Chulalongkorn Medical Journal

Volume 35
Issue 3 *March 1991*

Article 6

3-1-1991

Treatment of diabetic distal symmetrical small-fiberpolyneuropathy with gangliosides.(part III : prognostic factors)

Sompongse Suwanwalaikom

Kammant Phanthumchinda

Sek Arksaranugraha

Srichitra C. Bunnag

Montchai Chalaprawat

นิพนธ์ต้นฉบับ

Treatment of diabetic distal symmetrical small-fiber polyneuropathy with gangliosides. (part III : prognostic factors)

Sompongse Suwanwalaikorn*
Kammant Phanthumchinda* Sek Arksaranugraha**
Srichitra C Bunnag* Montchai Chalaprawat*

Suwanwalaikorn S, Phanthumchinda K, Arksaranugraha S, Bunnag SC, Chalaprawat M. Treatment of diabetic distal symmetrical small-fiber polyneuropathy with gangliosides. (part III : prognostic factors) Chula Med J 1990 Mar; 35(3) : 157-161

Gangliosides have been used for the treatment of various forms of peripheral neuropathies. Recent studies of gangliosides in the treatment of diabetic neuropathies showed variable outcomes. An open self-controlled study designed to evaluate the therapeutic effects of gangliosides in non-insulin dependent diabetes mellitus with distal symmetrical small-fiber polyneuropathy was performed by using gangliosides 40 mg/day for 8 weeks period. The response rate demonstrated by nerve conduction study was 60% (18/30). The electrophysiological outcome was concordant with the clinical outcomes. There was no significant difference among the responders and non-responders regarding to the sex, body mass index, duration of diabetes and associated late diabetic complications. The significant factors which may influence the outcomes of therapy were age, duration of neuropathy and hyperesthesia.

Reprint request : Suwanwalaikorn S, Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
Received for publication. February 12, 1990.

* Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University.
** Department of Orthopedic and Rehabilitation Medicine, Faculty of Medicine Chulalongkorn University.

สมพงษ์ สุวรรณวลัยกร, กัมมันต์ พันธุมจินดา, เสก อักษรานุเคราะห์, ศรีจิตรา บุนนาค, มนต์ชัย ชาลาประวรรตน์. การรักษาโรคประสาทส่วนปลายชนิด ดิสตัล ซิมเมตติคอล สมอล ไฟเบอร์ โพลีนิวโรพาทรี ในผู้ป่วยเบาหวานด้วยแกงกลีโอไซด์. (ตอนที่ 3 : ปัจจัยการทำนายผลการรักษา) จุฬาลงกรณ์เวชสาร 2534 มีนาคม ; 35 (3) : 157-161

แกงกลีโอไซด์ได้ถูกนำมาใช้ในการรักษาโรคของระบบประสาทส่วนปลายหลายชนิดด้วยกัน ในเรื่องของเส้นประสาทพิการจากเบาหวานนั้น ผลของแกงกลีโอไซด์จากการวิจัยในที่ต่าง ๆ จะแตกต่างกันออกไป กลุ่มผู้วิจัยได้ทำการศึกษาแบบ open-self controlled เพื่อประเมินประสิทธิภาพของแกงกลีโอไซด์ ในการรักษา distal symmetrical small-fiber polyneuropathy ในผู้ป่วยเบาหวานที่ไม่พึ่งอินซูลิน โดยการใช้แกงกลีโอไซด์ 40 มิลลิกรัมต่อวัน เป็นเวลา 8 สัปดาห์ ผลการตอบสนองจากการมีการนำกระแสประสาทและอาการทางคลินิกดีขึ้น 60% (18/30) เมื่อได้ทำการวิเคราะห์ปัจจัยที่จะช่วยทำนายผลการรักษาพบว่า เพศ ครรชนีย์น้ำหนักตัว ระยะเวลาที่เป็นเบาหวาน และการมีภาวะแทรกซ้อนนอกระบบประสาทส่วนปลาย ไม่เป็นปัจจัยที่จะบ่งถึงการตอบสนอง ส่วนอายุ ระยะที่เริ่มมีอาการทางระบบประสาทส่วนปลาย และอาการปวดเสียวจะเป็นตัวบ่งถึงการตอบสนองต่อการรักษาในผู้ป่วยกลุ่มนี้

The therapeutic effect of gangliosides treatment in diabetic neuropathy has been evaluated in many clinical trials including our own series (parts I and II of the series). The variable responses may be caused by various factors, but the most important factor is the clinical subgroup of diabetic neuropathy. Several clinically, pathologically and electrophysiologically distinct types and subtypes of diabetic neuropathy have been ideneified[1,2]. Diabetic neuropathy of various sub-groups may have different and consequently differently influenced by treatment. In our series, we have decided to study the effect of gangliosides in diabetic distal symmetrical predominantly small-fiber polyneuropathy which represents early neuropathy and may give a more promising result than other subgroups of diabetic neuropathy[3]. Our group was thus a homogeneous group of diabetic neuropathy and the variable response of treatment due to differences in subgroups of diabetic neropathy and may give a more promising result than other subgeneous group of diabetic neuropathy and the variable response of treatment due to differences in subgroups of diabetic neuropathy was therefore deleated. In this part of the series we attempt to evaluate other potential prognostic factors among the responders and non-responders in the gangliosides therapy.

Materials and Methods

The study design, the study population, the intervention and the outcomes of the study has been previously described in the first two parts of the series.

The characteristics which were evaluated among the responders and non-responders were

- Age in years
- Sex either male or female
- Body Mass Index (BMI) defined by body weight devided by (height)^2
- Duration of diabetes mellitus in years
- Duration of neuropathic symptoms in years
- Degree of diabetic control defined by HbA1 level (< 8% = good, 8-10% = fair, >10% = poor)
- Associated nephropathy defined by presence of proteinuria > 2+ by dipstix
- Associated retinopathy defined by presence of background or proliferative retinopathy, diagnosed by ophthalmologist
- Presence of hyperesthesia
- Regular alcoholic consumption

The responders and non-responders were defined according to the improvement in nerve conduction study of two or more nerves. The electrophysiological responses was in concordance with the clinical response. There were 18 responders and 12 non-responders.

Results

Baseline characteristics of the patients were demonstrated in Table 1.

Table 1. Characteristic of the patients.

Characteristics		Mean + S.E.		Range
Age (yr)		60.4 ± 8.5		42 - 76
Sex		male = 6		Female = 24
BMI (kg/M^2)		25.3 ± 4.6		21 - 29
Duration of DM (yr)		9.7 ± 6.3		1 - 20
Duration of (yr) symptoms		2.1 ± 1.3		1 - 5
Mode of treatment				
		Diet alone		3 cases
		Oral agents		16 cases
		Insulin		11 cases
Diabetic complications				
		Nephropathy		13 cases
		Retinopath		11 cases
		Good	Fair	Poor
Degree of diabetic control	before Rx	8	15	10
	during Rx	7	16	7

Baseline characteristics of the responders and non-responders were demonstrated in Table 2.

Degree of diabetic control, associated nephropathy, retinopathy, presence of hyperesthesia and consumption of alcohol were demonstrated in Table 3.

The comparison between the responders and non responders according to various characteristics were shown in Tables 2 and 3. The factors which were significantly different among the two groups were age, duration of neuropathy and presence of hyperesthesia. After application of the multivariate analysis (log-linear model) these prognostic factors remained significant.

Table 2. Base-line characteristics of the responders and non-responders.

Characteristics	Responders 18	Non-responders 12	P-value
Age	60.5 ± 5	66.2 ± 5	< 0.01
Sex M:F	3:15	3:9	NS
Duration of DM	8.8 ± 5	9.0 ±	NS
Duration of neuropathic symptoms	1.2 ± 8	2.2 ± 1.2	< 0.01
BMI	24.4 ± 3	25.4 ± 3	NS

Table 3. Degree of diabetic control, retinopathy, nephropathy alcoholic consumption and presence of hyperesthesia.

Characteristics	Responders 18	Non-responders 12	P-value
Degree of DM control (HBA_1)	10.8 ± 3	11.0 ± 3	NS
Retinopathy	10/18	6/12	NS
Nephropathy	8/18	5/12	NS
Hyperesthesia	15/18	4/12	< 0.01
Alcohol	3/18	2/12	NS

Discussion

In our study, the response rate of gangliosides therapy in diabetic neuropathy was 60% (18/30). According to previous trials, the response rate in gangliosides therapy ranged from 50-80%[4-7]. Factors which may have influence on the response rate include type of diabetic neuropathy, methods of outcome measurements, diabetic control, and other prognostic factors[8-9].

In our series we have studied a limited subtype of diabetic neuropathy, thus the difference in response among the responders and non responders will not be caused by a difference in the pathogenesis of the neuropathy. We have probed the potential important factors which might influence the response in our group. In our series, the most important demographic factors which have an effect on the response of diabetic neuropathy in gangliosides therapy were, age and duration of neuropathic symptoms.

Naturally, the deterioration in neurological function and to normal aging process usually occur after the age of 50 years[10]. The conduction velocity

of the peripheral nerve is one of the well-known physiological change which is significantly affected by age[10]. This may explain the correlation between poorer response with increasing age in our series.

The longer the duration of neuropathic symptoms reflect the longer duration of the disease and eventually the more severe degree of the neuropathic change in the nerves[10]. The more severely damaged nerves will not respond to treatment as demonstrated in our cases.

The hyperesthesic group showed more favorable effect than the patient without these symptoms. This may reflect the mechanism of gangliosides in promoting nerve sprouting, and consequently reduced pain (discussed in part I).

Other prognostic factors which might have, effects on diabetic neuropathy include, sex, body mass index, and diabetic control[10] did not have any significant prognostic value in our series. The presence of diabetic retinopathy and nephropathy which reflect microvascular late complications of diabetis mellitus had no influence on the outcomes of the therapy. Alcoholic consumption which may directly be a toxic agent to the peripheral nerve or may cause nutritional neuropathy and may act as a confounding factor did not play any significant role in gangliosides treatment in this series.

Conclusion

Gangliosides are helpful in diabetic neuropathic patients especially for those who are relatively young, with a short duration of neuropathic symptoms and those who have hyperesthesia.

Acknowledgement

The authors with to thank FIDIA Research Laboratories for funding and generous supplies of gangliosides (Cronassial[R] used in this study.

References

1. Thomas PK. The clinical syndromes of diabetic neuropathy. Intern Med 1986 Jul; 2(3): 138-51
2. Dyck PJ, Thomas PK, Asbury AK, Winegrad AJ, Porte D, eds. Diabetic Neuropathy. Philadelphia : WB Saunders, 1981.
3. Said G, Salma G, Selva J. Progressive centripetal degeneration of axons in smallfiber diabetic polyneuropathy. A clinical and pathological study. Brain 1983 Dec; 106(4): 791-807
4. Abraham RR, Levy DM, Abraham RM. Changes in thermal sensaions in diabetic patient after treatment with gangliosides. Diabetic Research 1988 Mar; 7(3): 129-35
5. Barsi S, Albizzati MG, Calloni E, Frattola L. Electromyographic study of diabetic and alcoholic polyneuropathic patients treated with gangliosides. Muscle Nerve 1982 May-June; 5(5): 351-6
6. Horowitz SH. Gahgliosides therapy in diabetic neuropathy. Muscle Nerve 1986 Jul-Aug; 9(6): 531-6
7. Linger C, Pernet A, Moody JF, Assal JPH. Effect of gangliosides on diabetic neuropathy. In : Ward JD. Goto Y, eds. Diabetic Neuropathy. Chichester : John Wiley & Sons, 1990. 471-5
8. Comi G, Canal N, Lozza L. Diabetic peripheral neuropathy : therapeutic approach. Intern Med 1986 Jul; 2(3): 152-7
9. Sanchez AP. Monitoring of pharmacological results. (Controlled clinical trials). Intern Med 1986 Jul; 2(3): 164-7
10. Abraham RR, Levy DM. Diabetic neuropathy : Measurement and quantitation. In : Ward JD, Goto Y, eds. Diabetic Neuropathy. Chichester : John Wiley & Sons, 1990. 259-68