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The savings potential of implant accupuncture according to Werth for the treatment of Parkinson's disease – a retrospective pilot study

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Conceptual fomulation and objective:

Can a reduction in direct medical costs incurred for Parkinson's disease patients be attained by means of permanent accupuncture implants according to Werth, without aggrevation of the pathology? In order to investigate this question, a retrospective enquiry of data was conducted in Germany in 2006. An analysis of the data should provide information about the evidence of this issue.

Method:

The completed case report forms (CRFs) (n=210) were evaluated. These CRFs were completed by patients who already underwent the treatment (n=134), as well as patients not yet treated (n=76) with permanent accupuncture implants. The following data was documented in the CRFs: Intensity of Parkinson's pathology (modified UPDRS according to Werth), age, gender, duration of the disease, and daily dose of drugs administered for the treatment of Parkinson's disease. Besides the comparison of parameter averages, a covariance analysis (ANCOVA) is also conducted.

Results:

The direct daily therapy costs for drugs were less for the treated group (therapy group) than the untreated (control group). The unadjusted averages were € 4.04 (±3.70) and € 6.03 (±6.41) respectively, resulting in a significant difference of € 1.99 (p=0.005). The patients in the therapy group were on average 69.67 (±7.59) years of age, weighed 74.09 kg (±16.77), have been suffering from Parkinson's disease for 79.09 months (±58.92), and have been under drug therapy for 72.1 months (±61.46). In comparison, the patients in the control group were on average 69.82 (±7.62) years of age, weighed 73.63 kg (±10.85), have been suffering from Parkinson's disease for 65.24 months (±50.96), and have been under drug therapy for 60.84 months (±49.71).

After adjustment by means of the ANCOVA method with the covariants age, gender, weight, duration of the disease, duration of antiparkinson drug therapy, as well as the score of the modified UPDRS-scores, the average difference in daily therapeutic costs amounted to € 1.85 (p=0.009) in favour of the therapy group. In addition, the therapy group, on average, also experienced less hyperkinesia, muscle rigidity, rigour, tremor, and were in a better state of mind than the patients in the control group.

The result from this statistical evaluation indicated that the implant acupuncture according to Werth for the treatment of Parkinson's disease, has a savings potential in the direct drug costs. It is hereby recommendable to conduct prospective, controlled, clinical trials to prove the superiority of implant acupuncture with regard to the effect on neurogenesis and neuroplasticity over a drug only therapy.

Table of contest

1 Introduction 4
1.1 Hypothesis of the pilot study 7
2 Method 8
2.1 Patients 8
2.2 Study design 9
2.3 Evaluation of the effect 9
2.4 Documentation of drug therapy costs 11
2.5 Data analysis 12
3 Results 14
3.1 Patient characteristics 14
3.2 Variance analysis 15
4 Limitations 18
5 Conclusion and recommendation 19
Summary of variables 21
References 22

1 Introduction

Typical for the Parkinson syndrom is the degeneration and resulting loss of pigmented dopamine-secreting (dopaminergic) cells, secreted by the same cells, in the pars compacta region of the substantia nigra. The neurotransmitter dopamine is a messenger and mainly responsible for movement regulation.[1]

The causes of Parkinson's disease as well as the basic molecular mechanism by which cells are lost have not been fully elucidated up to now. Usually the symptoms occur between the ages of 40 and 70 years. The average age at which symptoms begin is 55 years. Parkinson's disease is a degenerative disorder of the central nervous system and progresses with time. It is characterised by typical symptoms such as loss of physical movement (akinesia), muscle rigidity (rigour), and tremor. Apart from these, the patients often suffer from psychological disorders and cognitive disfunction.

Parkinson's disease is one of the most common neruological diseases. The prevalence in Germany regarding the total population is estimated at 0.1-0.2%, regarding the population aged over 65 years at 1.8%, and at 3% for the population aged over 80 years.[2,1]

Men are affected almost twice as often as women. Dorsey et al. (2007) conducted a prevalence study in 2005 and came to the conclusion that the number of Parkinson's disease patients will double until the year 2030.[3]

Up to date drug therapies focus on enhanced dopamine action. However, these therapies only provide intermediate relief of symptoms without preventing the progression of the disease. Presently the research concentrates on dopamine substitutes or substances that artificially increase the efficiency of dopaminergic synapses. The most widely used form of treatment is L-dopa. The treatment should be extended as long as possible to avoid long-term complications. The probability of incidence of these complications correlate with duration and dosage of L-dopa therapy. One of the hypothesis for these complications is the accelerated destruction of dopaminergic cells by L-dopa.[1]

A further problem with this therapy is the increasing fluctuation in action over a specific time period, which implies that within the daily routine fluctuations in

mobility and additional occurrence of dyskinesia arises. In accordance with the pathophysiological hypothesis, the physiologically more stable striatal dopamine level starts to fluctuate with the L-dopa plasma level.

Parkinson's disease results in a progressive increase in the pathology and a lifelong depency on drug therapies.

The "Deutsche Gesellschaft für Neurologie" („German Association of Neurology") defined the therapeutic goals of the treatment of Parkinson's disease in their treatment guidelines:[2]

1. Sustainment of independent conduct of everyday activities
2. Prevention/reduction in the necessity of high-maintenance care
3. Sustainment of independency within the family and society (social competence)
4. Sustainment of a professional life/occupation
5. Sustainment/regain of the health-related quality-of-life
6. Avoidance of secondary orthopaedic and internistic concomitant diseases
7. Prevention of motor and non-motor complications
8. Prevention of dopaminergic side effects

Apart from the suffering experienced by the patients and their relatives, they also incur medical costs. The direct costs, implying the costs of the drug therapy that are directly attributable to the cost of illness, consist of the cost for the medical treatment, in-patient and out-patient medical services, and remedies and aids.

In the retrospective study conducted by Dodel et al. (1997), data on costs for 40 Parkinson's patients were documented. The results indicate that the yearly direct drug therapy costs contribute about 44%, in-patient medical services 38%, aids 7.5%, and out-patient and remedies each 4% of the medical costs.[4]

From a health-economical point of view it is necessary to portray a therapy's quality and cost-effectiveness. Therefore, any therapeutic approach that delivers at least the same relevant effects in patients (effectiveness)[5] as the prevail-

ing therapeutic options, as well as a savings potential, for instance by reducing treatment costs or by substituting a cost intensive component with a less cost intensive component, should be regarded as an innovation.

A starting-point to reduce treatment costs of Parkinson's disease is provided by the costs of drugs. To put it in perspective, it should be added that drug therapies are in general favourable, because they oblitirate surgery and, with decreasing average costs, possess considerable rationalisation potential.[6]

Furthermore, it should be acknowledged that the drug therapy, especially with regard to the pathology, has been of great assistance to Parkinson's disease patients during the past years and will remain so in the future. However, from newly gained knowledge from neurobiology, a therapy consisting *mainly or solely* of drugs does not suffice. The aspect of plasticity of the nervous system should be emphasized more when regarding variances in the disease and therapeutic options. Considering the nervous system as a whole – with numerous colaborating neuron systems – the possibility exsists that dopaminergic neurons are not lost due to primary degeneration, but rather by means of secondary degeneration due to extreme conditions of the whole system, especially stress situations caused by shortage of impulses.[7]

On the other hand, the reason for the collapse of the plasticity of the nervous system at the onset of the disease, has not been elucidated. Also, therapeutic options that could enhance the plasticity of the nervous system and hence deliver longterm positive results, should be investigated. New therapies that will improve the quality-of-life of the patient over a long period and simultaneously contribute to the facilitation of drug therapy costs for the German health sector are required.

The implant acupuncture according to Ulrich Werth MD fulfils the requirements of such an innovative therapeutic option. This method was developed from implant-ear-acupuncture. Ear acupuncture entails a few externally placed acupuncture needles over a ***short time*** period and often requires regular treatments. This method is not applicable for diseases such as Parkinson's disease. The method developed by Dr. Werth entails the **implantation** of titanium

pins, which reduces the risk for infections and assures a more intensive effect. The improvement of the therapy group was also confirmed in a study conducted by Teschmar (2003).[8] The implant acupuncture developed by Dr. Werth differs in so far that considerably more titanium implants are used, which seems to avoid habituation of the stimulus. The mode of action of implant action is to trigger neurohumoral factors of the subcutaneous receptors of the outer ear. Certain regions in the brain are hereby stimulated, which redresses the balance. Hereby unstable regulatory systems, especially in the extrapyramidal system, are stabilised and the drug dosage can be reduced over a period of a few months.

1.1 Hypothesis of the pilot study

Fluctuation in Parkinson's disease drug therapy's effect, which increases with time, as well as other complications / side effects, such as pharmacogenic psychosis, sleeping disorder, and depression, results in the prescription and administration of more drug therapies, which progressively leads to higher drug therapy costs.

Therefore the hypothesis of this pilot study states the following:

If the implant acupuncture according to Werth has a positive effect on the pathology and quality-of-life of the Parkinson's disease patient, the drug therapy costs (antiparkinsonika) of the group treated with this method should be less than the drug therapy costs incurred for the untreated group (same duration of the disease). The drug therapy cost amount is considered as the proxyvariable of the drug intake, contrary to the DDD (defined daily doses) usually applied.

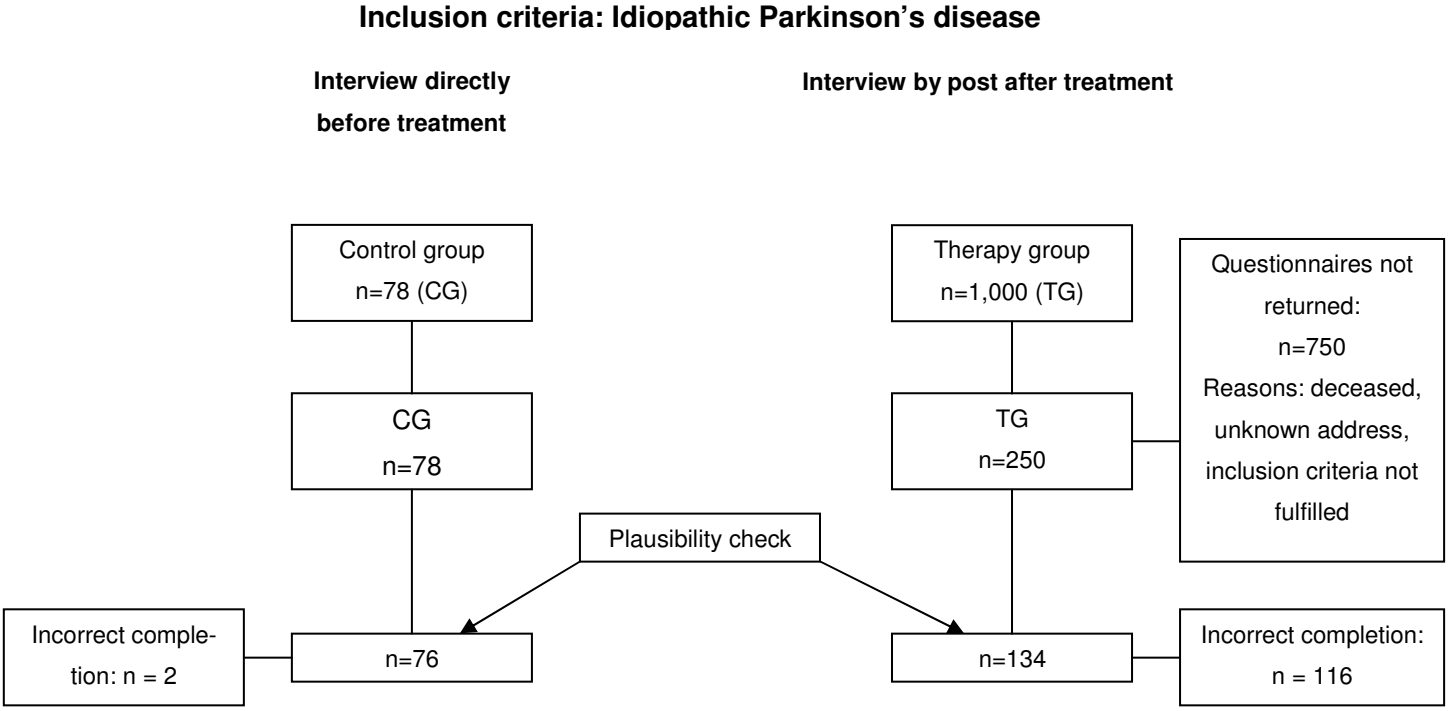
The implant acupuncture according to Werth offers a savings potential of direct drug therapy costs.

2 Method

2.1 Patients

In June 2006, 1,000 patients who have been treated with the implant acupuncture (therapy group) at the "Institut für Akupunktur und gesunde Medizin" and 78 patients who still had to undergo the treatment (control group), were interviewed by means of a questionnaire by post (therapy group) or directly on site (control group). The following information was recorded: pathology, age, gender, daily drug dosages, duration of the disease, and the duration of drug therapy for Parkinson's disease. Inclusion criteria was a diagnosed, primary Parkinson's disease (ICD10-code G20), especially idiopathic parkinsonism. 25% of the patients in the therapy groups returned the questionnaires. Every patient was included as long as the implant acupuncture treatment took place within 3.5 years from June 2006. Reasons for not returning the questionnaire were for instance that the patient has passed away, a change of address, or the diagnosis was essential parkinsonism, eg. an essential tremor, instead of idiopathic parkinsonism. The reason for incorrect completion of the questionnaire can be attributed to misinterpretation. The patients in the control group completed their questionnaires on site and could hence clarify uncertainties directly with the medical staff (see Figure 1).

Figure 1: Study population



2.2 Study design

The patients were requested to complete the questionnairs with regard to the pathology and daily drug therapy dosage of the four weeks preceeding the receipt of the questionnaire. Hereby possible fluctuations by "on" and "off" phases should be eliminated. The analysis is retrospective and based on a specific point in time, because the patient can only fill in one value for the respective period in the past. This also aplies to the variables such as duration of the disease or drug intake.

2.3 Evaluation of the effect

As a rule the stage and severity of the Parkinson's disease are assessed by means of 42 questions in the comprehensive UPDRS-scale.[1] However, the assessment and allocation of points are performed by trained medical staff within an examination, by relatives, and by the patients. The UPDRS-scale is the assessment scale applied most frequently for Parkinson's disease.[9]

An analysis of 20 Parkinson's disease patients, conducted in 2002, verified the UPDRS-values taken every 14 days over a 3 month period after the treatment

with implant acupuncture. The average total scores of the UPDRS-scale were 44.35 points at the start and 34.35 points after 3 months. The results of the analysis, conducted in the Parkinson-Clinic in Bad Nauheim under the supervision of Prof. Henneberg, are portrayed in Table 1.[10]

Table 1: UPDRS-scores of the first Parkinson's disease study after implant acupuncture according to Werth

Patient	V	N	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
1	20	15	15	16,5	13	11,5	7,5	7,5
2	52	40	38	37.5	18	25	17.5	19
3	40	33	42	42	42	39	35	28
4	27.5	19	20	17.5	12	8	12.5	20
5	50	35	42	42	k.A.	k.A.	k.A.	k.A.
6	88	61	78	86	72	-	82	56
7	58	56.5	46	50	49.5	49.5	51	51
8	60	57.5	52	52.5	52	53	53.5	53.5
9	76	68.5	-	68	69	61.5	58	59
10	42.5	42.5	36	36	30	32	23	32.5
11	36.5	35	15	30	25	15	6	5
12	36.5	32	27	18	7.5	11,5	k.A.	11.5
13	68	58	25	32	29	27,5	k.A.	k.A.
14	72	72	53	41	51.5	43	k.A.	k.A.
15	74	74	55	51	52	45	k.A.	k.A.
16	46	42.5	25	5	6	10	k.A.	k.A.
17	49	35	27	39	32	25	k.A.	25
18	14	12	7.5	11	7	6	k.A.	6
19	32	28	20	19	20	22	41	49
20	75	68	67	67.5	67	67	71	78
Average*	**44.35**	**39.45**	**35.1**	**36.85**	**32.85**	**32.2**	**31.8**	**34.35**

- Average of the patients who completed all data records at all the observational points in time
- k.A. no entry
- V = directly before the treatment
- N = directly after the treatment

In this pilot study the questions regarding pathology were phrased in such a way that the patient or relative who received the questionnaire by post could answer them. The time dependant intensity of the symptoms, regarding involuntary movements, muscles rigidity (rigour), gait, tremor, and mood disturbances, were recorded. This modified version is a simplification of the original UPDRS, but also with an ordinal scale. The following combinations were made for the analysis:

- Questions 1-3 modified to UPDRS1, with the focus on hyperkinesia
- Questions 4-10 modified to UPDRS2, with the focus on rigour, tremor and gait

- Questions 11-13 modified to UPDRS3, with the focus on mood

With an increase in the intensity of the symptoms, the score for the modified UPDRS1 becomes lower and for the modified UPDRS2 higher. A low score for the modified APDRS§ indicates better moods and more social contact. Table 2 depicts the scores for the respective questions.

Table 2: Part of the questionnaire regarding Parkinson's pathology

Symptom/intensity	incessantly	often - daily	sometimes	seldom - monthly	never	
Involuntary movement of eg. an arm or leg	0	1	2	3	4	Mod. UPDRS1
Involuntary twisting in my movement	0	1	2	3	4	
Fidgetiness, eg. inability to sit still	0	1	2	3	4	
Rigidity of the body and limbs	4	3	2	1	0	Mod. UPDRS2
Feeling of inability to move	4	3	2	1	0	
Short steps / shuffling while walking	4	3	2	1	0	
Tremor in the arms or legs	4	3	2	1	0	
Problems with the digestive system	4	3	2	1	0	
Stooped, forward-flexed posture when walking	4	3	2	1	0	
Feeling of uneasiness	4	3	2	1	0	
Good mood	0	1	2	3	4	Mod. UPDRS3
Feeling of loneliness / exclusion	4	3	2	1	0	
Social contact with friends and acqaintences	0	1	2	3	4	

2.4 Documentation of drug therapy costs

All the drugs were considered that were administered in the treatment of the pathology of Parkinson's disease (mono- or combination therapies), as well as against end-of-dose fluctuation. The patient had to fill in the trade name, form of application, amount of active pharmaceutical ingredient in the application form, and the daily intake. The daily intake amounts of the altogether 16 active agents are assessed together with the price per mg of the respective agent. It is hereby avoided that variances in the manufacturers' prices have an influence on the total drug therapy costs. The drug costs documented in this way exclusively concern direct costs contributable to the drug therapy.[11] In Table 3 the active agents, price per mg, and the indication are listed.

Table 3: Active pharmaceutical agents and price per mg

Active agent	Price/mg	Indication
α-Dihydroergocryptine	0,1009 €	Idiopathic Parkinson's disease
Amantadine	0,0014 €	Rigour, tremor

Biperidene	0,0844 €	Rigour, tremor
Bromocriptine	0,1726 €	Idiopathic Parkinson's disease
Budipine	0,0671 €	Comb. with end-of-dose-fluctuation
Cabergoline	2,0400 €	Idiopathic Parkinson's disease
Entacapone	0,0076 €	Comb. with end-of-dose-fluctuation
Levodopa/Carbidopa	0,0016 €	Idiopathic Parkinson's disease
Lisuride	3,3620 €	Comb. with end-of-dose-fluctuation
Metixene	0,0292 €	Rigour, tremor
Pergolide	2,4514 €	Idiopathic Parkinson's disease
Pramipexole	5,5890 €	Idiopathic Parkinson's disease
Rasagiline	4,2540 €	Idiopathic Parkinson's disease
Ropinirole	0,9157 €	Idiopathic Parkinson's disease
Selegeline	0,0840 €	Idiopathic Parkinson's disease
Tolcapone	0,0194 €	Comb. with end-of-dose-fluctuation

* Prices from the Roten-Liste www.rote-liste.de for N3-Package

2.5 Data analysis

The arithmetical group averages and standard deviations of various parameters were calculated and compared with descriptibe statistics and by utilising MS Excel. The focus of this observational study was on the average costs of drug therapy comparison between the two groups. Subsequent to the descriptive statistics, a variance analysis (ANOVA) for adjusting the differences in average drug therapy costs was conducted.

The variance analysis is often used to verify whether the differences between arithmetical averages from various populations are significantly different from zero. The refute / nullification of this study's hypothesis (null hypothesis) states that the various patients from the control and therapy groups originate from the same population with regards to daily drug therapy costs. Therefore it is irrelevant in which group the patient was, the drug therapy costs remain the same. With this formulation the risk of an unjustified nullification of the null hypothesis (type-1 risk of error) is minimised with an additional selection of a lower significance niveau. The variable "group membership" is the nominal scale factor whithin the scope of the variance analysis. To ascertain the effects of the cause variable, the summations of the squares of the deviations from the averages over both groups as a rest variation (total variation in daily drug therapy costs) are seperated from the summmation of the square of the observed effects of the factor "group". The test statistic to be tested is determined from this

seperation. It comprises the quotients from the average square sum of the factor "group" (sum of the squared observed effect of the factor group divided by the number of degrees of freedom) and the average square sum of the rest (rest variation divided by the number of degrees of freedom). This quotient follows a F-distribution and is compared with a critical F-value (corresponding to a fixed significance niveau traditionally 10%, 5% or 1%). If the quotient should be higher than the critical F-value, it indicates a corresponding probability of less than 5% on the right hand side of the distribution and the null hypothesis can hence be refuted.[12]

It can however be assumed that the amount of the drug therapy costs also depends on the age, gender, weight, duration of the disease, and duration of drug intake, and not solely on the "group membership". The method of variance analysis described above has to be extended by incorporating the covariants. In this case the special type of variance analysis, namely covariance analysis (ANCOVA), can be applied. The total procedure is connected to a regression analysis with this incorporation of covariants. In this case the daily drug therapy costs of each patient are corrected by considering the influence of these variables.[13]

3 Results

3.1 Patient characteristics

As mentioned before, the therapy group consists of patients who have undertaken the implant acupuncture treatment according to Werth and the control group consists of patients who have not undertaken this treatment.

From Table 3 it can be derived that the patient populations from both groups do not differ considerably with regard to age, gender, and weight. On the contrary, the patients from the therapy group have been suffering from Parkinson's disease for 79.9 months, and on average 14.66 months longer, than the patients from the control group. The duration of the disease is associated with the duration of drug intake. It follows that the patients from the therapy group have been taking drugs against Parkinson's disease for 72.1 months on average versus only 60.84 months in the control group. 56% and 59% of the patients in the therapy group and control group respectively, received a combination therapy. Despite the longer average duration of the disease and drug intake, merely 11% of the therapy group had to take drugs for end-of-dose fluctuation. In reference to the Parkinson's pathology (see Table 2), the therapy group suffered less from involuntary movements (higher score for mod. UPDRS1), experienced less rigidity (lower score for mod. UPDRS2), and were in a better state of mind / mood (lower score for mod. UPDRS3).

Table 4: Patient characteristics

		Control gr. (n=76)		Therapy gr. (n=134)	
		Average		Average	
Variable	Description		SD		SD
GESCHL	Gender 0=Male,1=Female	0,30	(0,46)	0,36	(0,48)
Alter	Age in years	69,82	(7,62)	69,67	(7,59)
kg	Weight in kg	73,63	(10,85)	74,09	(16,77)
erkr_dau	Duration of the disease in months	65,24	(50,96)	79,90	(58,92)
med_dau	Months since first intake of medication for Parkinson's	60,84	(49,71)	72,10	(61,46)
HERZIN	Cardiac insufficiency 0=no,1=yes	0,12	(0,33)	0,20	(0,40)
UPDRS1	UPDRS modified according to Werth 2006 (Hyperkinesia)	7,22	(3,32)	8,69**	(2,89)
UPDRS2	UPDRS modified according to Werth 2006 (RIgour)	16,34	(6,06)	14,17**	(5,99)
UPDRS3	UPDRS modified according to Werth 2006 (Mood)	4,20	(2,91)	3,83	(2,42)
AKU_DAUER	Months since implantation	0,00	(0,00)	8,28	(8,69)
Kombi	Proportion of patients receiving combination therapy	0,59	(0,49)	0,56	(0,50)
FLUK	End of Dose-Fluctuation	0,16	(0,37)	0,11	(0,32)
L-DOPA	Proportion of patients receiving L-Dopa therapy	0,76	(0,43)	0,74	(0,44)
med_kost	Daily drug therapy costs for (€/day) antiparkinsonika	6,03	(6,41)	4,04*	(3,70)

* on a level of less than 0.05 significant difference from null (T-test for independent samples)

and on a level of less than 0,1 significant difference from null in accordance with Kolmogorov-Smirnoff-Test (non parametric)

** on a level of less than 0,05 significant difference from null Mann-Whitney-Wilcoxon-Test (non parametric)

SD=Standard Deviation

*** average of the dichotomous variables (0/1-specificity) as the percentual proportion

3.2 Variance analysis

In accordance with paragraph 2.5 the influence of all the variables in Table 3 should be compared with regards to the averages. The difference in daily drug therapy cost of €1.99 under "group membership" is also confirmed with genden, age, weight, duration of the disease, duration of drug intake, the modified UPDRS-score, and whether a patient received a combination therapy for end-of-dose-fluctuation or a L-Dopa therapy. Table 4 depicts the parameters of the model and their variations in daily drug therapy costs accounted for by the extent of influence. The significance of the variation of the parameter is given with the responding Power.

It is noticeable that the variation in daily drug therapy costs is substantially accounted for when a patient received combination therapy or end-of-dose therapy.

In the following table, the averages adjusted with the extent of influence, are compared with drug therapy costs:

Table 5: Results of the covariance analysis (ANCOVA)

	Tests on intermediate subject effects				
Source	**Square summation Typ III**	**Square average**	**F**	**Significance**	**Power(a)**
Korrigiertes Modell	1,930.902	137.922	8.514	0.000	1.000
Konstanter Term	24.451	24.451	1.509	0.221	0.231
L_DOPA	66.769	66.769	4.122	0.044	0.524
KOMBI	612.485	612.485	37.808	0.000	1.000
FLUK	349.174	349.174	21.554	0.000	0.996
GESCHL	1.619	1.619	0.100	0.752	0.061
ALTER	26.088	26.088	1.610	0.206	0.243
HERZIN	1.746	1.746	0.108	0.743	0.062
UPDRS1	0.104	0.104	0.006	0.936	0.051
UPDRS2	5.956	5.956	0.368	0.545	0.093
UPDRS3	1.131	1.131	0.070	0.792	0.058
AKU_DAU	2.138	2.138	0.132	0.717	0.065
KG	51.677	51.677	3.190	0.076	0.428
MED_DAU	8.534	8.534	0.527	0.469	0.112
ERKR_DAU	9.983	9.983	0.616	0.433	0.122
GRUPPE	111.523	111.523	6.884	0.009	0.742
Error	3,142.796	16.200			
Total	9,861.175				
Corrected total variation	5,073.698				
a	Calculated with Alpha = 0.05				
b	R-square = 0.381 (corrected R-square = 0.336)				

The adjusted averages of daily drug therapy costs are depicted in Table 6 based on stated standardised values of the covariates. The adjusted difference in daily drug therapy costs amounted to €1.85 in favour of the therapy group. This difference is significant on an α-level of ≤ 0.05 (p=0.009).

Table 2: Adjusted group averages of the drug therapy costs

Variable	standardisierter Wert
L-DOPA	0.75
KOMBI	0.57
FLUK	0.13
GESCHL	0.33
ALTER	69.73
HERZIN	0.17
UPDRS1	8.2
UPDRS2	15.03
UPDRS3	3.98
AKU_DAU	5.29
KG	73.92
MED_DAU	68.34
ERKR_DAU	74.43
mittlere tägliche Arzneimittelkosten KG	**5.96 €**
mittlere tägliche Arzneimittelkosten TG	**4.11 €**
Mittelwertdifferenz	**1.85***

* on a level of 0.05 a significant difference from null

4 Limitations

The limitiations associated with this study and the study design have to be mentioned.

As seen from 2.1, the questionnaires were completed by the patients or the caring relatives. This holds the risk that the patient could misinterpret the questions. On the other hand, especially with respect to the patient's own perceiving of the pathology, it is advantageous and the personal quality-of-life as perceived by the patients / relatives is represented strongly. The study design depicts that the health status can only be assessed by the patient / relative.[6]

Another disadvantage of the study design is the retrospective and time bound method of documentation. In order to attain a higher evidence level, a prospective study over a period of at least one year should be conducted.[14]

With respect to the variance analysis, this method strictly speaking requires a normal distribution of the dependant variables to ensure the validity of the hypothesis. However, this is a restrictive limitation, because only F-test were conducted within the scope of the variance analysis. These F-tests are considered robust towards the non-fulfillment of normal distribution, but still deliver interpretible results and evidence.[12] To support this evidence, non-parametric tests, with no prerequisite for normal distribution (see 3.1 and Table 4), are applied. These tests also reveal the significance of the differences between averages.

The method of standardising the amount of active over the price of the drug is not unproblematic, but preferential to the DDD method. The DDD method, at the most, accounts for comparisons between large amounts of active agents, but does not reflect the dosage of comparable drugs with which the same treatment results are reached. [15]

5 Conclusion and recommendation

This pilot study proved that differences in daily drug therapy costs can incur for patients treated with implant acupuncture according to Werth versus not treated patients. The deviations in the unadjusted and adjusted averages of daily drug therapy costs were calculated at €1.99 and €1.85 respectively, both times in favour of the therapy group.

Statistical evidence of the savings potential in direct drug therapy costs with implant accupuncture according to Werth is hereby provided. Therefore, the hypothesis that patients treated with implant accupuncture according to Werth incur less drug therapy costs is confirmed by this study.

In accordance with this evidence, it is recommendable to conduct a follow-up randomised, controlled, multicentre, prospective study to analyse the efficacy of implant acupuncture according to Werth for the treatment of Parkinson's disease. The pathology and progression of the disease should be assessed over a period of at least one year on preliminary established fixed dates. These dates should be fixed with consideration of the generally used scales such as the UPDRS, Hoehn and Yahr, Northwestern University Disability Scale (NUDS) or the Webster Scale. The following intrinsic problems occur with this treatment method, namely incorporation of a placebo group, observation of the relevant area of the brain by means of brain imaging techniques in a prospective study, and to include patients with similar characteristics who are distinguished solely by being treated or not treated.

If the evidence provided in this pilot study should be confirmed by other studies, the implant acupuncture treatment according to Werth may be regarded as a process innovation.[6]

For the follow-up health-economic evaluation, modelling, by means of a cost-efficiency-analysis or cost-utility-analysis, is recommended within the scope of stochastic models of the disease's progression. This is beneficial insofar that the results from previously conducted clinical trials can be applied to analyse various scenarios and to deliver information on economical benefits of specific

treatments, which would otherwise have taken a lot of time and effort to acquire.

Summary of variables

Variable	Description
med_kost	Daily drug therapy costs for Parkinsons's disease
gruppe	Group (0=control,1=therapy)
kombi	Combination drug therapy (0=no;1=yes)
fluk	End-of-Dose Fluctuation
geschl	Gender (0=Male;1=Female)
alter	Age in years
herzin	Cardiac insufficiency (0=no;1=yes)
updrs1	UPDRS1 modified according to Werth 2006 (Tremor)
updrs2	UPDRS2 modified according to 2006 (Rigor)
updrs3	UPDRS3 modified according to 2006 (Mood / state of mind)
aku_dua	Months since implantation
kg	Body weight in kg
med_dau	Months since the first intake of drugs for Parkinson's disease
erkr_dau	Months since the first diagnosis of Parkinson's disease

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