Juvenile Recurrent Parotitis: A Retrospective Comparison of Sialendoscopy Versus Conservative Therapy

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Objectives/Hypothesis: There are several therapeutic approaches to treat juvenile recurrent parotitis. The aim of this study was to compare sialendoscopy, including prophylactic cortisone irrigation, with observation and a conservative approach of antibiotic therapy alone.

Study Design: Retrospective study, tertiary clinical center.

Methods: The charts of patients treated for juvenile recurrent parotitis between November 2004 and June 2011 were reviewed. Initial acute flares were always treated with a course of antibiotics. Subsequent treatment consisted of either salivary gland endoscopy including cortisone irrigation or additional pure antibiotic therapy. Patients treated with salivary endoscopy were compared to patients treated with antibiotics alone with regard to the number of inflammatory episodes and pain intensity pre- and posttreatment.

Results: Thirty-six patients were treated during the period of study, 15 with salivary endoscopy with cortisone irrigation and 21 with antibiotic therapy alone. A significant reduction in recurrent episodes and pain intensity following therapy was found in both groups. With respect to these two outcomes, the comparison showed two therapeutic options of equal merit.

Conclusions: Salivary gland endoscopy is an option in the management of juvenile recurrent parotitis that helps in confirming the diagnosis and that also provides therapeutic intervention. However, although there are further advantages, the definitive value of salivary gland endoscopy requires ongoing evaluation in further prospective studies.

Key Words: Juvenile recurrent parotitis, salivary gland endoscopy.

Level of Evidence: 4.

INTRODUCTION

Juvenile recurrent parotitis (JRP) is an inflammatory disease of the salivary gland of unknown etiology. It occurs between the ages of 4 months and 15 years, but is usually self-limiting with puberty. Boys are affected more often than girls. Despite its rareness, it nevertheless represents the second most common inflammatory salivary gland disease of childhood after mumps. Symptoms include unilateral, rarely bilateral, swelling of parotids with redness, pain, occasional fever, and hyposecretion of the affected salivary gland. The disease flares up for 1 or 2 days on average, but in rare cases it may last for weeks. The interval between flares can extend to several years. Imaging of the asymptomatic side usually shows the typical findings of sialectasis to a lesser degree than viewed in the symptomatic gland.[1] The typical sonogram shows a hypoechoic picture with multiple hypodensities and loose cloud-like structures.

A theory of multifactorial etiology is generally preferred today, although many other views exist. In 1945, Bailey proposed the presence of a congenital abnormality.[2] He drew a parallel to bronchiectasis of the lungs with a congenital dilatation of the duct system, which would predispose infection. Congenital changes in the ductsystem,[1,3–6] autosomal dominant inheritance,[7] autoimmune disease,[1,8] immune deficiency,[9–11] and disrupted enzyme activity[12] have all been discussed. Some have looked for the origin of disease in bacterial or viral infections. Pus is occasionally found during acute exacerbations, but it is otherwise present in only the most isolated cases. There is usually a grayish white flocculent secretion; therefore, the administration of antibiotics in the absence of bacterial infection is disputed.[13] A viral infection such as mumps as the underlying cause hasn't been confirmed.[9] Finally, a further hypothesis refers to the endoscopic picture of the salivary ducts. The reduction of blood vessels seen in affected ducts may depress the gland's ability to secrete saliva, thereby causing chronic infection.[14,15]

In addition to clinical diagnostic methods, B-scan ultrasonography is the imaging method of choice and replaces invasive procedures such as sialography.[16]

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Further imaging methods are computed tomography, magnetic resonance (MR) imaging, and MR sialography. A relatively new diagnostic investigation is salivary gland endoscopy (SGE), which can be used to directly observe changes in the duct system: In such cases, the salivary ducts are usually of a whitish surface with a clear reduction in the normally visible blood vessels.[14,16]

The treatment of JRP has previously been merely symptomatic and not standardized. Currently, antibiotic therapy is the standard treatment for acute flare-ups, often with analgesics, sialagogues, and gland massage. Other methods include intraductal injection of substances such as Ethibloc (Ethicon, Norderstedt, Germany)[17]; tetracyclines[18]; or methyl violet,[19] which cause glandular atrophy; intravenous injection of the kallikrein inhibitor; aprotinin [20]; irradiation of the gland, which is now obsolete;[21] and surgical measures such as tympanic neurectomy[22] and ligature of the parotid duct.[23] Parotidectomy is a method of last resort. Galili et al.[5] found that sialography also had a therapeutic effect, which they attributed to irrigation with the contrast medium. The therapeutic application of SGE, first used in the early 1990s, was developed from this observation. The effect is thought to be due to the irrigation of the tissues, the cleansing of debris, and the application of antiinflammatory solution such as cortisone.[13]

SGE with cortisone irrigation, or alternatively conservative measures with antibiotic therapy alone, are established methods of treatment within our department. The retrospective study presented here compares these two therapeutic approaches with respect to the number of postinterventional recurrent episodes and pain intensity.

MATERIALS AND METHODS

This project was approved by the ethics committee at the University of Erlangen–Nuremberg. Between November 2004 and June 2011, 36 patients with confirmed JRP presented for treatment. Clinical and ultrasound findings led to the diagnosis of JRP. B-scan ultrasonography (Siemens Acuson S 2000) was carried out with frequencies between 5.0 and 7.5 MHz. Clinical criteria were: age between 4 months to 15 years; symptoms unilateral or bilateral; and no other identifiable pathology, including stones in ultrasound.

The initial acute flare was always treated with antibiotics. After explaining further therapeutic options to the patients and/or parents, they were given the choice of prophylactic SGE including irrigation with sodium chloride and cortisone (Group SGE+), or of further clinical observation including antibiotic therapy for acute exacerbations (Group SGE−). All selected patients remained in the same group. Treatment was carried out as described below.

Group SGE+

SGE was performed only once—with the exception of two patients, who were treated on more than one occasion for recurrent, intense symptoms at the request of their parents. We did not perform the endoscopy in the acute phase. It was carried out under local or general anesthetic, depending on the age and compliance of the patient. Depending on symptoms and clinical and ultrasound findings, SGE was performed uni-or bilaterally.

We used semiflexible endoscopes (Erlangen type; Karl Storz, El Segundo, CA) with an external diameter of 0.8 mm or 1.1 mm. The parotid duct opening was dilated using conical bougies, and the duct system was dilated by continuous irrigation until the secondary and tertiary ducts could be visualized. The solution consisted of 100 mg prednisolone, a synthetic cortisone derivative, dissolved in 50 ml sodium chloride. Antibiotic therapy (aminopenicillin, possibly with a β-lactamase inhibitor) was given peri- and postoperatively for 5 days.

Group SGE−

Antibiotics were administered during individual flare-ups, usually orally. Intravenous therapy was required only for patients with severe symptoms. Treatment mostly consisted of aminopenicillins in combination with β-lactamase inhibitors; for example, sultamicillin (alternatively, cephalosporins or macrolide antibiotics).

Data for the retrospective study were collected from medical records, together with telephone interviews with the parents and/or the children. Participants estimated the number of flares in the pre- and posttherapeutic periods. The pretherapy period in the SGE+ group was defined as the time from the first episode until the intervention; the posttherapy period was defined as the time between the intervention and the telephone interview. The posttherapy period for the two patients treated more than once was defined as the time between the first and second intervention. The pretherapy period in the SGE− was viewed as the time between the first event and the clinic visit in which our therapy was started. The posttherapy period was the time between this visit and the telephone interview.

In addition, the average pre- and posttherapeutic pain intensity was determined using a scale of 0 (no pain) to 6 (maximum pain).

Because of the scale used and the distribution of the outcome measures, data were analyzed with nonparametric tests. We analyzed, if there had been a change in frequency of flares or in pain intensity. As the follow-up period covered a wide range, calculations were made on the basis of the relative frequency (flares/month). The Wilcoxon Signed Rank Test was used to analyze the pre- and posttherapeutic frequency of flares and the pain intensity of each group.

In addition, the two therapeutic approaches were compared directly with one another. As the number of flares and the follow-up period have a direct relationship, and the evaluation of success with respect to posttherapeutic flares/pain intensity depends on the pretherapeutic values, the comparison was made on the basis of the differences of the relative pre- and posttherapeutic frequency of flares and pain intensity, using the Mann-Whitney U test.

The level of significance was set at $\alpha = 0.05$.

RESULTS

Twenty-five (69%) of the 36 patients were male and 11 (31%) were female. The median age was 6 years (absolute: range: 2–15; mean: 6.6. SGE+: median: 7; range: 3–15; mean: 7.5. SGE−: median: 6; range: 2–11; mean: 6.4). Symptoms and abnormal ultrasound findings were bilateral in 39% of the cases and unilateral in 61%. Two children presented during the first episode of disease.

Fifteen patients (42%; 10 male, 5 female) opted for cortisone irrigation (SGE+ group), while 21 patients (58%; 15 male, 6 female) chose conservative treatment

TABLE I.
Comparison of Pre- and Posttherapeutic Relative Frequency of Flares and Pain Intensity.

Pre- and Posttherapeutic Results of Treatment						
		Pretherapy		Posttherapy		
		Median	Mean	Median	Mean	*P* Value
Frequency of Flares	SGE+	0.4	0.6	0.2	0.2	0.005
	SGE−	0.4	0.6	0.03	0.2	0.001
Pain Intensity	SGE+	4	4.5	1	1.9	0.005
	SGE−	5	4.8	2	2.2	<0.001

SGE+ = sialendoscopy group; SGE− = pure antibiotic therapy group.

with antibiotics (SGE−). General anesthesia was given in 80% of the endoscopies; in 20% of the endoscopies local anesthetics were applied. Endoscopy was bilateral in six cases (40%) and unilateral in the remaining nine cases (60%). One of the two patients with several endoscopies received two treatments; the other one received six treatments; and the additional treatments weren't included in our calculations. Antibiotic therapy in the SGE− group was applied intravenously in two severe cases (9.5%), but it was otherwise administered orally as an outpatient (90.5%).

Initially, the relative frequency and pain intensity of pre- and posttherapeutic flares in the two treatment groups was investigated. Table I shows the progression of episodes using the Wilcoxon Signed-Rank test. Both groups showed a reduction in the number of flares per month. The median relative frequency of pre- and posttherapeutic flares fell from 0.4 flares per month before treatment to 0.03 after therapy in the SGE− group; while the corresponding figures in the SGE+ group fell from 0.4 to 0.2. This reduction in frequency was significant in both groups (SGE−: $P = 0.001$; SGE+: $P = 0.005$), so both led to improvement.

With respect to pain intensity, 27% of children in the SGE+ group had a maximum pain of 6 prior to treatment; but only 7% reported maximum pain afterward and 40% had no further pain. The median intensity in this group decreased from 4 to 1 ($P = 0.005$). In the SGE− group, 33% had maximum pain before treatment, but only 10% reported maximum pain afterward and 48% had no pain at all. The median intensity here was reduced from 5 to 2 ($P < 0.001$). Therefore, both treatments showed a significant reduction in pain intensity after therapy (Table I).

The direct comparison of the methods on the basis of the difference in the relative frequencies of pre- and posttherapeutic flares per month is presented in Table II using the Mann-Whitney U test. It shows that flares are to be expected to the same extent in both groups ($P = 0.822$). This can be demonstrated with the values obtained for the means and standard deviations of the differences. Although there was a difference in the means, the scatter of the values was virtually the same, with an almost identical standard deviation. These values were therefore in the same order of magnitude.

Comparison of the differences in pre- and posttherapeutic pain intensity also showed little difference between the groups ($P = 0.922$). The means and standard deviations further demonstrate this point: These values were likewise in a similar range (Table II).

Thus, the direct comparison showed no significant difference with respect to the posttreatment pain intensity and number of flares.

Notably, with two exceptions SGE only had to be performed once; but in case of strong flares, sporadically posttherapeutic antibiotics were administered as well

The pre- and posttherapy periods (months) between the two groups differed (SGE+: pre: median 46, mean 50.6; post: median 12, mean 18.2. SGE− : pre: median 21, mean 30.3; post: median 42, mean 44.1). In particular the duration of follow-up differed, as in the course of time more participants favored endoscopy (Median follow-up: SGE+: 12; SGE−: 42).

DISCUSSION

Our study compared conservative observation with antibiotics as needed with prophylactic cortisone irrigation via SGE in the treatment of JRP. Both approaches reduced not only the postinterventional frequency, but also the pain intensity of the flares, so they are similarly promising.

Antibiotic therapy has been the established treatment of the acute flare for many years. But JRP is not a purulent infection; studies have shown that the leucocyte marker myeloperoxidase can be found only on the first day of illness.[13] Although antibiotics provide symptomatic relief, causative treatment cannot be achieved in the absence of an infection of the gland. The therapeutic success may indicate an association between acute flare-ups and bacterial infections of the upper respiratory tract. Ericson et al.[1] considered that infections of the upper airways lead to dehydration, and as a result to reduced saliva flow with an increased risk of inflammation. During the interviews, many parents reported a relationship between acute flares and prior infections in the children. One advantage of antibiotics is the simplicity of treatment. However, with rising microbial resistance their use must be regarded critically. Our patients

TABLE II.
Comparison of the Difference Between the Relative Pre- and Posttherapeutic Frequency of Flares and Pain Intensity.

Difference in the Pre- and Posttherapeutic Values					
		Median	Mean	SD	*P* Value
Frequency of flares (difference between relative pre- and post-therapeutic values)	SGE+	0.34	0.34	0.40	0.822
	SGE−	0.18	0.40	0.41	
Pain intensity (difference between pre- and post-therapeutic values)	SGE+	2	2.5	2.4	0.922
	SGE−	3	2.6	2.2	

SD = standard deviation; SGE+ = sialendoscopy group; SGE− = pure antibiotic therapy group.

sometimes had flares every month over a period of up to 83 months. If each flare is treated with antibiotics, then the development of multiresistant organisms is a potential risk.

While we focus in this study on the therapeutic effect, SGE already has the advantage of being an excellent diagnostic tool for JRP. Studies have attributed greater diagnostic value to SGE than to ultrasonography.[24,25] The antiinflammatory cortisone irrigation is particularly suitable for removing accumulated proteins that have leaked out because of disrupted permeability.[13] The cortisone is administered intraductally in the irrigation solution, so adverse systemic effects are unlikely to occur. Despite these advantages, it must be remembered that the patients, often very young, frequently need a general anesthetic for this invasive procedure, but they may be amendable to local anesthesia in select circumstances depending on the age and compliance of the child.

The therapeutic effect of SGE is likely due to the irrigation of the tissue. Antoniades et al.[26] showed that irrigation of the gland with penicillin or NaCl alone relieved symptoms. In 1986, Galili et al.[5] described the therapeutic effect of irrigation during sialography. Besides the improvement in symptoms, 86% of the 22 children treated in his way had a notable regression in flares.[5] In a long-term study, Shacham et al.[15] treated 70 children with cortisone irrigation as part of the SGE, of whom 56 were symptom-free in the follow-up period of 6 months to 36 months. However, all of them had previously been investigated with bilateral sialography. Nine out of 10 children treated with cortisone irrigation in a study by Quenin et al.[24] were free of symptoms in an average follow-up period of 11 months. Martins-Carvalho et al.[25] treated 18 children with SGE; only four children had postinterventional recurrence.

In this first retrospective comparison, we confirm this therapeutic effect of SGE. During the acute phase SGE builds onto the standard treatment, and during the nonacute phase SGE offers an option of prophylactic treatment, showing similarly good outcomes.

Another important point is the low number of required endoscopies. Nahlieli et al.[14] propose that the characteristic duct changes cause disordered saliva transport and therefore chronic inflammation. Hence, SGE may offer a way of significantly combating the disease directly. This could also explain the low number of treatments required and should be taken into consideration in the choice of management in the individual case. The antiinflammatory effect of cortisone, combined with irrigation of the duct system and subsequent dilatation of the ducts, seems to be an excellent therapeutic option for JRP. However, in case of intense posttherapeutic episodes, children of the SGE+ still had to receive antibiotics: During a strong acute phase, it would be unethical not to treat them at least with antibiotics.

A further point is the duration of follow-up. An equally good outcome was achieved in the SGE treatment group, as in the antibiotic therapy group, in a median absolute follow-up period that was considerably shorter. The median follow-up period depends on several different determinants; further studies must be carried out to determine whether the duration of treatment of endoscopic therapy is shorter.

Finally, although not quantified in the data, it is important to note that without exception parents interviewed in our study were very satisfied with the SGE treatment and success. In two cases the parents even insisted on further SGE treatments, given the perceived improvement of the children's state. It has to be remembered, however, that the frequency of flares and pain intensity were purely subjective assessments by the parents/children of events, which were often well in the past and are therefore possibly subject to recall bias. This point and the rareness of the disease with a small number of patients might be a reason that the pre- and posttherapy periods covered such a wide range. A future prospective multicenter trial would help to clarify the best treatment approach to this patient population.

CONCLUSION

In conclusion, both approaches are valid treatment alternatives. SGE, however, has several potential advantages: First, It is a good tool for diagnosis that may even have therapeutic effects during the nonacute phase of JRP. Second, Despite the low number of required endoscopies, the median follow-up period was shorter than with conservative treatment, yet with similar results and third, parents repeatedly expressed subjectively that the symptoms improved significantly. In view of the ever-increasing problem of multiresistant organisms from repeated antibiotic therapy, we believe that these results warrant a further continuation of this method to increase the number of treated patients and data for further analysis of SGE outcomes. Prospective trials with longer follow-up and larger sample size would help determine the best treatment paradigm.

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