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Posterior vitreous detachment

A combined clinical and physicochemical study

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Abstract. Sixty-one postmortem eyes were examined with clinical methods (slit lamp) and later sectioned for measurement of the liquid and gel vitreous. The amount of liquid vitreous was found to be progressively greater with increasing posterior vitreous detachment (PVD), and it was concluded that slit-lamp examination is a reliable method of evaluating the rheological state of the vitreous in the living eye. The total content of sodium hyaluronate (NaHA) in the vitreous was measured. Eyes proven to have no PVD had a higher concentration of NaHA than eyes with total PVD. Also, females had a lower concentration than males. There was no significant difference in NaHA concentration between the gel and liquid vitreous. The role played by different structural elements for the stability of the vitreous gel is discussed.

Introduction

Posterior vitreous detachment (PVD) is the clinical description of changes in the vitreous due to syneresis, causing collapse of the vitreous gel and its separation from the posterior retina. PVD can be complete or incomplete, depending on the size of the vitreous area that becomes separated from the retina. PVD is known to be more common in the ageing eye, but there is a discrepancy between the incidence figures arrived at with clinical and histopathological methods (Favre and Goldmann 1956; Heller et al. 1972). This may be due to population differences in the study material or, more probably, to different techniques.

The histopathological results are based on gross sectioning of the eyes and visual estimation of the amount of gel vitreous. The clinical results are based on slit-lamp examination. The picture obtained in the slit lamp represents the light scattered from the collagen fibrils of the vitreous gel. The areas with strong scattering are easily recognized, whereas areas with widely spaced fibrils might be mistaken for pools of liquid vitreous.

By combining slit-lamp evaluation of the state of the vitreous with physical control of the amount of fluid and gel vitreous in the same eye, we tried a new approach to assess the reliability of the biomicroscopical diagnosis of PVD. In the mechanochemical vitreous model proposed by Balazs (1961), sodium hyaluronate (NaHA) is considered to be a very important structural element with regard to providing stability to the collagen fibril network (Balazs 1973). Its role in the pathogenesis of PVD is, however, still unclear.

The aim of this investigation was to study the variability of the sodium hyaluronate concentration in the vitreous and its relationship to the instability of the gel in the ageing eye.

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Materials and methods

Both eyes from 40 adult corpses were obtained from the Department of Pathology (Malmö General Hospital) and enucleated not later than 24 h postmortem, with the intention of subjecting all eyes to clinical, physical, and biochemical examinations. The material comprised 15 males and 25 females aged 45–93 years (Table 1). Cases with clinical records available at the Eye Department were chosen, but otherwise no selection was made. Due to ophthalmic operations, myopia and technical mishaps, 9 eyes were excluded. Among the remaining 71 eyes, pathological findings were recorded in 21 (Table 2). These were treated as a separate group in the final analysis of results. The frequency distribution of the material is presented in Fig. 1. Ten eyes were excluded from clinical examination for technical reasons.

After enucleation the remaining conjunctiva and extraocular muscles were removed. The eye was immersed in 4% glutaraldehyde for 30 min and then mounted with the

Table 1. Age and sex distribution of patients

	No	Median age	Range (years)
Males	15	71	55–84
Females	25	72	45–93

Table 2. Pathological findings in clinical records

Diagnosis	Males	Females
Macular degeneration	–	6
Diabetic retinopathy	1	6
Myopic degeneration	2	–
Retinal vein occlusion	2	2
Retinal arterial occlusion	–	2

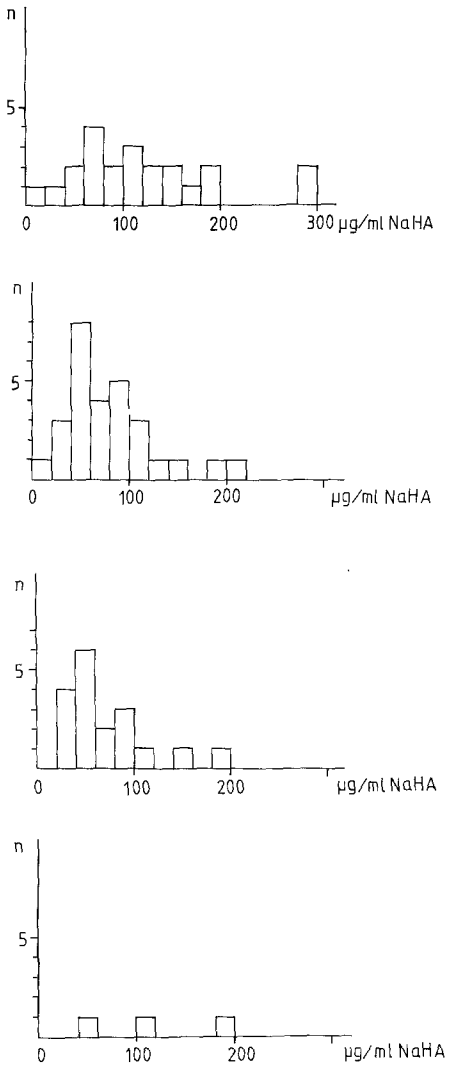

Fig. 1. Frequency distribution of (from top): normal eyes (males) $n=22$, (females) $n=28$; pathological eyes (females) $n=18$, (males) $n=3$

cornea facing upward in a metal support consisting of two limbus-parallel circular frames. These were adjusted to support the anterior and posterior segments without causing excessive pressure on the eye. The bulb was opened at the limbus with a scalpel and the cornea removed using curved scissors. In order to make biomicroscopy of the vitreous possible, the lens nucleus was extracted in eyes with cataract, leaving the posterior capsule to prevent escape of the vitreous. In a few eyes the whole lens was removed. In these cases careful handling generally allowed the vitreous to be inspected through an intact anterior surface. Sixty-one eyes were available for biomicroscopy. The bulb, supported by the frames, was held manually in the slit lamp with the insertion of the superior rectus muscle in the 12 o'clock position and the anterior segment facing the observer, thus allowing the eye to be studied in the same positions as when a clinical slit-lamp examination is performed.

It was noted if the posterior surface of the vitreous was seen as a vertical line anterior to the centre of the eye, if there was arching toward the posterior pole, or if it appeared that the gel was intact. The extent of syneresis was thus estimated and recorded as "complete, partial or no

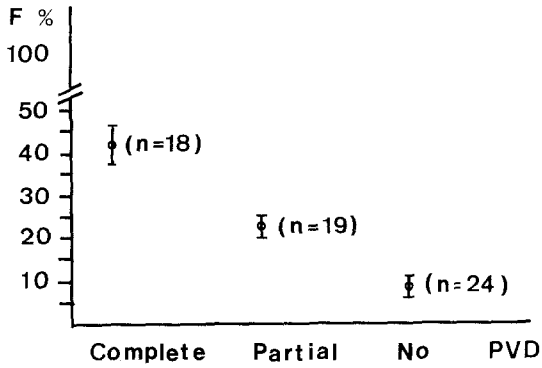

Fig. 2. Volume of fluid vitreous in different stages of PVD F% = Volume of fluid vitreous × 100/vitreous volume. Mean ± SEM respectively 42.19 ± 4.34, 23.43 ± 2.22, 8.99 ± 2.10

PVD." With this method it was not possible to establish the difference between complete posterior vitreous detachment and extensive syneresis within the vitreous body or to make a distinction between partial posterior vitreous detachment and moderate syneresis within the vitreous body. However, this did not interfere with the evaluation of the proportions of fluid and gel vitreous. A macroscopic evaluation of the results was achieved by gently sectioning the eye horizontally with a Thomas tissue slice blade (Arthur H. Thomas Co., Philadelphia, USA) in the equatorial zone exposed between the metal frames. All escaping liquid vitreous was weighed. The bulb segments were frozen and the formed vitreous carefully dissected from the adjacent structures and weighed. The two fractions were again frozen and kept at −20° C until analyzed.

Biochemical analysis

After removal from the freezer, the vitreous was transferred to centrifuge tubes, melted and centrifuged at 105,000 *g* at +4° C (International IEC/B-60 ultracentrifuge). The supernatants were dialyzed against large volumes of buffered saline. The samples were assayed for hexuronic acid using the modified uronic acid carbazol reaction (Bitter and Muir 1962). Hyaluronic acid values were calculated from the hexuronic acid contents, using a conversion factor of 1.95. The means and differences were compared by using the paired and unpaired *t*-test.

Results

In the 61 eyes studied biomicroscopically after removal of the lens, complete separation of the posterior hyaloid from the retina was noted in 18 (29.5%) and partial detachment in 19 (31.2%), but no detachment could be detected in 24 eyes (39.3%). In a macroscopic comparison after the eye had been sectioned, the amount of fluid vitreous was found to be progressively greater with increasing vitreous detachment. The results are presented in Fig. 2, with the fluid phase calculated as percentage of the total vitreous volume, the mean ± SEM being 42.19 ± 4.34, 23.43 ± 2.22, and 8.99 ± 2.10, respectively, for the three groups. It was concluded that the clinical method correlates well with the physical control.

In the biochemical analysis the NaHA concentrations in the vitreous were compared in 50 normal eyes from men

Table 3. Concentration of vitreous hyaluronate in males and females

Sex	No. eyes	Concentration hyaluronate (μg/ml)
Males	22	120.89±75.44
Females	28	79.53±48.17

Mean±SD

Table 4. Concentration of vitreous hyaluronate in different stages of PVD

Group	PVD	No. eyes	Concentration hyaluronate (μg/ml)
A	Complete	11	82.00±66.50
	None	19	131.88±70.72
B	Complete	7	60.21±37.88
	None	5	80.65±40.66

A=normal; B=pathological
Mean±SD

Table 5. Concentration of hyaluronate in fluid and gel vitreous in different stages of PVD

Group	PVD	No. eyes	Concentration hyaluronate (μg/ml)	
			Fluid	Gel
A	Complete	11	103.91±90.33	68.36±53.19
	Partial	10	88.00±74.74	77.40±43.05
B	Complete	7	65.86±44.88	55.86±35.29
	Partial	9	82.33±58.44	90.22±69.06

A=normal; B=pathological
Mean±SD

and women. The latter were found to have lower concentration, the difference being significant at a 1% level (Table 3). In 21 pathological eyes (3 males and 18 females) no significant difference was found ($P<0.06$).

The NaHA concentration was analyzed in both eyes from the same individual in 20 normal cases (8 males and 12 females). It was found to be of the same magnitude in both eyes of either sex. The difference between the eyes calculated as percentage of the highest NaHA value was 18.76±19.33 for male eyes and for female eyes 26.33±23.31 μg/ml. No statistically significant difference could be demonstrated. In 11 pairs of eyes with a pathological finding in one or both eyes (1 male and 10 females), no significant difference was found ($P<0.37$).

Eyes with no PVD (group A) showed higher concentrations of NaHA ($P<0.04$), although in 4 cases it was less than 70 μg/ml. In the small number of pathological eyes, it could not be verified that there was a corresponding difference between the concentrations in complete versus no PVD ($P<0.19$, Table 4).

No significant difference was found in the distribution of NaHA between fluid and gel vitreous in normal or pathological eyes with complete or partial vitreous detachment (Table 5).

Discussion

In the classic study by Favre and Goldmann (1956) otherwise normal eyes were examined with a three-mirror lens and the slit lamp. The incidence of PVD was reported as 65% in patients over the age of 60. If cadaver eyes are examined after fixation and gross sectioning, the rate of PVD in the corresponding age group is 31% (Heller et al. 1972).

Two factors might explain the high incidence in the clinical investigations. One is the inherently selective nature of clinical studies using subjects. Another factor may be related to the clinical optical methods used. Since the slit lamp picture of the vitreous is based on the scattering of incident light by the orientation and distribution of the collagen network, areas with very widely spaced collagen fibrils might be falsely identified as liquid pools.

None of these factors seem to have influenced the present investigation as far as total PVD is concerned. In our case material (median age, 71 years) using the amount of fluid vitreous as a control for slit-lamp evaluation, the relatively low incidence of complete PVD (29.5%) correlates fairly well with the findings of others (Foos and Wheeler 1982).

The incidence of partial PVD (31%), as compared with Foos' results (3% partial PVD and 30% syneresis with large liquid pools), reflects the difficulty in discriminating between syneresis and partial PVD.

The NaHA distribution in the vitreous is along a gradient, with the highest concentration in the posterior part close to the retina (Swann and Constable 1972). It was therefore surprising to find that also in eyes with total PVD, where the liquid vitreous occupies the posterior part of the vitreous space, there is no difference in NaHA concentration between liquid and gel vitreous. This is in agreement with the results of Balazs and Denlinger (1982), if the present material is considered to be on the borderline between 60 and 70 years (the medium age 71 years), as these investigators found the same NaHA concentration in both gel and liquid vitreous from 20 to 70 years of age but a dramatic increase of NaHA in the liquid vitreous after 70 years of age.

In studies on the macromolecular composition of the vitreous, it has been noted that there is a wide variability in the NaHA concentration in different individuals from the same age group (Balazs 1960; Balazs and Flood 1978). Since the same variability has been found regarding the degree of syneresis (O'Malley 1976) and NaHA is a proposed stabilizer of the vitreous gel (Balazs 1973), it seemed reasonable to try to find a correlation. For this reason, NaHA concentration was examined in eyes with a known degree of PVD. The results show that the NaHA concentration was higher in eyes with no PVD than in eyes with total PVD and argue in favor of NaHA playing a role as a stabilizer of the collagen gel. Foos and Wheeler (1982) have recently reported a higher rate of PVD in women (between 60 and 80 years of age), but could give no explanation for this observation. A similar distribution has been found by Novak and Welch (1984) Our finding that there

is a significantly lower NaHA concentration in the female vitreous, which is reported here for the first time, could be a possible explanation if the role of NaHA as a gel stabilizer is accepted.

As for the difference in concentration between men and women, the glucosaminoglycan (GAG) composition of connective tissue is known to be influenced by gonadal hormones (Szirmai 1966). NaHA synthesis seems to be the most sensitive of the GAGs for this type of stimulation. Vitreous might therefore be a "target tisssue" and the problem of vitreous syneresis and PVD a result of hormone withdrawal.

Although the findings described seem to be in line with the role of NaHA as a stabilizer of the vitreous gel, the low concentration of NaHA in certain eyes without PVD suggests that other components also contribute to the stability. Such components are, in addition to the obvious role of collagen, the vitreous-specific noncollagenous proteins (Swann 1980).

Careful mapping of the macromolecular constituents in eyes with a known degree of syneresis can eventually solve the question regarding the mechanism of PVD. The present study has demonstrated a good correlation between clinical methods and physical quantitative methods in evaluating the degree of syneresis. This finding is valuable since the investigator can alternate between the methods. When mapping the vitreous proteins known to change rapidly in concentration and nature postmortem, he can use specimens obtained at surgery from a patient previously examined by slit lamp. The quantity of NaHA and collagen concentrations does not seem to change postmortem and thus qualifies the physical method.

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