ORIGINAL ARTICLE

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PRE-TRANSPLANT SCREENING FOR MMP-9 IN ALLOGENEIC HSCT CANDIDATES

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ABSTRACT:

PURPOSE: InflammaDry® (Quidel Eye Health, San Diego, California), an FDA-approved point-of-care commercial test, measures matrix metalloproteinase-9 (MMP-9) levels in the tear film. MMP-9 is an inflammatory biomarker that is elevated in response to ocular surface stress, particularly observed in ocular graft-versus-host disease (oGVHD). The purpose of this study is to assess the prevalence of MMP-9 positivity and a score >4 on the OSDI-6 questionnaire in patients before allogeneic hematopoietic stem cell transplant (HSCT). **METHODS:** A prospective, observational, cross-sectional single center pilot study was conducted among 23 patients (46 eyes) undergoing planned allogenic HSCT. InflammaDry® results, OSDI-6 questionnaire results, and development of oGVHD were collected. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and chi-square test were calculated. **RESULTS:** InflammaDry® demonstrated high sensitivity (1.0) but low specificity (0.1429) for oGVHD development. The PPV was 0.25, while the NPV was 1.0. No statistical significance was found between InflammaDry® result and development of oGVHD (p-value> 0.05). **CONCLUSION:** InflammaDry® is not an effective tool for detecting the onset or predicting the risk of developing oGVHD. A significant percentage of patients exhibited ocular inflammation before allogeneic HSCT, suggesting that initiating prophylactic treatment could be valuable in reducing oGVHD development.

KEYWORDS: Matrix Metalloproteinase 9. Graft vs Host Disease. Transplantation, Homologous.

INTRODUCTION

Ocular graft versus host disease (oGVHD) is a serious complication that impacts many patients following allogeneic hematopoietic stem cell transplant (HSCT) and is associated with significant ocular morbidity and decreased quality of life. The pathophysiology of the development of oGVHD is not well-defined, but it is thought to be a complex interplay of T cell mediated damage to the lacrimal glands, eye lids, conjunctiva, and cornea.[1] Risk factors for developing oGVHD include being a male recipient of a female donor; skin, oral mucosa, liver, or GI tract involvement in acute or chronic stages of GVHD; lung involvement in chronic GVHD; history of diabetes mellitus; Epstein-Barr Virus (EBV) positive donors; and patients of Asian descent.[2] Furthermore, the prevalence of developing oGVHD is increasing as it currently affects 30-60% of patients who undergo HSCT and 60-90% of patients with systemic graft versus host disease (GVHD).[1-4]

The ocular manifestations associated with oGVHD include meibomian gland dysfunction (MGD), mechanical eyelid disorders (trichiasis, ectropion, entropion, lagophthalmos), persistent epithelial defects (PED), infectious keratitis, corneal scarring, conjunctival injection and chemosis, keratoconjunctivitis sicca, cicatricial conjunctival fibrosis, corneal perforation, and filamentary keratitis. It can also present with various ocular symptoms including redness, photophobia, excessive tearing, blurry vision, irritation, grittiness, foreign-body sensation, or burning.[1] These symptoms significantly impair vision and reduce the quality of life of these patients. A study employing the 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25), designed to evaluate patients' perception of their visual health status and the impact of ocular disease on their quality of life, revealed that in comparison to healthy populations without eye disease, individuals with oGVHD exhibited heightened levels of ocular pain, vision-specific role limitations, vision-specific mental health symptoms, challenges in near and distance vision, difficulties in general vision activities, increased vision-specific dependency, peripheral vision issues, and compromised general health.[5]

The diagnosis of oGVHD is based on diagnostic criteria proposed by the International Consensus Group of Ophthalmologists in 2013. The specific clinical parameters to assess oGVHD are as follows: (1) Schirmer's test without anesthesia, (2) corneal fluorescein staining, (3) conjunctival injection, and (4) ocular discomfort symptoms rated by the Ocular Surface Disease Index (OSDI). The variables are scored, and the total is used to determine disease severity (Table 1).[6]

Previously, the diagnosis of graft-versus-host disease (GVHD) was based on categorizing as acute, developing within 100 days of HSCT, or chronic, developing after 100 days following HSCT.[8] However, the NIH adjusted diagnosis guidelines to be based on the organs involved in manifesting symptoms, which then determine the difference between acute GVHD and chronic GVHD diagnosis. Specifically, symptoms involving the eye are a distinctive finding of chronic GVHD.[9]

The difficulties in the management of oGVHD are the early recognition of symptoms by the hematology/oncology providers and prompt referral to an eye care provider for evaluation. Education and training have been shown to significantly reduce the time interval between onset and symptoms to referral.[10] This is critical to identify patients in the initial stages of oGVHD and to prevent cicatricial changes to the ocular surface and vision loss. While symptom development is a key factor in recognizing the onset, studies have shown that varieties of inflammatory cytokines are present in the precorneal tear film.[11] One of the prominent cytokines is matrix metalloproteinase-9 (MMP-9).

MMP-9 is an endopeptidase that is secreted into the tears and can break tight junctions of the ocular surface epithelium, resulting in loss of ocular surface barrier function and desquamation. Multiple studies have demonstrated a significant correlation between the degree of MMP-9 elevation and clinical severity of ocular surface disease.[12-16] InflammaDry® is positive in 84.6% of patients with ocular surface disease and positive in only 6.3% of patients without ocular surface disease.[16] A recent study has shown that MMP-9 is present in over 90% of patients that have been diagnosed with oGVHD.[17] The presence of MMP-9 was shown to be present in all stages of oGVHD and persistent regardless of symptoms or therapeutic measures. An FDA approved point-of-care commercial test, InflammaDry®, a lateral flow immunoassay, was used in this study and is widely available to measure MMP-9 presence in ocular sur-

face disease patients. This test is easily administered, requires no topical anesthetic, and has minimal risk to the patient. The results can be scored as either positive or negative or can be graded on an ascending scale of 0 for a negative presence to 4, indicating a marked presence of MMP-9.[18] However, it is not known if MMP-9 is present pre-transplant in allogeneic HSCT candidates due to other chemotherapy or preconditioning procedures. If so, then testing with InflammaDry® after allogeneic HSCT would be inconclusive. Additionally, if there is MMP-9 present prior to allogeneic HSCT, pretreatment of any ocular surface inflammation could be advantageous to reduce any contributing factors in developing and exacerbating oGVHD.[19] Therefore, the purpose of this study is to determine whether MMP-9 is present prior to allogeneic HSCT using InflammaDry®.

METHODS

A prospective, observational, cross-sectional single center pilot study was conducted aimed at gathering InflammaDry® data on eligible participants undergoing planned allogeneic HSCT. This study was approved and conducted in compliance with the Medical College of Wisconsin's Institutional Review Board. The primary outcomes for this study were 1) Percent of patients who test negative on the InflammaDry® test; 2) Percent of patients who score less than 4 on the OSDI-6; 3) Percent of patients who test positive on the InflammaDry® test and 4) Percent of patients who score more than 4 on the OSDI-6. Further secondary exploratory outcomes of this study are 1) To investigate pre-transplant procedures or conditions that correlate with positive MMP-9 and 2) To establish if the presence of MMP-9 in the pre-transplant screening of allogeneic HSCT candidates would be viable screening tools in oGVHD. Prospective subjects, as defined by the inclusion/exclusion criteria, were considered for entry into the study. Determination if prospective subjects met the inclusion and exclusion criteria occurred by retrospective chart review of prospective subject's electronic medical records. Inclusion criteria required prospective subjects to be at least 18 years-old, the ability to consent, is scheduled for an allogeneic HSCT (and has not previously undergone an allogeneic HSCT) and the ability to read and speak English for completion of consent and OSDI-6 questionnaire. Exclusion criteria included prior diagnosis of ocular surface disease (keratitis sicca, meibomian gland dysfunction, infectious keratitis, exposure keratitis), prior use of topical ocular anti-inflammatories in the past 3 months, contact lens use prior to 1 month of examination, ocular surgery in past 3 months or ocular infection in past 3 months. Prospective subjects had to meet all inclusion criteria and none of the exclusion criteria in order to be considered for entry into the study. Of these prospective subjects, further retrospective chart review was completed to obtain additional background information. Information that was abstracted from the medical chart included cancer diagnosis as well as date of diagnosis; previous therapies prior to transplant [chemotherapy (including details of specific drugs), radiation (dose and location), immunotherapy, prior autologous transplants]; and ocular diagnosis (glaucoma, cataracts, ocular surface disease [dry eye, keratitis, lid malformation]).

Following retrospective chart review and determination of eligible prospective subjects, a subject was seen at their allogeneic HSCT consultation visit. The prospective subject was approached by a study team member who explained the study in detail, answered questions and provided a consent form to the subject. If the subject agreed to participate in the study, written informed consent followed by InflammaDry® and the OSDI-6 questionnaire were obtained. The InflammaDry® test was collected by a trained team member following manufacturer instructions (Figure 1). InflammaDry® results were recorded as either positive or negative and well as recorded on a scale of 0 to 4 (Figure 2).

InflammaDry® results were scored by two team members with the recorded result being an average of the two scores. External controls for each InflammaDry® package were performed with acceptable results for the positive and negative control.[20] The OSDI-6 questionnaire was completed by the subject and a score (0-24) was recorded. After informed consent, InflammaDry® and OSDI-6 were obtained, an additional retrospective chart review was completed for further medical history collection, including subject's age, gender, race, past medical history, and current medications. A follow-up phone call was performed by the principal investigator to determine if a subject experienced an adverse effect or had questions relating to the study or procedures performed.

Patients were followed for at least 12 months to monitor for development of oGVHD. Diagnosis of oGVHD was made using the oGVHD National Institutes of Health grading criteria.

Data analysis involved determining InflammaDry® sensitivity [number of patients who developed oGVHD with positive InflammaDry® result/ (number of patients diagnosed with oGVHD with positive InflammaDry® result plus number of patients diagnosed with oGVHD with negative InflammaDry® result)], specificity [number of patients without oGVHD diagnosis with negative InflammaDry® result/ (number of patients without oGVHD diagnosis with negative InflammaDry® result plus number of patients without oGVHD diagnosis with positive InflammaDry® result)], positive predictive value (PPV) [number of patients who developed oGVHD with positive InflammaDry® result/ number of patients with positive InflammaDry® result] and negative predictive value (NPV) [number of patients without oGVHD diagnosis with negative InflammaDry® result/ number of patients with negative InflammaDry® result]. Patients who died within analysis timeframe of 12 months were not included in calculations. Percent positivity [number of eyes with positive InflammaDry® result/ total number of eyes tested) *100] and percent negativity [number of eyes with negative InflammaDry® result/ total number of eyes tested) *100] was also calculated. A Chi-Square analysis was conducted to determine the statistical significance between InflammaDry® results and development of oGVHD. Furthermore, to evaluate InflammaDry® qualitative results, data were plotted with the x-axis as grade 0-4 and number of eyes as y-axis. Regarding evaluation of OSDI-6 questionnaire scores, all scores were used in the calculation of range, average and median along with percentage of scores ≥4 and percentage of scores <4.

RESULTS

Demographic data collected on study participants showed that the average age of subject was 61.52 years-old with an age range of 36 to 73. The races of the subjects were 91.30% White, 4.35% Black and 4.35% were of "other" race of which was not specified in the electronic medical health record. Of the sex of the subjects, 56.52% were male and 43.48% were female (Table 2).

The type of cancer each participant was diagnosed with was collected. These diagnoses included acute myeloblastic leukemia, acute lymphoblastic leukemia, prolymphocytic leukemia, aplastic anemia, myelodysplastic syndrome, chronic myelomonocytic leukemia, myelofibrosis, angioimmunoblastic T-cell lymphoma, and chronic myelogenous leukemia. Additional information regarding bone marrow transplantation including donor demographics, source of stem cells, and condition regimens are documented. 100% of stem cells were sourced from donor peripheral blood (Table 2).

InflammaDry® results collected on 46 eyes (23 participants) showed 91.30% of eyes were positive for MMP-9 and 8.70% were negative. Of the eyes that tested positive, 32 eyes were trace positive, 7 were weak positive, 2 were positive and 1 was strongly positive (Figure 3).

A comparison of oGVHD diagnosis related to InflammaDry® results was completed (Table 3).

Each participant had either positive InflammaDry® results in both eyes or negative InflammaDry® results of both eyes, which allowed for this comparison to be possible. Of the participants who had positive InflammaDry® results, four developed oGVHD while twelve did not. Out of the four subjects who developed oGVHD, seven out of eight eyes had an InflammaDry® score of 1 (trace positive) while one eye had an InflammaDry® score 2 (weak positive). Of the participants who had negative InflammaDry® results, zero participants developed oGVHD. From these results, InflammaDry® sensitivity, specificity, PPV and NPV were calculated. InflammaDry® was found to have a sensitivity of 1, specificity of 0.1429, PPV of 0.2500 and NPV of 1. Chi-square analysis revealed a chi-square value of 0.64. With 1 degree of freedom, the p-value was >0.05, and therefore no statistical significance was found between InflammaDry® results and the development of oGVHD.

An OSDI-6 questionnaire was collected on all 23 participants. The scores ranged between 0 to 9 with an average score of 2.78 and median score of 2. The majority of participants (60.87%) had a score of less than 4 while 39.13% had a score of 4 or above (Figure 4). Of the four subjects who developed oGVHD, two had an OSDI score of 4 or greater (score of 4 and 5) while the other two subjects had an OSDI score of 1 and 0.

To further investigate potential reasons for positive InflammaDry® results, the history of ocular treatments and past medical history of the patients were evaluated (Table 4 and Table 5). Additionally, chronic GVHD characteristics and NIH score of oGVHD of participants who developed oGVHD were collected (Table 6).

DISCUSSION

While InflammaDry® was found to have a sensitivity and NPV of 1 in detecting oGVHD development, the specificity of InflammaDry® was low at 0.1429, meaning that this point-of-care test resulted in many false positives. Additionally, the PPV of InflammaDry® was low at 0.2500, meaning that while the majority of participants had a positive InflammaDry® result, few participants developed oGVHD. No significant difference was found between patients who developed oGVHD versus patients who did not develop oGVHD and their InflammaDry® result (p-value> 0.05). Overall, these results conclude that InflammaDry® has limited application in determining which patients are at risk of developing oGVHD. Furthermore, InflammaDry® was positive in 91.30% of eyes that were tested, meaning that most participants were experiencing ocular inflammation, whether symptomatic or asymptomatic. Literature has shown that prophylactic treatment may be helpful in reducing development of oGVHD; however, no participants in this study chose to initiate treatment. Given that the vast majority of eyes tested positive and that it can be assumed InflammaDry® would continue to test positive following completion of HSCT, InflammaDry® would not be a helpful tool for providers to use to help determine if a patient is developing oGVHD.

Each participant completed an OSDI-6 form with score result possibilities of 0 to 24. The higher the score indicates more severe ocular surface disease symptoms; however, even a score of 4 or more suggests that the participant has ocular surface disease.[21] OSDI-6 results show that most participants (60.87%) were experiencing little to no ocular surface disease symptoms and did not have ocular surface disease (Figure 4). In fact, the average OSDI-6 score was 2.78 and median score of 2. However, 91.30% of participants had a positive InflammaDry® test (Figure 3). This indicates ocular inflammation is present but participants are asymptomatic. This ocular inflammation may be secondary to multiple causes including history of chemotherapy, systemic diseases, history of ocular disease and ocular treatments. Four participants developed oGVHD, all of which had positive InflammaDry® tests of both eyes. Two of these participants had systemic autoimmune diseases; rheumatoid arthritis and rosacea, both of which have been shown to cause ocular inflammation.[22,23] The participant diagnosed with rheumatoid arthritis also had Type II DM, which is a known risk factor for the development of oGVHD.[3] The inflammation detected by InflammaDry® may also be due to history of ocular disease and treatments (Table 4).

Three subjects, each of which had positive InflammaDry® testing and one of which developed oGVHD, had previously undergone cataract surgery, which is highly associated with ocular surface disease and therefore may have caused ocular inflammation in these participants.[19] In contrast, one patient was receiving intravitreal bevacizumab for exudative macular degeneration. Subconjunctival bevacizumab has been shown to be effective in ocular surface disease treatment and can therefore decrease ocular inflammation.[24] However, this patient, who was not receiving other ocular treatments and did not have additional ocular diseases, had positive InflammaDry® results in both eyes, suggesting that another cause for ocular inflammation may be secondary to other medications this patient was receiving such as chemotherapy.

A limitation of this study is the small sample size. At the start of the study, it was expected that 35-40 subjects would be recruited over three months. However, over nine months 124 subjects were screened for eligibility. Of these subjects, 75 were eligible for participation following the inclusion and exclusion criteria. However, only 23 subjects were enrolled in the study. Reasons for non-enrolment were for the following reasons: subject not wishing to participate in study or team member was unable to meet with subject during their allogeneic bone marrow transplant consultation visit. To combat the low recruitment rates, an information pamphlet about the study was made and included in the information packet each patient received at their allogeneic HSCT consultation visit. The addition of the pamphlet was implemented two months after the study was initiated. However, given the continued difficulty of recruit-

ing patients after extension of study period, it was decided to conclude the study with only 23 participants. The small sample size may be a limitation of this study. However, despite the smaller than expected participant recruitment, the data shows strong evidence that InflammaDry® should not be used as a screening tool to detect the onset of oGVHD given that there was no significant difference in the development of oGVHD based on InflammaDry® results (p-value > 0.05).

Another limitation of this study is the generalizability. While the study recruited nearly a 50:50 ratio of genders (56.52% male and 43.48% female), this study lacked variability in the race of participants. The majority of participants (91.30%) were White. This lack of variety may have been secondary to the population that was being screened given that Whites have a higher rate of developing leukemia of all types as compared to Black and Asian-Pacific Islanders.[25]

Lastly, another limitation of this study is the amount of data that was able to be collected. Past medical history, treatment history and follow-up history were limited by the fact that only information gathered within our hospital system's electronic health record (EHR) was able to be collected. Any data (diagnoses, surgical history, past medical history, etc.) not documented in our system could not be collected or included in our data analysis. Additionally, there is the possibility of non-documentation of oGVHD development within the EHR, which could have further impacted our data collection.

CONCLUSION

Of the eligible participants undergoing planned allogeneic HSCT, 91.30% tested positive for InflammaDry®, suggesting participants were already experiencing ocular inflammation secondary to multiple factors including chemotherapy, systemic disease, or previous ocular therapies. However, only 39.13% of participants were noted to be experiencing ocular surface disease symptoms related to this detected ocular inflammation. Despite the evidence that these participants have MMP-9 present in their tear film, on patient follow-up after completion of allogeneic HSCT, InflammaDry® was found to have a low specificity of 0.1429 and low PPV of 0.25. No statistical significance was found between InflammaDry® result and development of oGVHD (p-value > 0.05). These data suggests that InflammaDry® would not be a useful tool to detect the onset of oGVHD nor would InflammaDry® be helpful to predict which patients are at risk of developing oGVHD. While InflammaDry® may not be the tool for earlier detection of oGVHD, this study clearly showed that a high percentage of patients have ocular inflammation prior to undergoing allogeneic HSCT. Therefore, initiation of prophylactic treatment may be the best option for decreasing risk of development of oGVHD. Given that oGVHD continues to be a cause of high morbidity and reduced quality of life of patients, further research should be completed to determine a test for earlier detection of the disease along with determining prophylactic treatment regimen.

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TABLE 1: Ocular Surface Disease Index (OSDI-6) developed by Dr. Heiko Pult and Dr. James Wolffsohn to efficiently detect ocular surface disease based on patient symptoms. Adapted from Pult, 2019.[7]

Ocular Surface Disease Index 6 (OSDI-6)					
	Constantly	**Mostly**	**Often**	**Sometimes**	**Never**
Light sensitivity	4	3	2	1	0
Blurred vision	4	3	2	1	0
Difficulty driving at night	4	3	2	1	0
Difficulty watching TV (or similar)	4	3	2	1	0
Ocular discomfort during windy conditions	4	3	2	1	0
Ocular discomfort in places or areas with low humidity	4	3	2	1	0

The scores for each symptom are summed to obtain a total score. If the subtotal score is greater than 4, ocular surface disease is likely present

TABLE 2. Demographic information of subjects; N=23. Demographic data collected includes age, race, gender, and diagnosis of participants; donor age and gender; and conditioning regimen and course of stem cells used for bone marrow transplant.

Demographics		
Age	Range (years)	Median (years)
	36-73	63
Race	Number of Participants	Percentage of Participants (%)
White	21	91.30
Black	1	4.35
Other	1	4.35
Gender	Number of Participants	Percentage of Participants (%)
Male	13	56.52
Female	10	43.48
Donor Age	Range (years)	Median (years)
	19-62	27
Donor/Patient Gender	Number of Participants	Percentage of Participants (%)
Female/female	8	34.78
Male/male	8	34.78
Female/male OR Male/female	7	30.43
Diagnosis at Transplant	Number of Participants	Percentage of Participants (%)
Myelodysplastic Syndrome (MDS)	7	30.43
Acute Myeloblastic Leukemia	4	17.39

Myelofibrosis	3	13.04
Acute Lymphoblastic Leukemia (ALL)	2	8.70
Chronic Myelomonocytic Leukemia	1	4.35
MDS/Myeloproliferative Neoplasm	1	4.35
Angioimmunoblastic T-cell Lymphoma	1	4.35
Chronic Myeloid Leukemia/ALL	1	4.35
T-cell Prolymphocytic Leukemia	1	4.35
Acute Undifferentiated Leukemia	1	4.35
Aplastic Anemia	1	4.35
Conditioning Regimen	Number of Participants	Percentage of Participants (%)
Reduced Intensity	20	86.96
Non-myeloablative	3	13.04
Source of Stem Cells	Number of Participants	Percentage of Patients (%)
Peripheral Blood	23	100

TABLE 3. Comparison of InflammaDry® test results to subjects diagnosed with oGVHD and subjects who have not been diagnosed with oGVHD. N=18 participants.

	Subjects Diagnosed with oGVHD	Subjects without Diagnosis of oGVHD	Total
Positive InflammaDry® Test	4	12	16
Negative InflammaDry® Test	0	2	2
Total	4	14	18

TABLE 4. History of ocular treatments in participants. Treatments of participants who tested positive for InflammaDry® are compared to treatments of participants who tested negative for InflammaDry®. N=23 participants.

Ocular Treatments in InflammaDry® Positive Participants	Number of Participants
Radial keratotomy	1
Bimatoprost	1
Cataract surgery	3
Fluoroquinolone topical antibiotic	2
Prednisolone acetate	1
Polyethylene glycol	1
Intraocular Avastin	1
Polyvinyl alcohol	2
No treatment	14
Ocular Treatments in InflammaDry® Negative Participants	
No treatment	2

TABLE 5. Past medical history (PMH) of participants. PMH of participants who tested positive for InflammaDry® are compared to PMH of participants who tested negative for InflammaDry®. N=23 participants.

Past Medical History in InflammaDry® Positive Participants	Number of Participants
Asthma	1
Hyperlipidemia	1
Rosacea	1
Spinal stenosis	1
Rheumatoid arthritis	1
Type II Diabetes Mellitus	1
Past Medical History in InflammaDry® Negative Participants	Number of Participants
Polycystic kidney disease	1
Hypertension	6
Hyperlipidemia	6
Migraine	2
Transverse myelitis	1
Coronary artery disease	2
Stroke	1
Thrombus (deep vein thrombosis, pulmonary embolism)	3
Type II Diabetes Mellitus	1
Calcium pyrophosphate deposition disease	1
Inflammatory arthritis	1
Asthma	1

TABLE 6. Characteristics of chronic GVHD of participants who developed ocular GVHD. N=4 participants.

Participant	Number of Sites Involved	Location of Sites Involved	NIH Score of oGVHD
1	3	Gastrointestinal, Skin, Eyes	3
2	3	Gastrointestinal, Skin, Eyes	2
3	2	Skin, Eyes	2
4	3	Gastrointestinal, Skin, Eyes	1

FIGURES

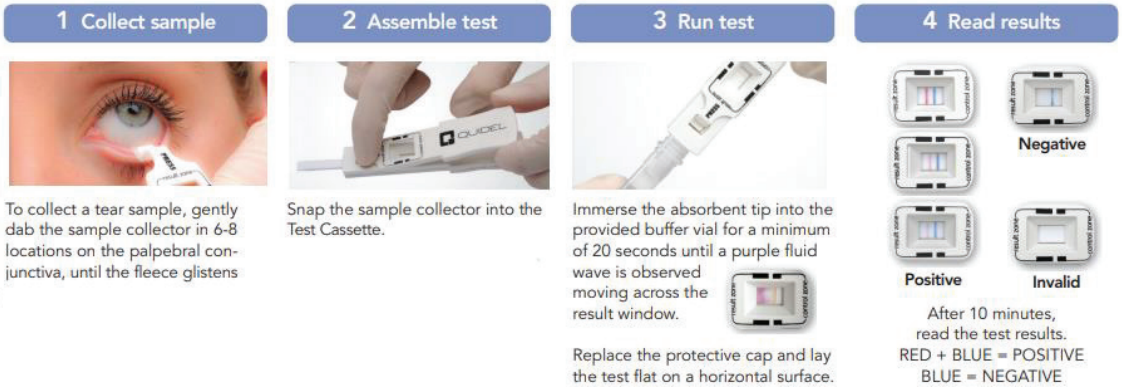


FIGURE 1. Four step process on correct usage of InflammaDry®, adapted from InflammaDry®, 2021.20 InflammaDry® Result

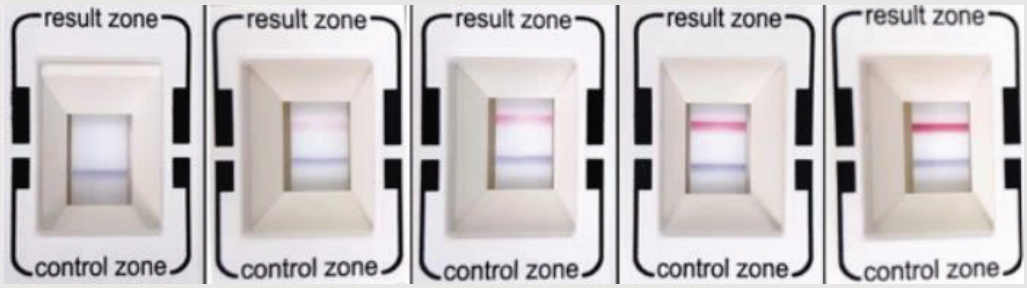
InflammaDry® Result					
	result zone / control zone	result zone / control zone	result zone / control zone	result zone / control zone	result zone / control zone
Interpretation	Negative	Trace	Weak Positive	Positive	Strong Positive
Grade	0	1	2	3	4

FIGURE 2. **InflammaDry® grading assessment, adapted from Kim, 2021.18**

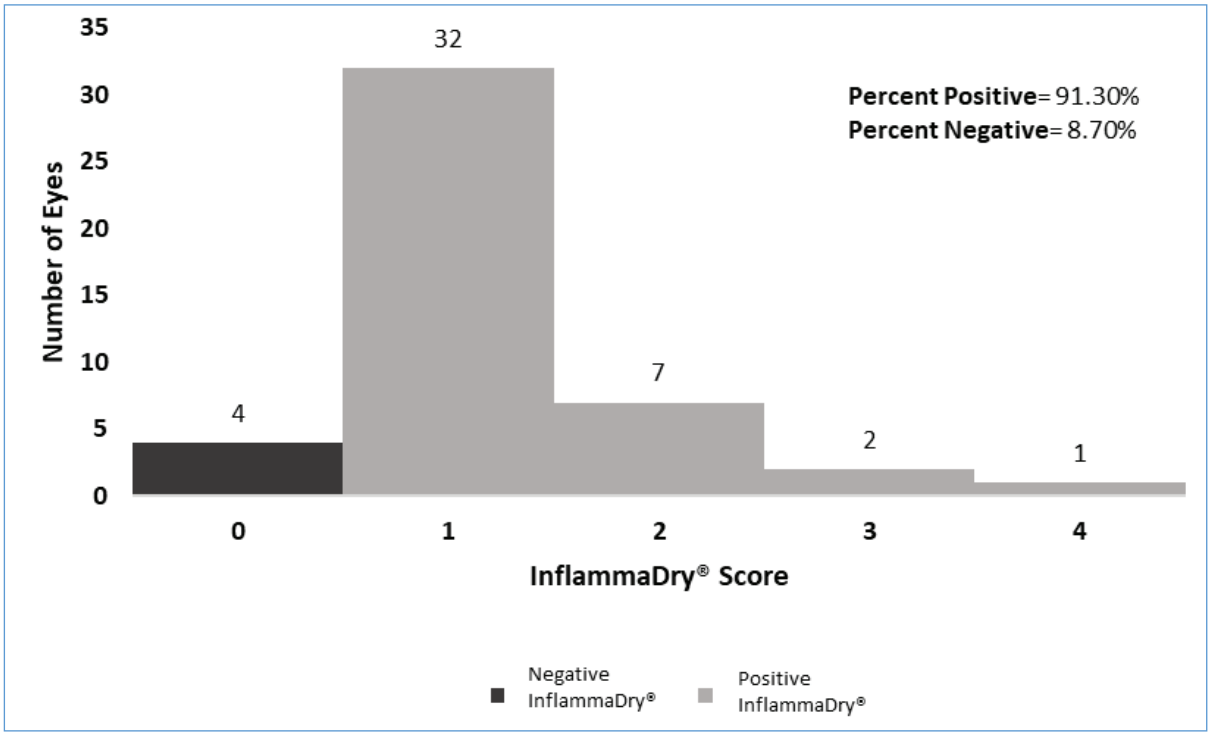
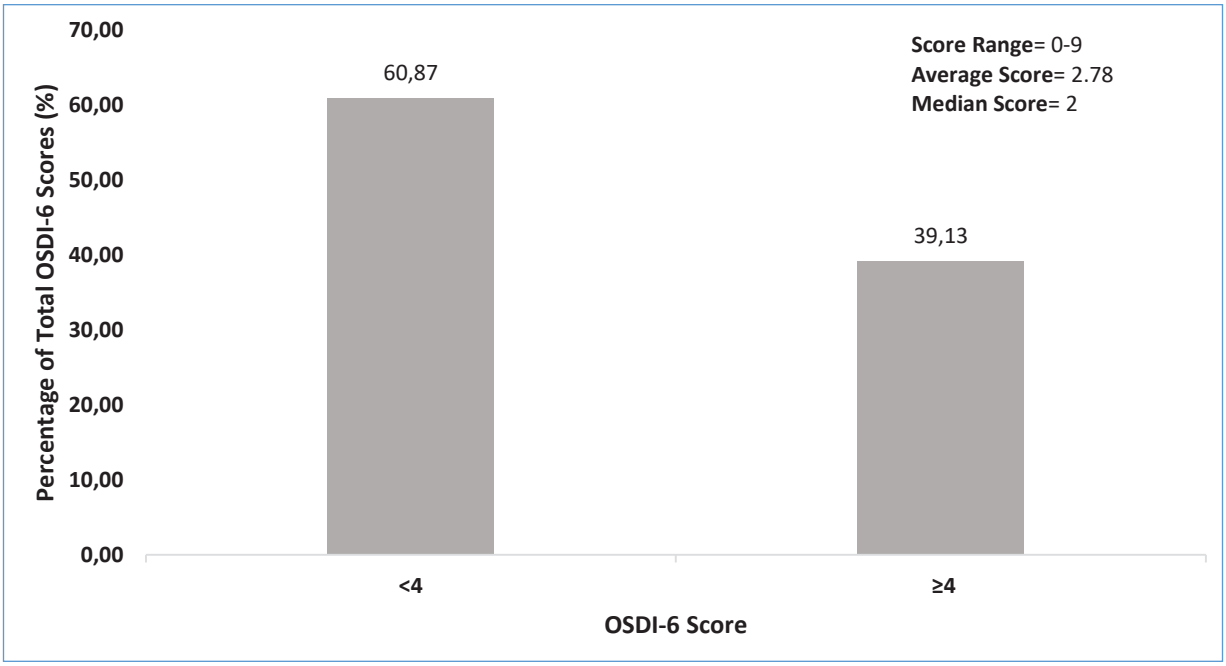


FIGURE 3. **Analysis of InflammaDry® test results. Positive InflammaDry® tests were scored on a scale of 1 (trace) to 4 (strong positive). Negative InflammaDry® tests were given a score of 0. N=46 eyes (23 participants). Of the 46 eyes tested with InflammaDry®, 91.30% resulted positive and 8.70% resulted negative.**



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