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CLINICAL RESEARCH

Quantitative Assessment of Dacryoscintigraphic Images in the Evaluation of Epiphora

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ABSTRACT *Background*: At the present time, only visual analysis is implemented on dacryoscintigraphic images and quantitative assessments are not routinely obtained. The authors have designed a novel, simple, quantitative method for the diagnosis of sac and post-sac obstructions based on the dacryoscintigraphic images. *Method*: Fifty-nine patients with severe unilateral epiphora were included and the contralateral asymptomatic eyes were used as controls. After ocular instillation of 0.1 cc isotonic saline containing 4 MBq ^{99m}TcO4, dynamic images were obtained for 20 minutes. Visual interpretation was done by two blinded specialists in nuclear medicine. A Time-Activity Curve (TAC) was generated for each eye and its pattern was divided to plateau type, shallow-down sloping and deep-down sloping. The excretion ratio (expressed as the percentage of drained activity) in the 2nd, 3rd, 5th, 7th, 10th, 15th and 20th minute of the study was calculated based on the following formula: (the total count in the region of interest (ROI) in the 1st minute – the total ROI count in the 2nd, 3rd, 5th, 7th, 10th, 15th or 20th minute/the total ROI count in the 1st minute) × 100. The results of the quantitative analysis were compared with the clinical symptoms, visual analysis and TAC pattern. *Results*: At the optimal cut-off points for the 2nd, 3rd, 5th and 7th minute, the sensitivity of the prediction of obstruction was 76%, 72%, 71% and 69%, respectively. The correlation between visual interpretation and the TAC pattern was statistically significant. *Conclusion*: The quantitative evaluation of dacryoscintigraphic images would contribute greatly to achieving an easier and more objective interpretation of the scintigraphic results and also provides a reliable tool for inter-individual comparison and the follow-up of patients. As it is the first time that this innovative method has been examined clinically, it will be necessary to investigate its clinical utility in a larger series of patients.

KEYWORDS Dacryoscintigraphy; lacrimal system; epiphora; image assessment

INTRODUCTION

Epiphora is a relatively common ophthalmologic complaint, particularly in the elderly (Linberg & McCormick, 1986; Traquair, 1941). Stenosis of the nasolacrimal duct (such as the development of involutional stenosis with aging) is probably one of the most common causes of this symptom; women are affected twice as often as men (Lanciego et al., 2001). Over the years, numerous diagnostic techniques have been used to evaluate the lacrimal drainage system (Becker & Berry, 1989; Guzek et al., 1997; Hoehn et al., 1976; Manfre et al., 2000; Massaro et al., 1990; Rose & Clayton, 1985; Rubin et al., 1994; Toprak et al., 2002; Zappia & Milder, 1972), including irrigation, dacryocystography, dacryoscintigraphy, MRI, DDT and the Jones test (Guzek et al., 1997; Hoehn et al., 1976; Manfre et al., 2000; Rose & Clayton, Toprak et al., 2002); however, the need for development of a reproducible practical test to distinguish patients with different degrees of disease has been emphasized (Toprak et al., 2002).

For dacryocystography, the cannula is placed in the lacrimal sac. The major drawback of this method is its invasive nature and also that it evaluates only the lower lacrimal system (Guzek et al., 1997). Catheterization of the lacrimal system for contrast dacryocystography carries at least the same risk of trauma by probing as does its repair, and is probably not justified by the incomplete information obtained. Also, the procedure is most annoying to the patient, which limits its use in children (Hoehn et al., 1976). Rose & Clayton (1985) compared dacryocystography with scintigraphy and found better sensitivity (77% vs. 51%) for scintigraphy. In fact, this confirms the non-physiological character of dacryocystography. Moreover, Nixon et al. concluded that the results of dacryocystography have no relevant influence on the choice of treatment (Sorensen & Jensen, 1977). Hence, these findings do not support the routine use of this imaging technique in the assessment of the nasolacrimal drainage system. The same drawbacks are present in the use of computed tomography, so that its application as a screening test is also limited.

As an alternative technique, dacryoscintigraphy provides an objective tool to evaluate the lacrimal drainage system under physiologic conditions. However, the criteria for objective analysis of epiphora by means of dacryoscintigraphy have unfortunately not yet been clearly determined. A recent report on the quantitative analysis of dacryoscintigraphy has confirmed the usefulness of this approach in the assessment of epiphora (Jager et al., 2005). At the present time, however, only visual analysis is implemented on dacryoscintigraphic images and quantitative assessments are not routinely obtained. In view of the equivocal results that are sometimes obtained by qualitative visual assessment, quantitative analysis could be helpful in establishing the final definite diagnosis.

The diagnosis of lacrimal drainage system obstruction at the pre-sac level is relatively straightforward,based on the visual interpretation of scintigraphic images that reveal absence of radiotracer entry into the cannalicula and lacrimal sacs, but the diagnosis of obstruction at the sac and post-sac level is more difficult. Therefore, in this study, we applied a simple, non-invasive, quantitative method for the assessment of dacryoscintigraphic images for the diagnosis of sac and post-sac obstructions of the nasolacrimal drainage system.

MATERIAL AND METHODS

Study Population

The study was carried out between January 2004 and September 2005. As an inclusion criterion, only patients with unilateral epiphora were selected and the contralateral eyes were used as the control. As another inclusion criterion, we selected only those patients who had severe epiphora in the affected eye, meaning a severity of grade 3 or 4 based on the classification of Munk et al. (Jager et al., 2005). Hence, because of the severity of the complaints, all of our patients were candidates for dacryocystorhinostomy (DCR) or dacryocystoplasty (DCP).

All patients had undergone a routine ophthalmologic examination to exclude any cause of reflex epiphora (e.g., facial nerve palsy, lower eyelid laxity and posttraumatic deformity). Finally, 59 consecutive patients (36 females and 23 males) with a mean age of 51.9 ± 14.6years (age range: 21–87 years) who had not been previously undergone DCR or probing were entered into the study. All patients had normal palpebral statics and no ocular surface irritation or infection were present.

Dacryoscintigraphy

Routine dacryoscintigraphy was performed on all patients: the patient sat upright in front of a gamma camera with the head fixed in an adjustable stand (Hurwitz

et al., 1975b; Sorensen & Jensen, 1977). The distance between the cornea and the surface of the collimator was relatively equal and less than 20 mm for all patients. A single-head gamma camera (ADAC) equipped with a low-energy, high-resolution collimator was used and images were acquired in a 256 × 256 matrix. Image acquisition was performed for 20 min (at one frame per minute) following ocular instillation of 0.1 cc isotonic saline containing 4 MBq $^{99m}TcO_4$ at the lateral canthus of each conjunctival sac.

The visual analysis was performed by two experienced nuclear medicine specialists familiar with dacryoscintigraphy who were blinded to other clinical data, and the final diagnoses were made by consensus. The visual interpretation was categorized as: normal, partial obstruction or complete obstruction. These criteria were only based on the experience of our physicians. Notable drainage of activity from the lacrimal sac before the 5th minute of the study was considered normal. Delayed radiotracer washout from the lacrimal sac (in the presence of some drainage of activity after the first 5 minutes of the study) was considered partial obstruction; and the absence of notable radiotracer washout up to the end of the study was regarded as complete tear flow obstruction.

All patients had been referred by their ophthalmologist for a scintigraphic assessment and no additional intervention was performed on these patients. However, the purpose of the study was described to all patients and verbal consent was obtained.

Image Analysis

A region of interest (ROI) was drawn for each eye, positioned over the whole eyeball area plus the lacrimal sac. A Time–Activity Curve (TAC) was generated for the ROI. The pattern of the TAC was visually classified into three categories: plateau type, shallow down-sloping, and deep down-sloping (Figs. 1 and 2).

We calculated the excretion ratio (expressed as the percentage of drained activity) in the 2nd, 3rd, 5th, 7th, 10th, 15th and 20th minute of the study, based on the following formula: (the total ROI count in the 1st minute – the total ROI count in the 2nd, 3rd, 5th, 7th, 10th, 15th or 20th minute/the total ROI count in the 1st minute) × 100. After the quantitative analysis, the results were compared with the clinical symptoms, TAC pattern and visual analysis.

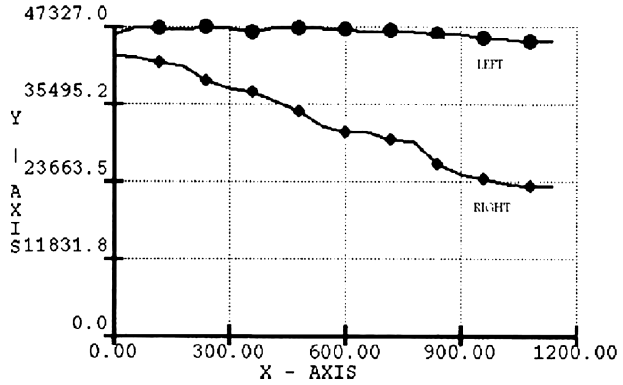

FIGURE 1 **TAC of a patient with unilateral epiphora (left eye). The TAC of the left eye shows a plateau-type pattern, while the TAC of the contralateral eye is deep down-sloping.**

Statistical Analysis

The percentage of drainage in the above-mentioned minutes was taken as a variable. The parameters in both eyes (symptomatic and asymptomatic) were compared using the independent student's t test. ROC analysis was performed with various cut-off levels and, subsequently, the corresponding sensitivities and specificities in the detection of abnormal tear clearance were determined for each cut-off level. SPSS for windows (release 11.5.0) was used for statistical analysis. Two-sided p-values less than 0.05 were considered significant.

RESULTS

As discussed earlier, we had decided to exclude all patients with pre-sac obstruction in the visual analysis; however, no case of pre-sac obstruction was seen in our study population.

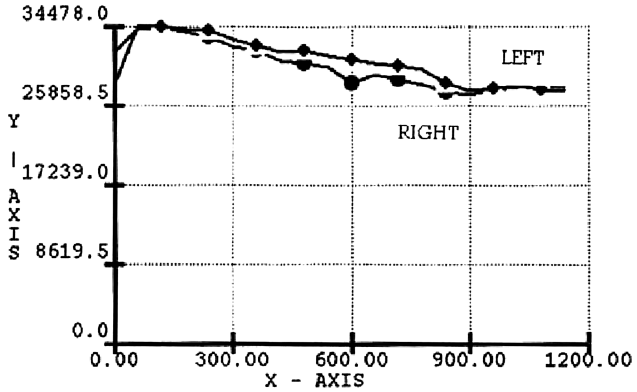

FIGURE 2 **TAC of a patient with unilateral epiphora (right eye). The TACs of both eyes show a shallow down-sloping pattern.**

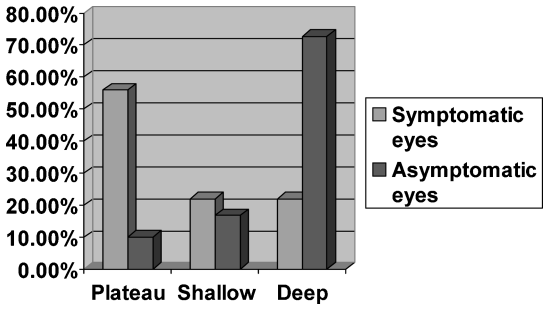

FIGURE 3 The frequency of different TAC patterns in two groups of symptomatic and asymptomatic eyes.

Time-Activity Curves

As shown in Figure 3, the TAC patterns in 59 symptomatic eyes evinced deep down-sloping in 13 patients (22%), shallow down-sloping in 13 patients (22%), and the plateau-type in 33 patients (55.9%). The respective patterns were detected in 43 (72.8%), 10 (16.9%) and 6 (10.1%) of the asymptomatic eyes. The difference was statistically significant ($P < 0.01$). The correlation between visual interpretation and the TAC pattern was also significant ($P = 0.0001$).

Excretion Ratio

The excretion ratios of the epiphoric and asymptomatic eyes are shown in Table 1. The differences between the two groups were statistically significant only in the 2nd, 3rd, 5th and 7th minutes of the study, not in the later 10th, 15th, and 20th minutes (all *P*-values >0.05). Based on the ROC analysis, we endeavor to find optimal cut-off points for the prediction of obstruction, the best results of which are presented in Table 2.

DISCUSSION

Based on our study results, it is possible to simply quantify the dacryoscintigraphic results in patients suffering from epiphora. Using this easily-performed quantification technique, presenting a quantitative parameter when reporting the results of dacryoscintigraphy may enable an ophthalmologist to arrive at a more objective assessment of the severity of the symptoms and thus improve his decision making; such a method, moreover, provides an objective criterion for further follow-up of the symptoms. As this is the first time that our innovative method of assessment has been examined, it will be necessary to investigate its clinical utility in comparison with other gold-standard methods for the investigation of the lacrimal drainage system.

We also found a significant correlation between the curve patterns and the visual interpretation. This finding may help us to determine the distinction between different severities of obstruction; however, this impression also requires further assessment.

In our study, we found that the closer we came to the end of the scintigraphy, the smaller the difference between the two groups in the clearance of the radioactivity. Taking into account the fact that previous studies have conclusively shown that a large part of the radiopharmaceutical drainage occurs in the very first moments after instillation, one of the main factors interfering with the diagnostic accuracy of our simple parameter is probably the long duration of image frames. Most likely, had the image frames been of shorter duration (e.g., 15 seconds) and had we calculated the percentage clearance in these frames of short duration, our diagnostic accuracy would have increased remarkably. Verification of the accuracy or validity of such a conclusion requires further research.

Unfortunately, in spite of inherent advantages of the dacryoscintigraphic analysis of the lacrimal drainage system over other competing methods (Amanat et al., 1979; Astakhov et al., 1999; Chmielowski et al., 2000;

TABLE 1 The excretion ratio of activity at different minutes of the acquisition.

Ratio of clearance	Symptomatic eyes	Asymptomatic eyes	*P*-value
2nd min	$.01 \pm .02$	$.12 \pm .09$	< 0.0001
3rd min	$.04 \pm .04$	$.17 \pm .10$	< 0.0001
5th min	$.09 \pm .08$	$.24 \pm .12$	< 0.001
7th min	$.19 \pm .18$	$.29 \pm .16$	< 0.01
10th min	$.20 \pm .18$	$.33 \pm .16$	$P > 0.05$
15th min	$.24 \pm .21$	$.43 \pm .17$	$P > 0.05$
20th min	$.28 \pm .22$	$.47 \pm .18$	$P > 0.05$

TABLE 2 Sensitivity and specificity of different cut-off points for the detection of lacrimal duct obstruction.

Variables	Cut-off point	Sensitivity	Specificity
Excretion ratio at the 2nd min	1.6%	76%	75%
Excretion ratio at the 3rd min	5.6%	72%	72%
Excretion ratio at the 5th min	13%	71%	30%
Excretion ratio at the 7th min	20%	69%	61%

Robertson et al., 1979), there have been only few previous attempts to quantify of these scintigraphic images (Hilditch et al., 1983; Hurwitz et al., 1975a,b; Jager et al., 2005). In these efforts, different and sometimes very complex kinetic models have been applied for the analysis of the disappearance of tracer from the eye and its subsequent passage to the lacrimal sac and nasolacrimal duct (Jager et al., 2005). In a recent study, Wearne et al. (1999) used qualitative factors such as pre-sac delay and pre-duct delay as output parameters. Despite the difficulty in the precise definition of these terms, they found a high sensitivity for dacryoscintigraphy. As emphasized by Jager et al. (2005), the complex parameters used in old studies are less valuable for clinical purposes and the simpler methods, such as those used in our study and that of Jager et al. may be more practical. Also, in some of these reports, the first 7 minutes of the study were excluded empirically; as is clear from our findings, these first 7 minutes of the study are extremely important and, in fact, provide the most reliable objective data from the scintigraphic images (Jager et al., 2005; Sorensen & Jensen, 1979).

In the recent study by Jager et al. (2005), a new quantitative physiological method was introduced. They presented two simple parameters for quantifying dacryoscintigraphy, based solely on the disappearance of tracer from the eye. In the investigators' opinion, the parameters *T*1 (the activity in the first minute after administration) and LCR (the proportion of activity that disappears from the eyeball in 15 min.) are easy to understand and have adequate sensitivity and specificity (77/95% for *T*1 and 71/100% for LCR) for the detection of tear drainage dysfunction. Therefore, over 70% residual activity after 1 min. and less than 50% disappearance of activity in 15 min. have been considered as parameters that accurately identify patients with severe tear drainage problems that may require intervention. However, this method has the same drawback as our method: These methods are not suitable for determining the exact anatomical site of obstruction further down the lacrimal drainage system, e.g., in the nasolacrimal duct (Jager et al., 2005).

In contrast to the findings of Wearne et al. (1999) and also those of Jager et al. (2005), our study results do not confirm the difficulty of using curves from the lacrimal sac for clinical purposes. In our study, the clearance of the activity up to the 2nd, 3rd, 5th and 7th minute was found to be a good and relatively sensitive diagnostic criterion for detection of lacrimal duct obstruction in normal subjects. However, our findings were not free of drawbacks: Lacrimal duct obstruction can be an involutional disorder, developing and becoming worse with aging. Our study was carried out on patients with unilateral symptoms and asymptomatic eyes were considered as controls; so it could be possible that the asymptomatic eyes were afflicted by the same involutional process and were not actually normal (they could have been in a subclinical state of obstruction). Ayub et al. (2003) also found great variability in dye flow between both eyes of the same volunteer, making the use of the contralateral eye as a control eye for similar investigations questionable. Therefore, to determine the excretion ratio, we suggest that a study should be carried out on normal and symptom-free individuals of different age groups, after which the results should be compared to those in the symptomatic patients of the same age group. Another explanation for discrepancy between the scintigraphic result and the patient's symptoms is the fact that there is a discrepancy between the degree of discomfort experienced by the patient and the severity of the underlying pathological process (Conway, 1994; Jager et al., 2005). While some epiphoric eyes are accompanied by patent lacrimal systems, there are also asymptomatic eyes with some degree of stenosis in the tear drainage ducts (O'Donnell & Shah, 2001; Jager et al., 2005). Also, it is well known from the analyses of volunteers that the transit time of a dye through the nasolacrimal ducts shows a high intra-individual variability (Ayub et al., 2003; Tucker & Codere, 1994). In the study by Ayub et al. (2003), the standard deviation was 3.23 minutes with minimum and maximum values of between 15 seconds and more than 18 minutes in one case. Several factors have been discussed that determine the high level of intra-individual variability in dye transit time: fluctuations within a single individual over time, family predisposition, emotional status, the fluid balance, blink rate, basal tear film production, atmospheric conditions of testing, tear pump efficiency, and hormonal status.

In our study, at the optimal cut-off points at the 2nd, 3rd, 5th and 7th minute, the sensitivity of prediction of obstruction was 76%, 72%, 71% and 69%, respectively. Our study findings and those of Jager et al. (2005) confirm the independent diagnostic value of dacryoscintigraphy in patients with epiphora, compared to clinical assessment. Therefore, it seems that a simple quantitative method provides objective data on the degree of

tear-flow disturbances. As emphasized by Jager et al. (2005), this could be helpful in the selection of patients that are more suitable for current invasive treatments such as dacryorhinoplasty or dacryorhinostomy. In fact, the quantitative methods of dacryoscintigraphy should be standardized and quantitative results (in different age groups) should be incorporated in the interpretation of final images. Combination of visual and quantitative analysis could be more helpful than each technique alone. Moreover, our simple parameters have the same drawback encountered by Jager et al. (2005) in calculating the T1: the calculated T1 parameter may be incorrect when the interval between the start of administration and the start of the dynamic study is long, as many studies have indicated that the initial tracer disappearance is very fast. Therefore, tracer administration should be carried out rapidly by an experienced technician in both eyes, and should always be complete within 15–20 seconds, thus minimizing the error in the subsequent minute.

CONCLUSION

In our view, the quantitative evaluation of dacryoscintigraphic images, no matter by what parameters they are evaluated (parameters devised by Jager et al. (2005) or those designed in our study), would contribute greatly to an easier interpretation of the scintigraphic results and also provides an objective method for the follow-up of patients; moreover, it provides a reliable tool for inter-individual comparison. Each and every nuclear medicine institute may avail itself of any of the parameters mentioned above in its interpretation of the images, but such a procedure requires that these parameters must be standardized among a large group of people, including both patients and controls.

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