for the 4th primary variable resulted in a p-value of 0.0001 between the 2 treatments. Thus, also for sneezing stimulus the level of significance was reached.

Nasal Itching
For the symptom nasal itching a low peak reaction with scores of 0.69444 was seen for 0.1 % DMM after 90 min. After a slight decrease between 90 and 120 min, during the third hour again a score increase from 0.63889 to 0.72222 could be detected. The score value decreased then reaching a score level of 0.52778 in the end of the provocation. In contrast, for placebo a strong increase in the first 30 to 60 min could be seen with scores of 1.2500 followed by a even higher plateau phase with a peak level of 1.4167 after a slight decrease in severity for the time point 210 min. The sequentially statistical analysis for the 5th primary variable resulted in a p-value of 0.0001 between the 2 treatments. Thus, also for nasal itching the level of significance was reached.

3.1.1.2 Secondary efficacy variables

Sneezing Frequency
As can be seen from Table 4 and Fig. 6 a lower sneezing frequency could be demonstrated for the active principle DMM 0.1%.

The sequentially statistical analysis for the 1st secondary variable resulted in a p-value of 0.0016 between the 2 treatments. Thus, also for sneezing frequency the level of significance was reached.
Global Assessment of Efficacy
The treatment with 0.1 % DMM led to a better rating for the Global Assessment of Efficacy (Table 4, Fig. 7) from the beginning until the end of the provocation.
The sequentially statistical analysis for the 2nd secondary variable measured by means of a 100mm-VAS resulted in a p-value of 0.0029 between the 2 treatments. Thus, also for the global assessment of efficacy the level of significance was reached.

Nasal Flow Reduction
As can be seen from Table 4 and Fig. 8 under 0.1 % DMM the subjects' nasal flow showed a medium decrease from −288.86 to −357.86 cm³/s. Only between the time points 30 min to 90 min a slight trend in favour for DMM 0.1% could be seen.
The statistical analysis resulted in a p-value of 0.7773 between the 2 treatments. Thus, the level of significance was failed.
Figure 1: Total Nasal Symptom Score; DMM vs. PLC (N=36)

Figure 2: Nasal Secretion; DMM vs. PLC (N=36)

Figure 3: Rhinorrhea (gravimetrically); DMM vs. PLC (N=36)

Figure 4: Sneezing Stimmulus; DMM vs. PLC (N=36)

Figure 5: Nasal Itching; DMM vs. PLC (N=36)

Table 3: Results in Primary Criteria; DMM vs. PLC (N=36)

<table>
<thead>
<tr>
<th>Primary Criteria</th>
<th>Mean</th>
<th>SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNSC (PLC)</td>
<td>3.7639</td>
<td>2.1171</td>
<td>= 0.0001</td>
</tr>
<tr>
<td>TNSC (DMM)</td>
<td>1.9965</td>
<td>1.4870</td>
<td></td>
</tr>
<tr>
<td>Nasal Secretion (PLC)</td>
<td>9.0186</td>
<td>10.923</td>
<td>= 0.0031</td>
</tr>
<tr>
<td>Nasal Secretion (DMM)</td>
<td>6.5406</td>
<td>8.5642</td>
<td></td>
</tr>
<tr>
<td>Rhinorrhea (PLC)</td>
<td>1.3090</td>
<td>0.77488</td>
<td>= 0.0032</td>
</tr>
<tr>
<td>Rhinorrhea (DMM)</td>
<td>0.89236</td>
<td>0.64167</td>
<td></td>
</tr>
<tr>
<td>Sneezing (PLC)</td>
<td>1.1319</td>
<td>0.73250</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Sneezing (DMM)</td>
<td>0.48958</td>
<td>0.54230</td>
<td></td>
</tr>
<tr>
<td>Nasal Itching (PLC)</td>
<td>1.3229</td>
<td>0.78625</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Nasal Itching (DMM)</td>
<td>0.61458</td>
<td>0.60162</td>
<td></td>
</tr>
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</table>
3.1.1.3 Further variables

The explorative analysed variables consisted of a ocular symptom score, its single symptoms ocular tearing and ocular itching, overall severity assessment (OSA) and the FEV reduction.

**Total Ocular Symptom Complex**

With mean values of $m=0.6$ ($\pm 0.9$) for verum and $m=1.1$ ($\pm 0.8$) for placebo with a sum score range from 0 to 8 the statistical analysis resulted in a $p$-value of 0.0015 for 0.1 % DMM vs. placebo.

**Ocular Tearing**

With mean values of $m=0.2$ ($\pm 0.3$) for verum and $m=0.3$ ($\pm 0.4$) for placebo with a score range from 0 to 4 the statistical analysis resulted in a $p$-value of 0.0193 for 0.1 % DMM vs. placebo.

**Ocular Itching**

With mean values of $m=0.6$ ($\pm 0.9$) for verum and $m=1.1$ ($\pm 0.8$) for placebo with a sum score range from 0 to 8 the statistical analysis resulted in a $p$-value of 0.0064 for 0.1 % DMM vs. placebo.

<table>
<thead>
<tr>
<th>Secondary Criteria</th>
<th>Mean</th>
<th>SD</th>
<th>$P$</th>
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</thead>
<tbody>
<tr>
<td>Sneezing (PLC)</td>
<td>2.1458</td>
<td>2.2861</td>
<td>0.0002</td>
</tr>
<tr>
<td>Sneezing (DMM)</td>
<td>0.9236</td>
<td>1.2643</td>
<td></td>
</tr>
<tr>
<td>Overall Efficacy (PLC)</td>
<td>1.3090</td>
<td>0.8278</td>
<td>0.0016</td>
</tr>
<tr>
<td>Overall Efficacy (DMM)</td>
<td>1.8924</td>
<td>0.8666</td>
<td></td>
</tr>
<tr>
<td>Nasal Flow Red. (PLC)</td>
<td>-357.42</td>
<td>319.46</td>
<td>0.7773</td>
</tr>
<tr>
<td>Nasal Flow Red. (DMM)</td>
<td>-370.95</td>
<td>262.84</td>
<td></td>
</tr>
</tbody>
</table>

**Overall Severity Assessment (OSA)**

With mean values of $m=15$ mm-VAS ($\pm 22$) for verum and $m=28$ ($\pm 22$) for placebo using a 100mm-VAS scale the statistical analysis resulted in a $p$-value of 0.0029 for 0.1 % DMM vs. placebo.

**FEV Reduction**

With a mean unit of $-2.9$ (7) for verum and $0.8$ (14) the statistical analysis resulted in a $p$-value of 0.7773 for 0.1 % DMM vs. placebo.

3.1.2. Safety

No systemic or topical adverse events were reported by the subjects after nasal application of the 2 test preparations. Thus, 0.1 % DMM spray could be rated as safe and locally very well tolerated galenic formulation.

4. Discussion

In this double-blind, randomized, and placebo-controlled 2 fold cross-over design, the clinical efficacy and safety of topically applied 0.1 % DMM
as nasal spray was studied vs. placebo as negative control.

DMM was used as nasal spray in a concentration of 0.1% DMM. According to the patient leaflet 1 spray puff into each nostril were applied two times daily. This results into a daily dose of 0.56 mg DMM in the active treatment group.

Thirty-six healthy subjects (17 female, 19 male) were enrolled, randomised and completed the trial according to protocol without protocol violations. All could be evaluated for efficacy variables and safety.

The VCC is a well accepted and validated clinical model used for several antiallergic products to prove the efficacy and safety in the indication seasonal and perennial allergic rhinitis.

As known effects of potent H1-antihistamines the histamine dependant subjective TNSC and the single symptoms running of the nose, sneezing stimulus and itching of the nose could be significant reduced by 0.1% DMM compared to placebo. Also the objective parameter nasal secretion measured gravimetricaly resulted in a significant reduction in the active treatment group. In consequence this phase III trial demonstrates a statistical significant and relevant efficacy for all sequentially analysed primary criteria. The fact that also the sequentially analysed secondary criteria “sneezing frequency” and “global assessment of efficacy” consistently resulted in a difference reaching the level of significance in favour for 0.1% DMM underlines the relevance of this trial.

Concerning the 3rd secondary variable “nasal flow reduction” the result reflects the known fact that H1-receptor antagonists show only little effects on variables of nasal obstruction [7].

The results of this phase III trial is also consistent with the findings of earlier own trials [2, 4] and by Terrier in patients with SAR with a DMM containing nasal gel formulation [6]. While DMM 0.1% was able to demonstrate an equal efficacy compared to azelastine, in an earlier own dose-finding-trial the therapeutic effect of 0.025 % DMM could be rated as very weak and no variable tested, differed significantly from placebo [4]. Additionally the efficacy and safety of 0.1 % DMM could be demonstrated as being equivalent to levocabastine in children suffering from seasonal allergic rhinitis under everyday life condition [1].

As no systemic and local adverse events were reported for 0.1 % DMM the nasal spray solution can be judged as a safe and efficient galenic formulation for patients suffering from seasonal allergic rhinitis (SAR).

5. References


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