Reports

Vitreous Glucose in Bacterial and Sterile Endophthalmitis

Bruce R. Garretson,* Thomas A. Deutsch,* J. Terry Ernest,* and Jacqueline J. Vernor*

Bacterial or sterile endophthalmitis was induced in rabbits. The vitreous glucose levels were then assayed. Severe intraocular inflammation, whether bacterial or sterile, resulted in marked lowering of vitreous glucose as compared to control levels. Moderate or mild inflammation failed to reduce the vitreous glucose. These data suggest that determination of vitreous glucose is not of value in the differentiation of bacterial from sterile endophthalmitis. Invest Ophthalmol Vis Sci 27:1541-1543, 1986

Bacterial endophthalmitis is an ocular infection with grave visual consequences. Early diagnosis and aggressive treatment are vital to the recovery of visual function.1,2 However, the diagnostic and therapeutic modalities may have serious side effects, and must be used only when there is sufficiently high suspicion to warrant them.

Previous investigators have suggested that the level of vitreous glucose may be helpful in distinguishing patients with bacterial endophthalmitis from those with severe sterile vitreous inflammations.3 The purpose of this study was to determine the level of vitreous glucose in both bacterial and sterile endophthalmitis in order to evaluate the potential clinical benefit of this test as a diagnostic tool.

Materials and Methods. Experiments were performed on 3–5 kg New Zealand White rabbits and complied with the ARVO Resolution on the Use of Animals in Research. Anesthesia was induced in all cases using an intramuscular injection of 175 mg Ketamine hydrochloride with 2.5 mg acepromazine supplemented as necessary. Proparacaine hydrochloride (0.5%) was used for topical anesthesia.

Vitreous samples were obtained using a 23-gauge needle on a 3 cc disposable syringe via the pars plana. Direct visualization of the needle tip through the pupil was done in order to insure sampling from the mid-vitreous. Contamination with blood occurred in approximately 10% of the vitreous taps; these samples were discarded. Simultaneous blood samples were obtained via cardiac puncture. All samples were centrifuged at 2000 rpm for 10 min prior to glucose determination.

The Beckman Glucose Analyzer 2 was used to measure the glucose levels in all samples after calibration. This instrument measures the consumption of oxygen in the conversion of Beta-D-glucose to gluconic acid and hydrogen peroxide. Three successive trials were performed at room temperature on all samples, and mean values are reported. A 10 μl sample was used for each trial, all of which were made within 1 hr of sampling.

Bacterial endophthalmitis: Bacterial endophthalmitis was induced using methods similar to those described by previous investigators.4 Using the MacFarland dilution technique, a solution of Staphylococcus aureus was produced at an approximate concentration of 10,000 organisms per cc of normal saline. Injection of 0.1 cc of this solution into the mid-vitreous was performed on all of these animals via the pars plana. Immediate anterior chamber paracentesis was performed via a 27-gauge needle to lower the intraocular pressure. Vitreous samples were taken at 24–48 hr after inoculation. Clinical red reflex was determined in all eyes prior to vitreous taps by one observer (BRG). This semi-quantitative assessment of intraocular inflammation was based on clinical experience and was subdivided into four groups, as follows: 3–4+ red reflex, minimal to no diminution of fundus red reflex; 2–3+ red reflex, moderate loss of red reflex intensity; 1–2+ red reflex, severe loss of red reflex intensity and clarity; and 0–trace red reflex, total loss or minimal hint of red reflex.

Sterile endophthalmitis: Sterile endophthalmitis was achieved as follows: immune sensitization to human normal serum albumin (HNSA) was accomplished using three consecutive weekly intramuscular injections of 250 mg (1 cc of a 25 gm% solution). In the fourth week, a mid-vitreal injection of 25 mg HNSA (0.1 cc of a 25 gm% solution) was performed. Anterior chamber paracentesis was done for intraocular pressure control. Mid-vitreous samples were taken at 48 hr after injection following determination of clinical red reflex as above. All samples were cultured on both blood and chocolate agar; when visible growth within 48 hr was detected, the sample was excluded.
Table 1. Vitreous glucose in NZW rabbits

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<thead>
<tr>
<th>Rabbit Number</th>
<th>Plasma Glucose</th>
<th>OD</th>
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<tr>
<td>1</td>
<td>130</td>
<td>62</td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>202</td>
<td>121</td>
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<td>3</td>
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<td>71</td>
<td>69</td>
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<tr>
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<td>132</td>
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<tr>
<td>5</td>
<td>137</td>
<td>69</td>
<td>66</td>
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Results. Vitreous glucose was measured in the right and left eyes of five normal rabbits. Simultaneous serum glucose was determined, and values are reported as the percentage of vitreous glucose with respect to serum level (Tables 1, 2). Vitreous glucose was 51% ± 6.1 of serum glucose (mean ± SD).

Bacterial endophthalmitis was created in 15 eyes of 8 animals. Glucose measurements were made after the determination of the clinical red reflex (Fig. 1). In nine eyes, the red reflex was graded at zero-to-trace. In this group of eyes, the vitreous glucose was reduced to 9% ± 3.7 of the serum values. In six eyes, the clinical red reflex was greater than zero-to-trace. In these eyes, the vitreous glucose was 34% ± 10.9 of serum values, which was significantly greater than those with severe inflammation (P < 0.00002).

Sterile endophthalmitis was created in 20 eyes using the model described previously (Fig. 1). All reported cases were culture negative. Severe vitreal inflammation with zero-to-trace red reflex could only be achieved in two eyes. Vitreous glucose was drastically reduced in these two cases, the levels being 12% and 14% of serum glucose. In the 18 eyes with greater than zero-to-trace red reflex, the vitreous glucose was 41% ± 7.2 of serum levels.

Discussion. Bacterial endophthalmitis is a dreaded ocular infection; when present, it is often a complication of intraocular surgery. Early diagnosis and treatment are essential to maximize ultimate visual outcome. Early in the postoperative course, the clinician may be confused between the appearance of early bacterial endophthalmitis and sterile intraocular inflammation.5 We performed this study to evaluate the potential clinical benefit of vitreous glucose level in the differentiation of these two situations.

Table 2. Vitreous glucose as % of plasma glucose in NZW rabbits

<table>
<thead>
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<th>OD</th>
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<tr>
<td>Mean</td>
<td>51.4%</td>
<td>50.8%</td>
</tr>
<tr>
<td>SD</td>
<td>6.2</td>
<td>6.7</td>
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<tr>
<td>Paired t-test</td>
<td>P = 0.304</td>
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Fig. 1. Combined data from eyes with bacterial (open circles) and eyes with sterile (closed circles) endophthalmitis.

Normal mean vitreous glucose in NZW rabbits was 51% of serum levels for the range tested (130–202). This value is comparable to those reported by previous investigators.6,7

Vitreous glucose was drastically reduced in all cases with severe vitreal inflammation, irrespective of how it was produced. In bacterial endophthalmitis with zero-to-trace red reflex, the mean vitreous glucose was 9% of serum values. Comparable inflammation could be achieved in only two eyes in the immune-mediated model. In each of these cases, vitreous glucose was markedly depressed, similar to the bacterial group with severe inflammation.

There was a modest reduction of vitreous glucose from normal with a red reflex of 1+ or greater. No statistical difference was found between the bacterial and sterile groups for this range of vitreous inflammation (P = 0.11).

The mechanism for reduction of vitreous glucose in endophthalmitis is unclear. Reduction in vitreous glucose may be secondary to increased retinal anaerobic glycolysis of the brain, as proposed in cases of bacterial meningitis,8 or to inflammatory cell utilization of glucose. Further study is needed in this area.

In the clinical setting, it is the cases with minimal-to-moderate intraocular inflammation which present the greatest diagnostic challenge. Since early treatment of bacterial endophthalmitis is essential to maximize the potential visual outcome, diagnostic vitreous tap with institution of appropriate therapy must be performed at the earliest possible indication of infection.9,10
Often, one must wait for routine cultures to become positive before the diagnosis is confirmed. This commits the patient to potentially toxic antibiotic treatment, both systemic and intravitreal, pending culture results. It was the hope of this study that immediate measurement of vitreous glucose level would provide the clinician with a rapid means of differentiating bacterial from sterile inflammations when the diagnosis is uncertain. This, unfortunately, does not appear to be the case.

Vitreous glucose is depressed in endophthalmitis; markedly so with severe inflammation. This reduction occurs regardless of the etiology of the inflammation and, instead, is related to its severity. Therefore, vitreous glucose determination does not appear to be of clinical value in the differentiation of bacterial from sterile endophthalmitis.

Key words: bacterial endophthalmitis, ocular inflammation, intravitreal glucose, rabbits


References

Corneal Epithelial Cells Produce Thromboxane in Response to Interleukin 1 (IL-1)

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Synthesis of thromboxane, a product of arachidonic acid formed via the cyclooxygenase pathway, was studied in rabbit corneal epithelial cells (SIRC cell line) under resting conditions and under the influence of interleukin 1 (IL-1). IL-1 potentiated the production of thromboxane 3-10-fold in a dose-dependent manner. This finding assumes added significance in view of the previous observations that the same cells are capable of producing IL-1. Thus, the corneal epithelial cells may be viewed in this context as an autocrine cell producing two biologically active substances which can serve as mediators of inflammation, one of which can augment the production of the other. Invest Ophthalmol Vis Sci 27: 1543–1545, 1986

Rabbit corneal epithelial cells in primary culture, as well as an established line of rabbit corneal epithelial cells, produce a cytokine referred to as CETAF with properties characteristic of interleukin 1 (IL-1). We have confirmed the findings of Grabner et al by demonstrating that SIRC cell line produces an IL-1-like substance spontaneously and in increased amounts when stimulated by silica, LPS, lactic acid, or serum deprivation (Davis et al, unpublished). Thus, corneal epithelial cells may play an important role in local or regional physiological activities, which may be initiated and/or regulated by IL-1. Such activities include immunological reactions through the participation of lymphocytes, and histopathological effects such as injury and tissue repair. IL-1 can also increase the synthesis of prostaglandins and thromboxanes. It was previously reported that corneal cells are capable of synthesizing prostanoids. We, therefore, proceeded to determine whether production of these substances would be increased in corneal cells through the action of IL-1. Our findings indicate that SIRC corneal epithelial cells, which produce an IL-1-like substance, also respond to IL-1 by synthesizing increased amounts of thromboxane.

Materials and Methods. Cells and culture medium: Rabbit corneal epithelial cell line (SIRC) was obtained from American Type culture collection, Rockville,