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Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00272532
		Study Code:	L_9892
Generic drug name:	Thiocolchicoside	**Date:**	15/Feb/2008

Title of the study:	Efficacy of Topical Thiocolchicoside in Myofascial Pain Syndrome: Three-armed, Single-blind, Randomized, Prospective, Phase IV Clinical Study		
Investigator(s):	Prof. Aysegul Ketenci Cakmak, M.D. Department of Physical Medicine and Rehabilitation, Istanbul University, Istanbul Medical School, Istanbul, Turkey		
Study center(s):	Single center		
Publications (reference):	NA		
Study period: Date first patient/subject enrolled:14-Apr-2005 Date last patient/subject completed: 31-Dec-2005		**Phase of development:** IV	
Objectives:	Primary objective To demonstrate how effective thiocolchiocoside ointment is as compared to trigger point injection for the control of pain in patients with myofascial pain syndrome in the cervical region. Secondary objectives To demonstrate how effective the combination of thiocolchicoside ointment and trigger point injection as compared to trigger point injection alone for the control of pain in patients with myofascial pain syndrome in the cervical region. To determine the safety of thiocolchiocoside ointment applied on trigger points in the control of pain in patients with myofascial pain syndrome in the cervical region.		
Methodology:	Three-armed, Single-blind, Randomized, Prospective clinical trial		
Number of patients/subjects:	Planned: 66	Randomized: 65	Treated: 59
Evaluated:	61	Safety: NA	Pharmacokinetics: NA
Diagnosis and criteria for inclusion:	If the patient • has applied to the policlinic with complaints of head and neck pain, • has been diagnosed with acute myofascial pain syndrome by the determination of active trigger points in the trapezius and/or interscapular regions according to the criteria of Simons and Travel, • has 1-8 active trigger points, • is aged between 18-50 years of age, • provides written consent to participate in the study.		

Investigational product:	Thiocolchicoside / Muscoril
Dose:	Ointments→0.25% percutaneous 2 times a day; Ampoules→ 4mg / 2 mg intramuscular 2 times, 4 mg / day for 5 days
Administration:	Patients were randomized to three groups: thiocolchicoside ointment, thiocolchicoside injection and thiocolchicoside ointment + injection. The injection dose was 8 mg/day. The ointment was applied to the painful site two times a day.

Brand name	Company	Dosage form	Strength	Route of administration	Recommended dose
Muscoril	Sanofi-aventis	ointment	0.25 %	percutaneous	2 times a day
Muscoril	Sanofi-aventis	ampoules	4 mg / 2 ml	intramuscular	2 times 4 mg/day for 3-5 days

Duration of treatment: Ointments→0.25% percutaneous 2 times a day; Ampoules→ 4mg/2 mg intramuscular 2 times 4 mg / day for 5 days	**Duration of observation:** 5 days

Reference therapy:	NA
Dose:	NA
Administration:	NA
Criteria for evaluation:	
Efficacy:	*Primary efficacy parameters:* Reduction of pain (VAS and Algometer) Increase in neck mobility (Goniometer) *Secondary efficacy parameter:* Patient - physician satisfaction
Safety:	Adverse events were observed throughout the study period, severity and significance, cause-result relationship with the study drug and clinical consequences. Laboratory tests including whole blood count, liver function tests, serum creatinine measurements and urine analysis were performed in all patients. An ECG recording was obtained from each patient.
Pharmacokinetics:	NA
Pharmacokinetic sampling times and bioanalytical methods:	NA
Statistical methods:	The demographic (age, sex) and other initial features were expressed using descriptive statistics (mean, median, ration, standard deviation, 95% confidence interval). Data of the initial and follow up visits were compared with paired Student's t-test if parametric test criteria were met and otherwise the Wilcoxon test was used. The difference between the frequency of adverse events between the initial visit and the follow up visits was compared using the McNemar test.

Summary:	A total of 65 subjects (mean age 34.95±10.71 years, 83.0% female) were included and 61 subjects were evaluated in the study. Patients were randomized to three groups: Group 1: treated with thiocolchicoside ointment for 5 days; n=19 (35.76 ± 10.8 years; 80.0% females) Group 2: treated with thiocolchicoside injection for 5 days; n=21 (32.16 ± 11.2 years; 91.3% females) Group 3: treated with thiocolchicoside ointment + injection for 5 days; n=21 (37.00 ± 9.95 years; 77.3% females). The injection dose was 8 mg / day. The ointment was applied to the painful site two times a day. Protocol deviations; lost in follow-up and / or withdrawn because of adverse events: All of 59 patients who received the study medication completed the study according to the clinical protocol. There were no protocol deviations. Two patients who never received the study medication were lost in follow-up and no patient was withdrawn because of adverse events.

Efficacy results/ Pharmacodynamic results:

Reduction of pain (Visual analog scale algometer)

VAS scores (mean ± SD)

Severity of pain for 24 h

	Baseline*	Day 1	Day 3	Day 5
All patients	52.4 ± 19.2	46.3 ± 20.1 b	37.5 ± 16.1 b	28.9 ± 17.6 b
Group 1+	56.5 ± 20.4	45.5 ± 19.7	33.2 ± 16.4	25.8 ± 20.1
Group 2+	55.9 ± 14.7	51.1 ± 20.2	41.3 ± 11.7	26.9 ± 14.6
Group 3+	45.0 ± 20.9	42.3 ± 20.3	37.7 ± 19.0	33.6 ± 17.7

Severity of pain with movement for 24 h

	Baseline	Day 1	Day 3**	Day 5
All patients	60.8 ± 19.6	50.3 ± 18.8 b	41.2 ± 15.9b	30.4 ± 17.4 b
Group 1+	57.0 ± 22.9	47.1 ± 14.5	32.9 ± 14.4	29.0 ± 14.9
Group 2+	66.1 ± 15.1	52.9 ± 21.1	45.4 ± 11.8	29.0 ± 15.3
Group 3+	58.9 ± 20.4	50.4 ± 19.9	44.4 ± 18.1	37.2 ± 20.2

ap<0.001 between 4 measurements by Friedman test; bp<0.001 vs baseline by Wilcoxon test; *p=0.029 between Groups 1, 2 and 3 by Kruskal-Wallis test; **p=0.010 between Groups 1, 2 and 3 by Kruskal-Wallis test; +p<0.001 with Friedman test.

Pressure Algometer scores (mean ± SD):

	Trigger point pain threshold			
	Baseline	Day 1	Day 3	Day 5
All patients	3.2 ± 0.9	3.3 ± 0.9 c	3.5 ± 1.0 b	4.0 ± 1.4 b
Group 1+	3.2 ± 0.8	3.4 ± 0.7	3.6 ± 0.8	4.5 ± 1.6
Group 2+	3.4 ± 0.9	3.5 ± 1.0	3.5 ± 0.9	3.4 ± 1.0
Group 3+	3.1 ± 1.0	3.1 ± 1.0	3.4 ± 1.4	3.7 ± 1.4

**p=0.010 between Groups 1, 2 and 3 by Kruskal-Wallis test; +p<0.001 with Friedman test.

Pressure Algometer scores (mean ± SD):

ap<0.001 between 4 measurements by Friedman test; bp<0.001 vs baseline by Wilcoxon test; cp=0.002 vs baseline by Wilcoxon test; +p<0.001 with Friedman test.

Efficacy results/ Pharmacodynamic results:

Increase in the neck motility (Goniometer)
Cervical ROM results (degree) (mean ± SD):

Right lateral flexion

	Baseline	Day 1	Day 3	Day 5
All patients	40.5 ± 7.2	42.1 ± 6.5 b	42.3 ± 5.9 b	42.5 ± 4.3 b
Group 1	39.2 ± 9.6	41.2 ± 8.7	42.7 ± 8.7	41.7 ± 4.2
Group 2	41.9 ± 5.7	43.6 ± 5.6	42.9 ± 3.8	43.7 ± 4.3
Group 3	40.2 ± 6.1	41.3 ± 5.0	41.4 ± 4.4	42.1 ± 4.3

Left lateral flexion

	Baseline	Day 1	Day 3	Day 5
All patients	41.4 ± 5.8	42.7 ± 6.6d	44.1 ± 8.4 b	43.0 ± 3.6 b
Group 1	40.2 ± 8.3	43.2 ± 10.9	44.7 ± 10.4	42.6 ± 4.1
Group 2	42.2 ± 3.9	42.9 ± 3.2	46.0 ± 9.4	44.4 ± 2.3
Group 3	41.5 ± 4.9	41.9 ± 3.5	41.6 ± 3.9	42.2 ± 4.1

Right rotation

	Baseline	Day 1	Day 3*	Day 5
All patients	81.9 ± 11.8	81.9 ± 11.8	82.8 ± 11.6 e	84.4 ± 9.4 b
Group 1	79.25 ± 12.9	79.6 ± 12.9	80.6 ± 12.8	81.8 ± 12.7
Group 2	86.7 ± 6.1	85.5 ± 8.3	87.1 ± 7.2	87.8 ± 7.2
Group 3	79.4 ± 14.1	80.4 ± 13.5	80.6 ± 13.1	83.5 ± 7.2

Left rotation

	Baseline**	Day 1	Day 3***	Day 5
All patients	81.6 ± 11.9	82.3 ± 11.0 g	83.2 ± 10.2 f	85.1 ± 7.6 b
Group 1	77.8 ± 11.9	80.2 ± 12.9	81.4 ± 10.0	82.4 ± 9.7
Group 2	86.8 ± 6.2	85.6 ± 8.5	87.6 ± 4.9	88.5 ± 4.5
Group 3	79.5 ± 14.7	80.8 ± 13.1	80.5 ± 12.7	84.3 ± 7.0

Efficacy results/ Pharmacodynamic results:

Increase in the neck motility (Goniometer)

Cervical ROM results (degree) (mean ± SD):

Right lateral flexion

	Baseline	Day 1	Day 3	Day 5
All patients	40.5 ± 7.2	42.1 ± 6.5 b	42.3 ± 5.9 b	42.5 ± 4.3 b
Group 1	39.2 ± 9.6	41.2 ± 8.7	42.7 ± 8.7	41.7 ± 4.2
Group 2	41.9 ± 5.7	43.6 ± 5.6	42.9 ± 3.8	43.7 ± 4.3
Group 3	40.2 ± 6.1	41.3 ± 5.0	41.4 ± 4.4	42.1 ± 4.3

Left lateral flexion

	Baseline	Day 1	Day 3	Day 5
All patients	41.4 ± 5.8	42.7 ± 6.6d	44.1 ± 8.4 b	43.0 ± 3.6 b
Group 1	40.2 ± 8.3	43.2 ± 10.9	44.7 ± 10.4	42.6 ± 4.1
Group 2	42.2 ± 3.9	42.9 ± 3.2	46.0 ± 9.4	44.4 ± 2.3
Group 3	41.5 ± 4.9	41.9 ± 3.5	41.6 ± 3.9	42.2 ± 4.1

Right rotation

	Baseline	Day 1	Day 3*	Day 5
All patients	81.9 ± 11.8	81.9 ± 11.8	82.8 ± 11.6 e	84.4 ± 9.4 b
Group 1	79.25 ± 12.9	79.6 ± 12.9	80.6 ± 12.8	81.8 ± 12.7
Group 2	86.7 ± 6.1	85.5 ± 8.3	87.1 ± 7.2	87.8 ± 7.2
Group 3	79.4 ± 14.1	80.4 ± 13.5	80.6 ± 13.1	83.5 ± 7.2

Left rotation

	Baseline**	Day 1	Day 3***	Day 5
All patients	81.6 ± 11.9	82.3 ± 11.0 g	83.2 ± 10.2 f	85.1 ± 7.6 b
Group 1	77.8 ± 11.9	80.2 ± 12.9	81.4 ± 10.0	82.4 ± 9.7
Group 2	86.8 ± 6.2	85.6 ± 8.5	87.6 ± 4.9	88.5 ± 4.5
Group 3	79.5 ± 14.7	80.8 ± 13.1	80.5 ± 12.7	84.3 ± 7.0

Efficacy results/ Pharmacodynamic results:

ap<0.001 between 4 measurements by Friedman test; bp<0.001 vs baseline by Wilcoxon test; dp=0.008 vs baseline by Wilcoxon test; ep=0.009 vs baseline by Wilcoxon test; fp=0.007 vs baseline by Wilcoxon test; gp=0.011 vs baseline by Wilcoxon test; *p=0.010 between Groups 1, 2 and 3 by Kruskal-Wallis test; **p=0.004 between Groups 1, 2 and 3 by Kruskal-Wallis test; ***p=0.015 between Groups 1, 2 and 3 by Kruskal-Wallis test Right lateral flexion.

Safety results	Totally 15 (25.4%), 11 (18.6%) and 5 (8.5%) patients had experienced adverse events as recorded at the first, third and fifth days, respectively. The most common adverse events were nausea (71.4%) and pruritus (8.6%). Most of the adverse events (82.9%) were mild in severity and 54.3% were found to be strongly related to the study drug. No serious adverse event was observed. Sixteen and 19 adverse events were observed in Group 1 and Group 2, respectively, while no adverse event was seen in Group 3. There was no significant difference between Group 1 and Group 2 in terms of adverse event severity (p=0.886, Mantel-Haenszel test). Fifty percent of the adverse events observed in Group 1 and 57.9% of the events in Group 2 were found to be strongly related to the study drug (p=0.458, Mantel-Haenszel test).
Date of report:	13-Nov-2007