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Treatment of gustatory sweating with botulinum toxin: A prospective study on long-term efficiency and quality of life

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Introduction

Frey's syndrome is a localized hyperhidrosis in the facial skin associated with eating or smelling food. It is present in almost all patients after parotid gland surgery [7, 10]. First mentioned by Duphenix (Duphenix 1757) the phenomenon was studied and described by Lucie Frey in 1923 [5]. The symptoms are dripping sweat frequently combined with erythema, local hyperthermia and swelling sensations in the preauricular and temporal region. The pathogenesis of gustatory sweating is not clear yet. It is considered to occur due to aberrant regrowth of postganglionic parasympathetic fibers from the otic ganglion to the sweat glands of the overlying skin after parotidectomy thus causing sweating on gustatory stimulation. Because severe gustatory sweating decreases quality of life there is a strong demand for treatment [6]. Injections of botulinum toxin A (BTX) into the affected skin have recently been described to be an effective and safe treatment [2, 3, 4, 8, 9, 6]. Naumann recommended BTX to be the treatment of choice in gustatory sweating [11]. However, recent data suggest that there is only temporary effectiveness of the intracutaneous injection of the toxin. This prospective clinical study was therefore designed to evaluate the long-term efficacy of BTX for treatment of Frey's syndrome both in terms of functional outcome and health related quality of life.

Method

Under permission of the local ethic-commission [Nr. 2157: Qualitative Begleituntersuchung bei intrakutaner Injektion von BTX zur Behandlung des gustatorischen Schwitzens nach operativer Entfernung der Ohrspeicheldrüse 8/99] 17 patients with gustatory sweating were included. All patients had undergone a lateral parotidectomy due to a benign tumor of the parotid gland. Minor's starch iodine test was used as an objective measure to detect gustatory sweating [11]. The severity of the disease was quantified by morphometry using a digital camera with subsequent image analysis (CCD camera: (Olympus Camedia 1400)). The image was transferred to a computer (Macintosh G3, Apple Cupertino, CA/USA) and the affected area was calculated with NIH-Image1.61 freeware software. Lyophilized BTX (Botox®, Merz & Co., Frankfurt/Germany) was reconstituted to a final solution of 10 IU/ml. To achieve a uniform effect a grid template was used to divide the affected skin area into fields of 1cm². BTX was injected intracutaneously once at a dosage of 1 IU (mouseunits) BTX (0.1 ml) per 1cm². Minor's test was performed one week after treatment to prove the efficacy of treatment. The evaluation of effectiveness and duration relied on self-assessment of patients and periodic examinations 4 weeks, 4, 8, 12 and 18 month after treatment by a Minor's test. A digital photograph was taken during each follow-up visit and for assessment calculation of the affected skin area as described above. Quality of life was assessed by using the SF-36 questionnaire [2] before, 6 and 18 month after treatment.



Fig. 1-3: The affected side of the patient's face was coated with an iodine solution followed by a dusting of starch. After that the patient was asked to eat an apple. Gustatory sweating was delineated by the dark blue color following the iodine-starch reaction catalysed by perspiration. The identified area was marked with a pen and photographed with a digital Camera after placing a standard of 1cm² on the skin. The area showing the sweating was divided into fields of 1cm² each for injection of BTX.

Results

After 4 weeks the objective data showed an excellent effectiveness of treatment with BTX injections. There was a reduction of affected skin area from mean 34.4 (±16.3) cm² before treatment to mean 3.8 (±4.6) cm² 4 weeks after intracutaneous injection of BTX (<p=0.001).



Fig. 4-6: A fortyseven years old man (M.M.) with 57.5 cm² effected skin surface before treatment (Fig. 4). BTX injections worked excellent in facial skin, but less effective in hairy temporal region with remnants of 12,5 cm² four weeks after treatment (Fig. 5). During follow-up there was a recurrence of sweating even in the facial region with clinical impact (Fig. 6).

This was decrease down to 11% of the initial surface. Because the perioral region was excepted there were some remnants of sweating in this area. In the temporal region treatment was little less effective than in the facial skin. 6 patients presented with some remnants of sweating in the temporal region (mean of 8.0 cm², range 3.5-16.6 cm²). Even in those patients the reduction of sweating was highly significant (from mean 43.7 (±22.6) cm² before treatment to mean 8.0 8 (±5.7) cm² four weeks after injection of BTX: p=0.006). During follow-up to 18 month 13 patients developed recurrence of gustatory sweating. 5 patients had no signs of recurrent sweating at all. Overall there was a slight increase in sweating during follow-up from minimum 3.8 (±4.6) cm² 4 weeks after treatment to 4.5 (±5.1) cm² after 4 month (p=0.685), to 4.8 (±5.4) cm² after 8 month (p=0.567), to 5.4 (±6.1) cm² after 12 month (p=0.392) and up to 8.2 (±10.2) cm² after 18 month (p=0.117). There was a recurrence of sweating from minimum 11% to 24% of the initially affected skin area 18 month later. Quality of life increased over the time. Significant levels could be seen in "Mental Health" and "Social Function".



Fig. 7-9: A thirtyfour old woman (P.A.) eight years after superficial parotidectomy presented with severe gustatory sweating. 48 cm² skin surface was effected (Fig. 7). By treatment with BTX the sweating could be reduced to 3 cm². She showed up with 7 cm² twelve month (Fig. 8) and with 8 cm² eighteen month (Fig. 9) after injection.

Conclusion

BTX has proven to be a save and highly effective in treatment of gustatory sweating which improves quality of life. 60% of the patients had an asymptomatic period of at least 18 month.

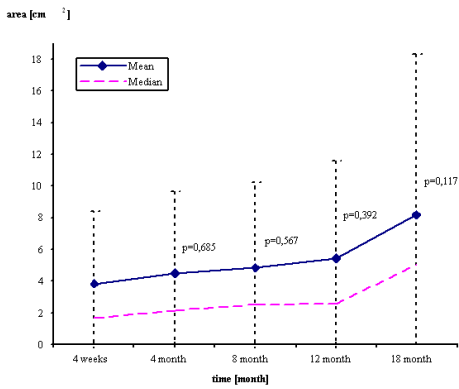


Fig. 10: Median increase of effected skin area during follow-up (n=17).

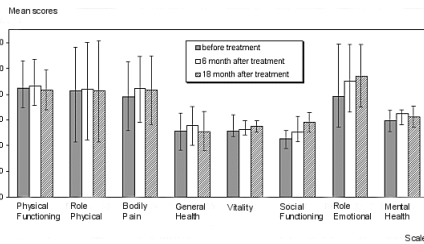


Fig. 11: Mean scores in FS-36 evaluation before treatment and after 6 and 18 month past injection (n=17).

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TREATMENT OF GUSTATORY SWEATING WITH BOTULINUM TOXIN A

A PROSPECTIVE STUDY ON LONG-TERM EFFICACY AND QUALITY OF LIFE

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Introduction:

Frey's syndrome is a localized hyperhidrosis in the facial skin associated with eating or smelling food. It is present in almost all patients after parotid gland surgery [1, 2]. First mentioned by Oskar Frey (1873) the phenomenon was studied and described by Lucie Frey in 1923 [3]. The symptoms are flapping sweat regularly correlated with or without local hyperthermia and swelling sensations in the preauricular and temporal region. The pathogenesis of gustatory sweating is not clear yet. It is considered to occur due to aberrant regrowth of postganglionic parasympathetic fibers from the ciliary ganglion to the sweat glands of the overlying skin after parasympathetic tract causing sweating in gustatory stimulation. There are several problems resulting decrease quality of life from it: a strong demand for treatment [3]. Injections of botulinum toxin A (BTX) into the affected skin have recently been described as an effective and safe treatment [2, 3, 4, 5, 6, 7, 8]. Neumann recommended BTX to be the treatment of choice in gustatory sweating [1]. However, recent data suggest that there is only temporary effectiveness of the intramuscular injection the skin.

Method:

Under permission of the local ethics commission (No. 2157, Qualitative Begleitende Untersuchung bei invasiver Injektion von BTX an Kehlkopf- und Kehlkopfnahe Operationsstellen) each cooperative Otolaryngologist (n=50) 17 patients with gustatory sweating were included. All patients had undergone a total parotidectomy due to benign tumor of the parotid gland 1-24 years before. After a search for the best site used as an objective measure to detect gustatory sweating [1]. The necessity of the disease was quantified by photography using a digital camera with subsequent image analysis (CCO camera, Olympus Camera, HD02). The image was transferred to a computer (Macintosh G3, Apple



Fig. 2: The affected side of the patient's face was covered with an adhesive foil followed by a coating of paper. After that the patient was asked to eat an apple. Gustatory sweating was followed by the skin's color under following the adhesive skin's reaction analyzed by photography. The identified area was marked with a grid and photographed with a digital camera after placing a standard of form on the skin. The area showing the sweating was divided into fields of 1cm² each for injection of BTX.

Computer, GAVISA) and the affected area was calculated with NIH Image 1.61 software. Lyophilized BTX (Botox, Merck & Co., Frankfurt/Germany) was reconstituted in a final volume of 10 ml in 0.9% NaCl. To achieve a uniform effect a grid template was used to divide the affected skin area into fields of 1cm². BTX was injected intramuscularly (Biotrakt 2.40 x 12mm BLUR) once at a dosage of 1 IU (concentration BTX 0.1 ml per 1 cm²). Minor's test was performed one week after treatment to prove the efficacy of treatment. The evaluation of effectiveness and duration: noted in self-assessment of patients and periodic examinations 4 weeks, 4, 8, 12 and 16 months after treatment by a Minor's test. A digital photograph was taken during each follow-up visit and the measurement calculation of the affected skin area as described above. Quality of life was assessed by using the SF-36 questionnaire [9] before, 6 and 18 months after treatment.

Results:

After 4 weeks the objective data showed an excellent effectiveness of treatment with BTX injections. There was a reduction of affected skin area from mean 34.4 (±14.3) cm² before treatment to mean 3.8



Fig. 4: A 44-year-old patient with mean (M.M.) and 37.9 cm² affected skin surface before treatment (Fig. 4). In this case BTX injections were not effective in facial skin, but less effective in fully temporal region with reduction of 12.8 cm² four months after treatment in this area (Fig. 4). During follow-up there was a recurrence of sweating area in the facial region with change (Fig. 6).

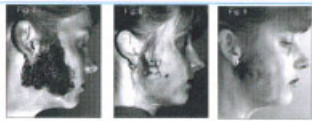


Fig. 7: A 48-year-old woman (P.A.) eight years after superficial parotidectomy presented with severe gustatory sweating. 60 cm² skin surface was affected (Fig. 7). By treatment with BTX the sweating could be reduced to 7 cm² skin showed up with 7 cm² before month (Fig. 8) and with 0 cm² eighteen month (Fig. 9) after injection.

(±4.6) cm² 4 weeks after intramuscular injection of BTX (p<0.001). This was a decrease down to 11% of the initial surface. Because the preauricular region was accepted from treatment there were some remnants of sweating in this area. In the

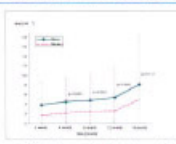


Fig. 10: Reduction of affected skin area during follow-up (n=17).

temporal region treatment was little less effective than in the facial skin. 5 patients presented with some remnants of sweating in the temporal region (mean of 6.0 cm², range 3.8-10.8 cm²). Even in those patients the reduction of sweating was highly significant from mean 43.7 (±12.6) cm² before treatment to mean 6.5 (±5.7) cm² four weeks after injection of BTX (p<0.001). During follow-up to 18 months 12 patients. Absorbed recurrence of gustatory sweating 5 patients had no signs of recurrent sweating at all. One had some a slight increase in sweating during follow-up from 9% from 3.0 (±1.6) cm² 4 weeks after treatment to 4.8 (±1.6) cm² after 8 months (p=0.01), to 6.4 (±1.1) cm² after 12 months (p=0.002) and up to 6.2 (±1.2) cm² after 16 months (p=0.11). There was a recurrence of sweating from minimum 11% to 24% of the initially affected skin area 16 months later.

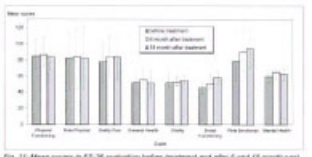


Fig. 11: Mean scores in SF-36 evaluation before treatment and after 6 and 18 months post-injection (n=17).

Quality of life increased over the time. Significant levels could be seen in "Mental Health" and "Social Function".

Conclusion:

BTX has proved to be a safe and highly effective in treatment of gustatory sweating which impairs quality of life. 40% of the patients had an asymptomatic period of at least eighteen months.

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