MEDICAL USE OF CANNABIS IN THE NETHERLANDS

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Abstract

Objectives: The purpose of this survey was to investigate for which indications *Cannabis sativa* was prescribed by which kind of licensed physicians and delivered through regular pharmacies in the Netherlands, and the possible efficacy and side-effects, documented by both the prescribing physicians and the patients.

Design: National survey consisting of two questionnaires: one for patients and one for prescribing physicians. All prescribed *Cannabis sativa* deliveries were accompanied by the questionnaires. Questionnaires were returned by patients and physicians separately, by regular prepaid mail, between October 1997 and February 1999.

Subjects: Patients receiving *Cannabis sativa* on prescription for medical indications.

Results: In the Netherlands, patients receiving Cannabis sativa on prescription were 45% male and 55% female; median age was 58 yrs; median weight 70. 0kg. Mean duration of Cannabis intake was 5.6 months. Indications treated were neurological disorders (38.8%), pain (26.7%). musculoskeletal/connective tissue disorders (20.7%), and symptoms associated with cancer (13.8%). Inhaled Cannabis was perceived as being more effective for most indications than oral administration ($p < 0.01$).

Conclusions: In the Netherlands, the medical use of *Cannabis sativa* is widely accepted and prescribed by physicians of various specialties and used by more middle-aged patients of both genders, mainly for symptoms like spasticity, anorexia/cachexia, fatigue, and (chronic) pain.

Introduction

Lately, there has been a renewed interest in the medical use of *Cannabis sativa* and its main constituent delta-9-Tetrahydrocannabinol (THC), both in scientific literature and in the media, in conditions like anorexia and cachexia in cancer and AIDS (Gorter, 1991; Gorter et al. 1992; Gorter, 1999), Multiple Sclerosis (Brenneisen et al. 1996; Ungerleider et al. 1987; Meinck et al. 1989), migraine, spinal cord injuries (Pertwee, 1997), movement disorders (Muller-Vahl et al. 1999) and chronic pain.

In 1997, in an anonymous questionnaire, 112 multiple sclerosis (MS) patients in the USA and the UK were asked about their medical use of Cannabis for the relief of symptoms. Respondents were about equally divided between the USA and the UK, and half male and half female patients. After Cannabis consumption, there was a strong improvement of spasticity at the onset of sleep, and upon awakening in the morning, as well as reduction in pain and tremor. Patients also reported improvement in the ability to walk, in recovery of balance, and in sexual function. There was only minor improvement in memory loss, faecal incontinence, and constipation (Consroe et al. 1997).

In another study in 1997, all 7407 members of the Dutch Society of Multiple Sclerosis, who had been diagnosed with MS, received an anonymous questionnaire to investigate knowledge and use of Cannabis among MS patients in the Netherlands. The response rate was 68.1%. Almost half of all respondents knew about the possible benefits of Cannabis in MS; 13% had ever used Cannabis for their symptoms; 5% indicated they used it regularly, at the time of the survey. Most patients started using Cannabis for relief of symptoms are of an elderly age and tended to live in cities with a population of 100,000 or more. In Amsterdam, above age 40, relatively more MS patients use Cannabis than the general population in this capital.

In the Netherlands as a whole, approximately 5% of the population above age 12 uses Cannabis occasionally, against 13% of all MS patients who responded (Zaadstra et al. 1999).

In 1998, an anonymous questionnaire about Cannabis use was distributed to patients in Germany, Austria and the German-speaking part of Switzerland. In one year, 170 patients returned their questionnaire; 128 could be evaluated. The most frequently mentioned indications for Cannabis were depression (12.0%), MS (10.8%), HIV-infection (9.0%), migraine (6.6%), asthma (6.0%), back pain (5.4%) and sleeping disorders (4.8%). The large majority had used Cannabis; in just 5 cases Dronabinol (delta-9-tetrahydrocannabinol, or Marinol ©) was taken by prescription. The route of administration was in 14.3% oral and in 49.2% by inhalation; and in 36.5%, both routes of administration were applied. Of the 128 patients, 72.2% stated that that the symptoms of their diseases were “much improved” by taking Cannabis; 23.4% were “slightly improved”, and 1.6% described their symptoms as gotten “worse” (Schnelle et al. 1999).

In the Netherlands, recreational use of Cannabis is illegal, but consumption of small amounts, under certain conditions, is condoned. The concept of using Cannabis for medical purposes seems to be acceptable by large parts of the Dutch population, and physicians are allowed to prescribe Cannabis through a pharmacy. There are Buyer’s Clubs in the Netherlands, which provide Cannabis to patients, in a similar way as it was done in California, USA. Founded in 1995, Maripharm, a non-profit patient-oriented organization in Rotterdam, delivers “medical grade Cannabis” (MGC) on prescription to pharmacies throughout the country. When a patient presents a prescription from his doctor for MGC, the pharmacy will forward the prescription to Maripharm, which delivers within 24 hours units of 25g or 5g of standardized, sterile and vacuum-packed MGM to the pharmacy. The THC content in MGM is standardized at 10.2%.

To augment existing information about the medical use of Cannabis in the Netherlands, a new questionnaire was developed to document for which indications MGC was taken, for which duration, whether a patient had any side effects and whether the patient was content with the effects of Cannabis. The objective was to obtain input not only from patients but also from physicians prescribing MGC. For this reason a standardized questionnaire accompanied each order of MGC, which was filled out by both the patient and the prescribing physician.

Materials and Methods

MGC was delivered by Maripharm in a vacuum plastic bag, which was placed in a plastic container. Each order of MGC, delivered to the pharmacy, was accompanied by two items along with self-addressed envelopes with pre-paid postage, placed in the plastic container by Maripharm.

The first piece was a letter addressed to the patient, explaining the reason of the anonymous survey and the importance of patient participation. It also contained the request to have the prescribing physician participate in filling out his/her part of the questionnaire.

The second piece was the questionnaire.

The questionnaire consisted of two sections. Section one was a letter to the prescribing physician, explaining the purpose of the survey. Section two was the questionnaire.

The first part of the questionnaire was filled out by the prescribing physician. He/she was asked to document his/her name and office address, his/her specialty; his/her patient's diagnosis, date of birth, weight, gender and for how many months the patient was taking

Cannabis. Then the physician was asked to rate the efficacy of the therapy with Cannabis as "not at all", "somewhat", "good" and "excellent", and how the Cannabis was administered (orally, by inhalation, or both).

The second part of the questionnaire was addressed to the patient and asked about symptoms and side-effects (eye irritation, feeling "high", short term memory loss, sleepiness, hunger, loss of concentration, decrease in motivation, anxiety, euphoria, depression, dry mouth and difficulties in coordination), about frequency of these symptoms (never, occasionally, regularly and always), and intensity of these symptoms (mild or intense). The filled-out questionnaires were sent to the International Institute for Oncological and Immunological Research in Amsterdam. The first 107 questionnaires, returned to the Institute in Amsterdam during the period October 1997 – February 1999, were analyzed.

Results

Of the 107 patients, who filled out their questionnaires, 48 (45%) were male and 59 (55%) were female. Median age was 58.0 years for the total patient population (52.5 for males, 60.0 for females). Median body weight was 70.0 kg (74.5 kg for males, 65.0 kg for females). Mean duration of Cannabis (MGC) intake was 5.4 months (7.3 months for males and 3.9 months for females) (see Table 1).

Among prescribing physicians, there were internists, oncologists, neurologists (usually from community based medical centers and university hospitals), and family practitioners in private practice. The specialists tended to prescribe Cannabis at the request of their patients, while the

family practitioners, on their own initiative, tended to discuss the possible benefists of Cannabis with their naïve patients, before Cannabis was prescribed.

The main reported diagnoses for which MGC was prescribed were neurological disorders, like multiple sclerosis and spinal cord injuries (N= 45, 38.8%), musculo-skeletal/connective tissue disorders (N=24, 20.7%); and malignant tumors for symptoms, like anorexia/cachexia and fatigue (N=16, 13.8%) and "other", which were often HIV infection, cerebro-vascular accident (CVA), and pain (N=31, 26.7%) (Table 1).

The correlation between efficacy and duration of intake Cannabis (GMC) is shown in Table 2. In 19 (18.4%) cases, no positive effects of Cannabis were documented. These patients stopped taking Cannabis between and 1-4 months. In contrast, a good or excellent effect of Cannabis was documented in 66 (64.1%) cases. Twenty-nine of these patients had taken Cannabis for five months or longer at the time of the survey. Sixteen patients took it for more than ten months.

Figure 1 shows efficacy in relation to duration of Cannabis intake. The perceived efficacy by the patient correlates positively with the duration of the intake of *Cannabis sativa* (Spearman $r=0.52$; $p<0.01$). Table 2 and Figure 1 show that negative experiences are more frequent at the first few months of intake. Positive experiences accumulate more when time progresses. This can mean one of the two things: those patients who experienced side effects or no efficacy, stopped after one to four months, or the perceived efficacy of Cannabis took time to develop.

Experienced efficacy is better in the group who inhaled only (68%of all patients) compared to those who took MGC orally only (32% of all patients). Thus, efficacy of MGC was better when inhaled (Mann-Whitney U Test, $Z= 4.7$; $p< 0.01$) (see Figure 2).

Table 3 shows the correlation between complaints (side-effects) and the duration of Cannabis (MGC) use at the moment of the survey. For all 12 listed side effects, the only documented side effect, which stands out as being present regularly or always is “dry mouth” in 27.4% of the cases. This might – in part- be related to the fact that most of these patients smoked Cannabis. Other side effects which were mentioned were “sleepiness (13.9%), “euphoria (13.3%), “loss of concentration (11.7%) and “feeling high” (10.6%).

Discussion

In the Netherlands, among MS patients, *Cannabis sativa* is used about equally by men and women (45% vs 55%), but the age of the women tends to be older (52.5 yrs vs 60.0 yrs). The fact that patients taking Cannabis are middle-aged people, strongly suggests that these individuals took Cannabis for its medical effects and not as a recreational drug.

The main indications for which Cannabis was prescribed are well described in both the lay press and in the scientific literature. Therefore, patients in the Netherlands have some awareness of its possible benefits for certain symptoms. Many physicians, on the other hand, are therefore willing, on request of the patient, to prescribe *Cannabis sativa*

The main indications, which are mentioned in the media and in the literature, are reflected in the use of this patient population. The main indications were neurological disorders (MS, Spinal cord injuries), musculo-skeletal and connective tissue disorders, consequences of cancer and AIDS, like anorexia/cachexia and fatigue, and various forms of pain. Interestingly,

patients with more chronic pains documented less of a beneficial effect than those patients with more acute pains (migraine).

Of the 107 evaluated questionnaires in this study, 66 (64.1%) patients documented a good or excellent effect for their symptoms. Of these patients approximately 44% used *Cannabis sativa* for 5 months or longer. It is likely, that patients receiving a benefit from Cannabis use will continue taking *Cannabis sativa* for the relief of their symptoms, while others, not experiencing a benefit during the first few weeks to months of intake, might have stopped within one to four months (fig 1). In addition, lack of efficacy experienced in the first few months might be attributed to the fact that certain medicinal effects of *Cannabis sativa* take a while to take effect, e.g. appetite stimulation and weight gain, and mood elevation.

Some of the described side effects, documented by a few patients, like appetite stimulation and weight gain, or "euphoria" were unwanted effects, by some but desired, who took it to treat caxechia, or their (reactive) depression..

The evaluations of efficacy and side effects by the prescribing physician and the patient were very similar. Therefore, it is likely that both patients and physicians were equally content or disappointed with regard to medicinal effects of the *Cannabis sativa*.

As in this study the prescribing physicians were internists, oncologists, neurologists (usually from community medical centers and university hospitals), as well as family practitioners in private practice, and the specialists tended to prescribe Cannabis at the request of their patients, while the family practitioners, on their own initiative, tended to discuss the possible benefits of Cannabis with their naïve patients, before Cannabis was prescribed, it is likely that

many physicians in the Netherlands are aware of the possible benefits of Cannabis and willing to prescribe it.

Acknowledgements

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Summary

In the Netherlands, *Cannabis sativa* is prescribed by physicians from various specialties and used by more middle-aged patients of both genders, mainly for symptoms like spasticity in MS and spinal cord injury, anorexia/cachexia and fatigue in cancer and AIDS, and various other forms of (chronic) pain.

In this survey, about 2/3 of all patients were satisfied with the effects of Cannabis for their symptom relief. Cannabis was very well tolerated and the only side effect, which stands out is dry mouth, which could - in part- be contributed to the inhalation of Cannabis. Other side effects were much less frequent and well-known effects from *Cannabis sativa*.

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Table 1. Reported diagnoses, sorted by frequency

Diagnose		frequency	percentage
neurological disorders		45	38.8
musculo-skeletal / connective tissue disorders		24	20.7
malignant tumors and symptoms thereof		16	13.8
Other		31	26.7
thereof:	pain	10	8.6
	HIV	5	4.3
	Stroke	3	2.6
	diabetes mellitus	2	1.7
	Hypertension	2	1.7
	other cerebro-vascular diseases	2	1.7
	Asthma	1	0.9
	depressive episode	1	0.9
	emotional shock or distress	1	0.9
	Emphysema	1	0.9
	Glaucoma	1	0.9
	Ménière disease	1	0.9
	Sarcoidosis	1	0.9
Total		116	100.0

Figure 1. Estimated efficacy vs. Duration of Cannabis intake

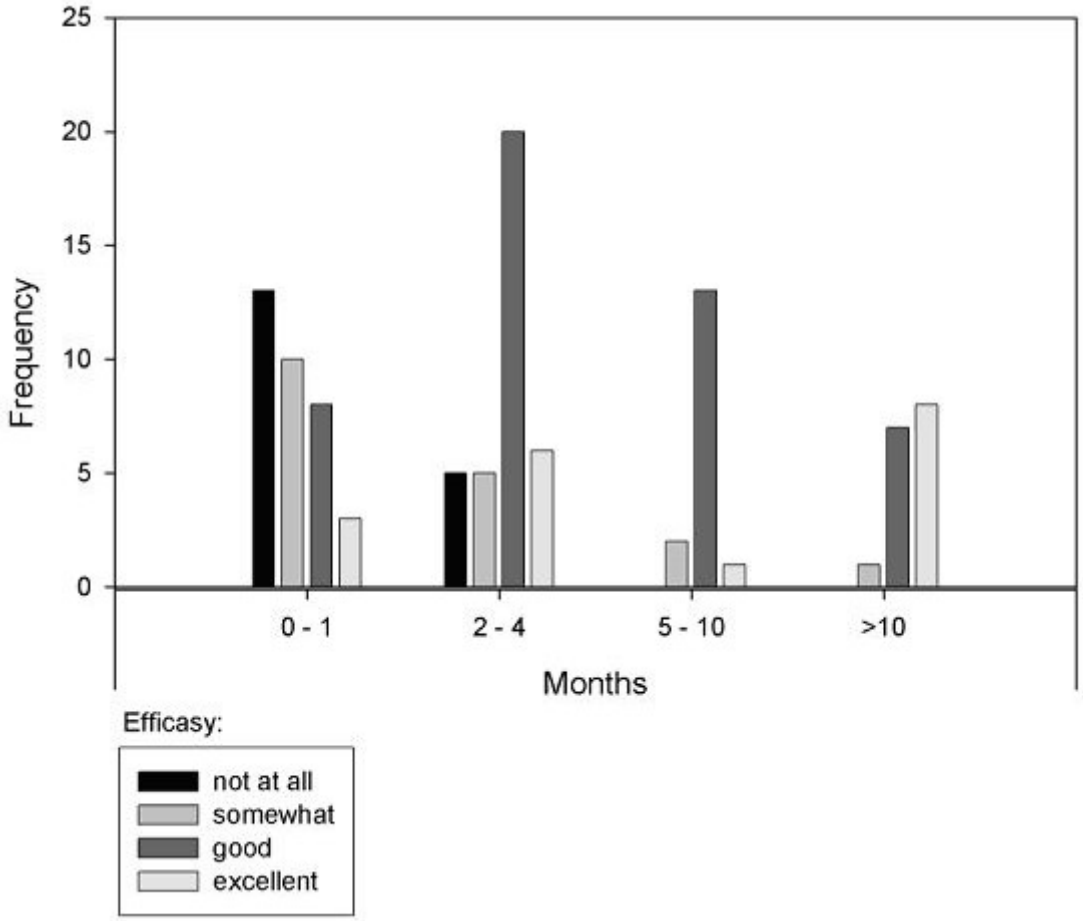

Fig. 1 shows efficacy in relation to duration of Cannabis intake. The perceived efficacy by the patient correlates positively with the duration of the intake of *Cannabis sativa* (Spearman $r=0.52$; $p<0.01$).

Figure 2. Differences in perceived efficacy between patients taking Cannabis orally and through inhalation.

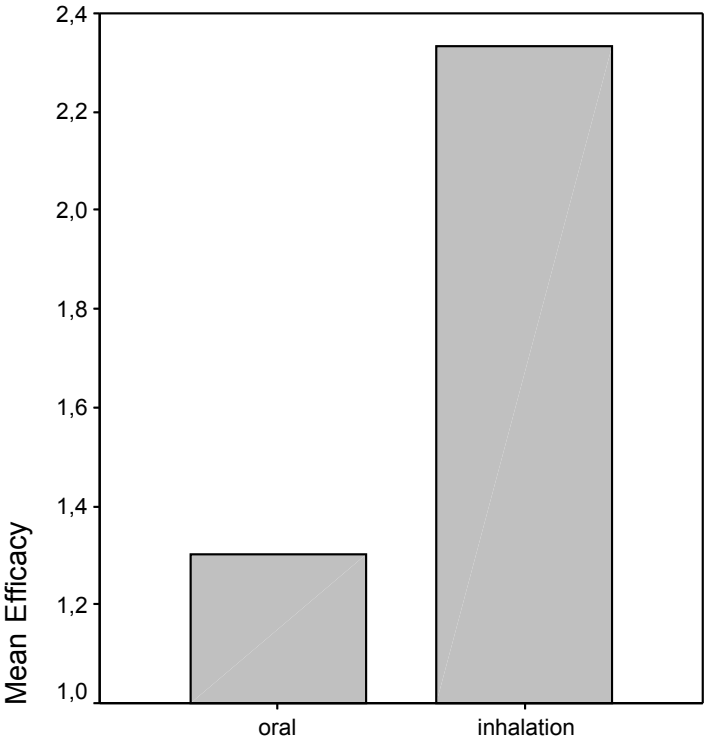

Fig. 2 Shows differences between perceived efficacy between patients taking MGC orally or through inhalation (Mann-Whitney U test $Z=4.7$; $p<0.01$).

Table 2. Correlation between estimated efficacy and duration of Cannabis intake

months	estimated efficacy								total	
	not at all		somewhat		good		excellent			
	freq	%	freq	%	Freq	%	freq	%	freq	%
0 - 1	13	38.2	10	29.4	8	23.5	3	8.8	34	33.0
2 - 4	5	13.9	5	13.9	20	55.6	6	16.7	36	35.0
5 - 10	0	0.0	2	12.5	13	81.2	1	6.2	16	15.5
>10	0	0.0	1	6.2	7	43.8	8	50.0	16	15.5
total	19 (one missing)	18.4	18	17.5	48	46.6	18	17.5	103	100.0

Table 3. Correlations between complaints (side-effects) and duration of Cannabis use

side effect	months	frequency									
		never		Occasionally		regularly		always		total	
		freq	%	freq	%	freq	%	freq	%	freq	%
Eye Irritation	0 – 1	30	90.9	2	6.1	0	0.0	1	3.0	33	32.4
	2 – 4	32	86.5	3	8.1	1	2.7	1	2.7	37	36.3
	5 – 10	14	87.5	1	6.2	1	6.2	0	0.0	16	15.7
	> 10	14	87.5	2	12.5	0	0.0	0	0.0	16	15.7
	total	90	88.2	8	7.8	2	2.0	2	2.0	102	100
Feeling High	0 – 1	19	59.4	8	25.0	3	9.4	2	6.2	32	31.1
	2 – 4	25	67.6	9	24.3	1	2.7	2	5.4	37	35.9
	5 – 10	12	70.6	5	29.4	0	0.0	0	0.0	17	16.5
	> 10	7	41.2	7	41.2	2	11.8	1	5.9	17	16.5
	total	63	61.2	29	28.2	6	5.8	5	4.8	103	100
short term memory	0 – 1	24	72.7	6	18.2	2	6.1	1	3.0	33	33.3
	2 – 4	28	77.8	8	22.2	0	0.0	0	0.0	36	36.4
	5 – 10	11	73.3	2	13.3	2	13.3	0	0.0	15	15.2
	> 10	9	60.0	5	33.3	0	0.0	1	6.7	15	15.2
	total	72	72.7	21	21.2	4	4.0	2	2.0	99	100
Sleepiness	0 – 1	13	40.6	8	25.0	9	28.1	2	6.2	32	31.7
	2 – 4	27	75.0	7	19.4	2	5.6	0	0.0	36	35.6
	5 – 10	10	58.8	7	41.2	0	0.0	0	0.0	17	16.8
	> 10	12	75.0	3	18.8	1	6.2	0	0.0	16	15.8
	total	62	61.4	25	24.8	12	11.9	2	2.0	101	100
Hunger	0 – 1	27	81.8	0	0.0	4	12.1	2	6.1	33	32.4
	2 – 4	25	67.6	5	13.5	7	18.9	0	0.0	37	36.3
	5 – 10	10	62.5	4	25.0	2	12.5	0	0.0	16	15.7
	> 10	7	43.8	5	31.2	4	25.0	0	0.0	16	15.7

	total	69	67.6	14	13.7	17	16.7	2	2.0	102	100

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side effect	months	frequency									
		never		occasionally		regularly		always		total	
		freq	%	freq	%	freq	%	freq	%	freq	%
loss of concen-tration	0 – 1	20	58.8	7	20.6	7	20.6	0	0.0	34	33.0
	2 – 4	28	75.7	7	18.9	2	5.4	0	0.0	37	35.9
	5 – 10	12	75.0	3	18.8	1	6.2	0	0.0	16	15.5
	> 10	12	75.0	2	12.5	1	6.2	1	6.2	16	15.5
	total	72	69.9	19	18.4	11	10.7	1	1.0	103	100
a-motivation	0 – 1	23	69.7	5	15.2	5	15.2	0	0.0	33	32.4
	2 – 4	33	89.2	3	8.1	1	2.7	0	0.0	37	36.3
	5 – 10	16	94.1	1	5.9	0	0.0	0	0.0	17	16.7
	> 10	10	66.7	5	33.3	0	0.0	0	0.0	15	14.7
	total	82	80.4	14	13.7	6	5.9	0	0.0	102	100
anxiety	0 – 1	29	85.3	4	11.8	0	0.0	1	2.9	34	32.7
	2 – 4	30	81.1	6	16.2	0	0.0	1	2.7	37	35.6
	5 – 10	16	94.1	1	5.9	0	0.0	0	0.0	17	16.3
	> 10	14	87.5	1	6.2	1	6.2	0	0.0	16	15.4
	total	89	85.6	12	11.5	1	1.0	2	1.9	104	100
euphoria	0 – 1	27	79.4	1	2.9	5	14.7	1	2.9	34	32.4
	2 – 4	31	83.8	2	5.4	3	8.1	1	2.7	37	35.2
	5 – 10	10	58.8	5	29.4	2	11.8	0	0.0	17	16.2
	> 10	11	64.7	4	23.5	2	11.8	0	0.0	17	16.2
	total	79	75.2	12	11.4	12	11.4	2	1.9	105	100
depression	0 – 1	25	80.6	5	16.1	1	3.2	0	0.0	31	31.3
	2 – 4	35	94.6	1	2.7	1	2.7	0	0.0	37	37.4
	5 – 10	10	62.5	3	18.8	3	18.8	0	0.0	16	16.2
	> 10	11	73.3	4	26.7	0	0.0	0	0.0	15	15.2
	total	81	81.8	13	13.1	5	5.0	0	0.0	99	100

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side effect	months	frequency									
		never		occasionally		regularly		always		total	
		freq	%	freq	%	freq	%	freq	%	freq	%
dry mouth	0 – 1	17	50.0	8	23.5	6	17.6	3	8.8	34	33.3
	2 – 4	14	37.8	11	29.7	9	24.3	3	8.1	37	36.3
	5 – 10	7	46.7	7	46.7	1	6.7	0	0.0	15	14.7
	> 10	3	18.8	7	43.8	5	31.2	1	6.2	16	15.7
	total	41	40.2	33	32.4	21	20.6	7	6.9	102	100
difficulties in coordination	0 – 1	25	73.5	6	17.6	3	8.8	0	0.0	34	34.0
	2 – 4	29	78.4	6	16.2	0	0.0	2	5.4	37	37.0
	5 – 10	9	69.2	3	23.1	0	0.0	1	7.7	13	13.0
	> 10	11	68.8	3	18.8	2	12.5	0	0.0	16	16.0
	total	74	74.0	18	18.0	5	5.0	3	3.0	100	100