

Contribution to the Study of Procyanidolic Oligomers: Endotelon Used In Diabetic Retinal Infections (30 observations) J.L. Arne

Introduction

Retinal infection represents a frightening sensory complication for a diabetic. Its prevention and treatment have been the object of a number of studies coming from the collaboration between doctors treating diabetes and ophthalmologists. Diabetic retinal infection puts into play the capillary lesions with the thickening of the basal membrane that vacuolizes and hyalizes thus infiltrating cellular debris. The number of pericytes progressively decreases. The retinal consequences of these capillary alterations appear as:

- Micro-aneurysms
- Hemorrhaging
- Exudation of plasmatic separation out of the capillary artery
- Neo-vascularization after hypoxic capillary occlusion

The evolution of retinal infection will bring about massive hemorrhaging and the detachment of the more or less extended retina.

As for the oedemas it is perhaps not always the immediate consequence of the disappearance of the capillary bed, it often proceeds very often to the modification of the structures of the endothelial cells of the micro-vessels.

The interest of the proposed work to put into evidence the capillo-protector effect of a new product composed of procyanidolic oligomers (Endotelon) seemed to correspond to our preoccupation into the research of new treatments in this area.

Its vasculoprotector power acting on the capillary permeability and the capillaro-venous resistance is defined in a number of previous studies.

The metabolism and pharmacology of O.P.C. were the subject of a detailed study (4) and the different works in pharmacology (3,5) and in clinics (1,2,6,7) showed its action in all the ailments where capillary permeability was the cause.

The results inspired us to do research into the treatment of diabetic retinal infections.

MATERIAL and METHODS

We studied 30 diabetics stricken with any sort of retinal infection in a double-blind trial (Endotelon and a placebo).

Each patient had to take 3 pills of 50mg a day (one at each meal). A numbered bottle containing either Endotelon or the placebo was given to each patient at the first three visits:

- The first was given during the initial examination

- The second was given on the thirtieth day
- The third on the sixtieth day

The last consultation took place on the ninetieth day.

Their glucidic diet was kept stable and the anti-diabetic treatment correctly adjusted. The examinations comprised:

- A clinical examination mentioning the age, sex, how long they'd been diabetic, weight, T.A.¹, capillary fragility index* and the type of antidiabetic treatment.

* The capillary fragility index is determined in the following manner: Numbering the red splotches using the following:

3 red splotches	= 0
3 to 5	= +
6 to 10	= ++
10	= +++
Ecchymosis	= ++++

Calculating the index:

Number of plus signs ϕ – 20 cmHg x 15 _____
 Number of plus signs ϕ – 30 cmHg x 10 _____
 Number of plus signs ϕ – 40 cmHg x 5 _____

Total of Index _____

- An ophthalmological examination with
 - The measurement of visual sharpness for distances (AVL) and nearness (AVP) with and with corrective lenses
 - The measurement of muscle tonicity
 - A bio-microscopic examination of the back of the eye
 - An examination of the F.O.²

These exams were done at each of the four consultations.

Specialized Exams

- Fluoresceinic angiographs

¹ Unsure what this stands for

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² Unsure what this stands for

- Retinographs from Day 0 to Day 90 in order to control the evolution of the lesions by objective procedures.

The analysis brings an evaluation of the stabilization or the worsening of the lesions at the back of the eye using the retinographs and fluoresceinic angiographs. Two different interpreters read the results in the blind.

AGE

The average age of Group A was 55.4 and the average age of Group B was 43.06. The comparison of the two averages by a test $t=2.33$ (for $ddl=28$) shows a significant difference ($p < 5\%$)³

This difference can cause an inconvenience in comparing the groups if we didn't know that the attack on the retinal micro-circulation is much more dependent upon the length of time the patient has had diabetes and how stable the diabetes is than the age of the patient.

DURATION OF THE DIABETES

Our calculations show that the difference is not significant ($t=1.03$ – $ddl=28$)⁴

WEIGHT

We also see that the difference between the two groups is not significant. ($t=1.03$ – $ddl=28$).

T.A.

There was also no significant difference on the first day of the study ($t=0.07$ $ddl=28$)

RESULTS

The Patients

The patients kept for this study were seen in consultation at the Ophthalmological Service at the Purpan Hospital at Toulouse.

They were referred to us by either diabetes specialist Dr. Denard or by the generalists for control and surveillance of the ophthalmological service.

Three patients dropped out of the study so we were left with data from 30 patients to analyze. They were divided into two groups:

³ Unsure of the meaning of these letters

⁴ Unsure meaning of paragraph

1. Those receiving Endotelon (3 pills a day for three months). There were eight men and seven women.
2. Those receiving the placebo in the same dosage and for the same length of time. There were seven men and eight women.

The analysis of the results led us to verify the homogeneity of the two groups and their comparability.

Clinical exam

Group	Men	Women
Endotelon	8	7
Placebo	7	8

The difference is not significant.

Nature of Diabetes

The diabetics were divided thusly:

Group	Insulin Dependent	Synthetic Hypoglycerin
Endotelon	8	7
Placebo	11	4

This distribution is homogenous in the two lots.

Capillary Fragility Index

Starting on Day 0 the comparison of the averages does not show any significant difference ($t = 0.17$) – ddl – 28

The Evolution of the Ophthalmological Parameters

The ophthalmological exam was made up of:

- The determination of the sharpness of distance vision (AVL)
- Examination of muscle tonicity
- Examination of the back of the eye
 - With fluoresceinic angiographs

- With retinographs

We determined that the AVL at the end of three months evolved thusly:

Group	Diminished	Stayed the Same	Got Better
Endotelon	7	19	4
Placebo	11	13	6

There was not much of a difference between the two groups.

Ocular Tonicity

In the same fashion the ocular tonicity was measured for each eye from Day 0 to Day 90.

Group	Diminished	Stayed the Same	Increase
Endotelon	7	19	4
Placebo	11	13	6

There was no significant difference between the two groups.

Exam of the Back of the Eye

This exam did not bring any information on the eventual changes between the two periods and the two groups of patients.

Fluoresceinic Angiographs and Retinographs

These were used to form a description of the back of the eye and an evaluation of the lesions from retinal infection from the beginning to the end of the treatment for each patient in each lot. This evaluation was done in the blind by two different evaluators.

At the end of the study we brought together the following distribution:

Group	Stabilized	Worsened
Endotelon	12	3
Placebo	7	8

Reading this graph the results appear clearly in favor of Endotelon (80% to 47%). However, the smallness of the groups does not allow us to say there was any significant difference.

Tolerance

Clinical Tolerance

All told the clinical tolerance was good. The group taking Endotelon showed a perfect tolerance for the product. No one complained being sick. A few noted some very minor and fleeting digestive problems.

Biological Tolerance

The stability of the biological controls was verified in both groups from Day 0 to Day 90.

Glycemia

For the Endotelon group there was no significant difference. There was no significant difference in the placebo group either.

These results underline very well an excellent control of diabetes by established treatments and carefully followed dietetic measures.

Glycosuria

We found in three patients the moderate presence of sugar in the urine. Once in the Endotelon group and twice in the placebo group.

Cetonic Bodies

Their systematic research did not produce any positive results.

Urinary Base

Normal for all of the patients throughout the treatment.

Proteinuria

Negative in all samples.

“Creatininemie” (translation not found)

No difference between Day 0 and Day 90 for both groups.

“Azotemia” (translation not found)

The constants did not vary throughout the study.

CONCLUSION

The vascular protector effect of Endotelon was evaluated on diabetic patients showing signs of serious retinal infection lesions using a placebo.

The treatment allowed us to obtain stabilization of the retinal infection lesions in 80% of the subjects treated with Endotelon. Stabilization occurred in only 47% of the placebo group.

Among the different vasculo-protector drugs that are available to us in the treatment of retinal infection Endotelon can be considered a medication of choice by reason of its good clinical and biological tolerance.