Nutrafoods (2019) 2 106-112. DOI 10.17470/NF-019-0015

Original Research

Retrospective analysis of the effects of a gum gel intended to treat signs and symptoms of teething in infants

Francesco Di Pierro [1*]
Paolo Risso [2]
Alexander Bertuccioli [3]
Guido Donato [4]

[1] Scientific Department, Velleja Research, Milan, Italy
[2] University of Genoa, Genoa, Italy
[3] D.I.S.B., Urbino, Italy
[4] ATS, Cuneo, Italy

*Corresponding author:
Francesco Di Pierro
f.dipierro@vellejaresearch.com

Abstract

Teething discomfort is a widespread disorder affecting a very high percentage of infants. It creates anxiety in parents, who look for help in paediatric clinics. The use of hyaluronic acid gels has been shown in the last 20 years to be an effective tool, generally devoid of side effects, in reducing oral mucosal inflammation in adults.

Recently, such results have also been confirmed in infants affected by teething. From our routine practice results, we have retrospectively reported the efficacy and the safety profile of Bonjela® Soothing Teething Gel, a teething gel capable of addressing in a significant way this infant complaint, which improves all of the clinical outcomes used in these types of study to describe the clinical condition of infants.

Keywords: Gums, redness, fever, paediatric, inappetence, sleep disturbance

Introduction

Teething is a natural physiological process that usually occurs without problems during the first months of life. It consists of the migration of the tooth from its intraosseous position in the jaw to eruption in the oral cavity [1].

Everyday parental and medical experience associates primary tooth eruption with alterations such as irritability, gingival irritation, increased salivation, fever, agitated sleep, diarrhoea and loss of appetite [2, 3].

Since these disturbances undoubtedly provoke discomfort and pain in the newborn/infant, they are often responsible for the common referral of many babies to paediatric clinicians. Parents in particular always ask for help and information relating to the probable relationship between these phenomena and the eruption of primary teeth.

From a scientific perspective at least, the relationship between tooth eruption and organic or worse, systemic, manifestations, such as fever for instance, in infants is controversial among paediatric clinicians and dentists, and within the scientific community in general [4]. Some authors report that it is unclear whether the disturbances are caused by the eruption of the primary teeth or whether they simply coincide with tooth eruption.

However, in any case, these disturbances are real and mainly observed during the eruption of the primary teeth and medical solutions, if possible those that are entirely devoid of potential side effects, must be used [5].

Apart from local discomfort, which affects almost 100% of infants, in a survey involving thousands of infants, it was observed that one or more systemic, and then surely important, symptoms were registered in 68% of subjects. Each manifestation appeared alone or in combination with others.

The most frequent clinical manifestations were: fever (16%), drooling (12%), diarrhoea (8%), fever–drooling (15%), fever–diarrhoea (8%), drooling–diarrhoea (6%) and the combination of fever–drooling–diarrhoea was found in 3% of the children [6].

The teething process in infants is therefore an important issue in medicine, and requires appropriate care and treatment.

From a pharmacological perspective, strategies for teething generally aim to achieve analgesia, anaesthesia, sedation or a combination of these. The use of acetaminophen or ibuprofen can reduce or halt discomfort and pain caused by teething [7]. Local anaesthetic agents, such as 20% benzocaine, are commonly found in teething preparations. However, benzocaine should be used with caution and is generally not recommended because of the risk of methaemoglobinaemia and it could interfere with the gag reflex, causing the infant to choke [8].

Apart from pharmacological agents, rubbing the gums and the use of teething rings have been described to help somewhat in reducing irritability in infants with no side effects at all [9, 10].

Recently, teething gels massaged over the gums with a clean finger have been demonstrated to provide relief, particularly if the formula included hyaluronic acid (HA) [11].

Even if the efficacy of HA is well accepted within the scientific community, its effectiveness in infants is also affected by the strength of HA retention over the oral mucosa. This is in turn affected by formulation and may vary between different products due to the different ingredients used; therefore, products may be distinguished not only, as expected, in terms of taste and texture, but also, with respect to functional characteristics.

We thus retrospectively report the results obtained by our recent paediatric experience of a newly developed HA-based medical device intended to counteract teething discomfort in infants.

Materials and methods

Tested product

The medical device tested is a teething gel (Bonjela® Soothing Teething Gel, Reckitt Benckiser, UK) intended for oral use and developed to counteract teething complaints in infants. The medical device is manufactured at Farmaceutici Procemsa S.p.A. in a facility located at Nichelino, Italy and it is distributed by Reckitt Benckiser, UK. The exact composition of the gel, ranked by weight is: xylitol, glycerin, *Rosa damascena* petal extract, xanthan gum, hyaluronic acid sodium salt (0.24%), pectin, potassium sorbate, sodium benzoate, citric acid, *Malva sylvestris* extract, *Chamomilla recutita* flower extract, *Aloe barbadensis* leaf extract.

Study protocol and endpoints

The study is the retrospective report of paediatric practice when treating infants with teething problems. The study was conducted in a paediatric clinic located in Cuneo under the supervision of a paediatrician and in accordance with the Declaration of Helsinki.

Between December 2018 and June 2019, a total of 40 infants, without ethnic limitations, of both sexes and between the ages of 2 and 12 months, affected by teething discomfort but considered otherwise healthy, have been analyzed retrospectively.

All of the infants were treated with teething rings filled with coolant. Fifty percent of subjects were also treated with the tested HA-based medical device. The double treatment (teething ring + teething gel) identifies infants within Group A. The single treatment (teething ring only) identifies Group B.

Single or double treatment was established by the paediatricians according to the opinion of the infants' parents. The infants were considered eligible for our retrospective statistical analysis only after their parents provided signed informed consent, with the relevant declarations of privacy and confidentiality.

At the time of enrolment, to establish eligibility, all of the infants' parents were also informed that both the clinical report and the statistical analysis would be performed under conditions of total anonymity to guarantee the subsequent possible publication of the data obtained.

All of the infants involved in this retrospective analysis had not previously been placed on immunosuppressive, cytotoxic, cortisone, antibiotic, antifungal and hormone therapy for at least 45 days prior to the use of the HA-based medical device. The paediatricians considered only subjects demonstrating at the first visit to have signs and symptoms of teething discomfort; that is, one or more signs of dental eruption, gum redness, excessive salivation, irritability, inappetence, sleep disturbance and unexplained cry, to be eligible for this report and for the statistical analysis. In the routine practice, the paediatrician, after prescription of the teething ring with or without the teething gel, scored (0–4, where 0 corresponds to absence of a symptom and 4 to the worst condition) for at least 1 month on a weekly basis the following outcomes: unexplained cry, irritability, sleep disturbance, inappetence, salivation, gum redness, number of days with fever and general well-being. In our retrospective report, these were considered primary endpoints. Tolerability, adherence to treatment, the need to use acetaminophen or ibuprofen, and the appearance of side effects were considered secondary endpoints.

These secondary endpoints were verified by reading the notebooks containing the daily transcription performed by parents and, with regards to the HA-based teething gel, through the analysis of the residual product content.

Statistical analysis

To test the difference between uncorrelated groups, treated subjects versus con-

trols, we used the non-parametric Wilcoxon rank-sum test. Data are represented as the mean ± standard deviation and the median value. JMP 10 for Mac OsX was used for statistical analysis and statistical significance was set at 95% (p<0.05).

Results

According to our retrospective report and analysis, the two groups did not differ in terms of age expressed in months (Group A: 4.7±1.5; Group B: 4.8±1.5), sex (Group A: 10 males and 10 females; Group B: 10 males and 10 females) and the number of teeth apparently involved in teething discomfort and checked on a weekly basis for 1 month (Group A: 1.3±1.0; 1.2±0.8; 0.7±0.6; 0.7±0.7 and Group B: 1.2±0.9; 1.2±0.9; 0.9±0.9; 0.7±0.9).

Since even the type of delivery and the type of feeding (breast milk versus formula) were overlapping (data not shown), we considered the two groups statistically comparable.

Regarding the primary endpoints (**Tables 1–8**), the use of the teething gel determined a better outcome, which was significant and appreciable from the 3rd visit for unexplained cry, sleep disturbance and general well-being, and from the 2nd visit for irritability, inappetence, salivation and gum redness.

Table 1 Scores (0–4) for unexplained cry (mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	2.1±1.0 [2]	2.1±1.1 [2]	n. s.
2nd	1.5±0.9 [1]	2.0±0.9 [2]	n. s.
3rd	0.8±1.0 [0]	1.6±0.9 [1]	<0.01
4th	0.4±0.7 [0]	1.8±1.1 [2]	<0.001
n. s.: Not significant			

Table 2 Scores (0–4) for irritability (mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	1.7±0.8 [2]	2.1±1.0 [2]	n. s.
2nd	1.2±0.8 [1]	2.0±0.9 [2]	<0.05
3rd	0.7±1.0 [0]	1.4±0.7 [1]	<0.01
4th	0.4±0.6 [0]	1.7±1.1 [1]	<0.001
n. s.: Not significant			

Table 3 Scores (0–4) for sleep disturbance (mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	1.4±1.0 [1]	1.8±1.0 [2]	n. s.
2nd	1.1±1.3 [1]	1.6±1.1 [2]	n. s.
3rd	0.5±0.8 [0]	1.3±1.1 [1]	<0.05
4th	0.2±0.4 [0]	1.1±0.8 [1]	<0.001
n. s.: Not significant			

Table 4 Scores (0–4) for inappetence (mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	1.4±0.8 [1]	1.4±1.4 [1]	n. s.
2nd	0.4±0.8 [0]	1.3±1.3 [1]	<0.05
3rd	0.2±0.7 [0]	1.2±1.2 [1]	<0.01
4th	0.2±0.5 [0]	1.5±1.2 [1]	<0.001
n. s.: Not significant			

Table 5 Scores (0–4) for salivation (mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	2.5±0.9 [2.5]	2.5±0.9 [3]	n. s.
2nd	1.8±1.2 [1]	2.5±1.0 [3]	<0.05
3rd	0.9±1.0 [0.5]	2.4±0.9 [2]	<0.01
4th	0.7±1.0 [0]	2.4±1.0 [2.5]	<0.01
n. s.: Not significant			

Table 6 Scores (0–4) for gum redness (mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	1.8±0.6 [2]	2.0±1.0 [2]	n. s.
2nd	0.9±1.0 [1]	1.7±0.8 [2]	<0.01
3rd	0.4±0.7 [0]	1.6±0.9 [2]	<0.001
4th	0.5±0.9 [0]	1.6±0.9 [2]	<0.001
n. s.: Not significant			

Table 7 Number of days per week with fever (mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	0.3±0.7 [0]	0.6±0.8 [0]	n. s.
2nd	0.2±0.5 [0]	0.4±0.7 [0]	n. s.
3rd	0.1±0.2 [0]	0.0±0.0 [0]	n. s.
4th	0.0±0.0 [0]	0.0±0.0 [0]	n. s.
n. s.: Not significant			

Table 8 Scores (0–4) for general well-being (the lower, the best; mean ± standard deviation; median in square brackets) observed in infants (N=20) treated with hyaluronic acid-based gel plus a teething ring (Group A) and in infants (N=20) treated with a teething ring only (Group B)

Visit	Group A	Group B	*p*
1st	1.5±0.8 [1]	1.7±0.7 [2]	n. s.
2nd	1.1±0.9 [1]	1.5±0.8 [1.5]	n. s.
3rd	0.6±0.8 [0]	1.5±0.7 [1]	<0.01
4th	0.5±0.8 [0]	1.2±0.9 [1]	<0.05
n. s.: Not significant			

Among the primary endpoints no difference was seen only in terms of days with fever, perhaps confirming what has previously been reported by others (see the Introduction). All of the secondary endpoints (tolerability, adherence, use of acetaminophen or ibuprofen) were non-significant in terms of a difference between the two groups, even if a mild tendency is probably visible in favour of Group A (teething ring + teething gel).

Discussion

Symptoms related to teething in infants are known to be generally self-extinguishing. For this reason they are often underestimated by physicians, even if the symptoms are extremely worrisome for parents. The situation is confirmed by the widespread use of anaesthetics and anti-inflammatory drugs, administered both topically and/or systemically. These molecules are readily absorbed by the oral mucosa and give the child rapid, albeit short-lived, relief. However, these drugs should be reserved for the most severe cases and used under medical supervision, due to the risk of adverse events, which can be serious although rare. Oral gels have been widely used in the last 20 years for various disorders affecting the oral cavity in adults. Some of these gels contain HA. Due to their effectiveness, ease of use and patient satisfaction, these products have garnered the interest of physicians and patients.

HA is a polysaccharide present in human tissue and in the oral mucosa. It plays an important role in epithelial protection and in maintaining intercellular exchange and water balance. Experimental studies have shown its effects in the treatment of mouth pathologies, providing evidence of anti-inflammatory, healing and anti-oedematous actions [12]. Several trials have described the clinical utility of HA in oral disorders such as gingivitis and gingival trauma [13], conditions similar to teething, and in treating teething discomfort [14]. Our retrospective study confirmed the positive role played by a HA-based teething gel in relieving teething discomfort and showed that the symptoms of teething abated more quickly in the group treated with the teething gel plus a teething ring than in the group just treated with the teething ring. We also observed that the use of the teething gel does not interfere in any way with acetaminophen or ibuprofen. This observation, along with the reports done by some parents describing

better results (data not shown) deriving from a concomitant use of the teething gel along with ibuprofen, prompt us to consider this option as an appropriate therapy.

Regarding the mechanism of action, the observed efficacy cannot be due only to the presence of HA. It is likely that the formula as a whole contributes globally to this efficacy.

In this perspective, an important role was surely played by the extract of *Rosa damascena*, recently described to be endowed with a likely soothing action on mucosa, being *Aloe barbadensis*, *Malva sylvestris* and *Chamomilla recutita* effective filming agents [15–18]. Regarding methodological aspects, a limitation of our retrospective report is the lack of a negative control or of a placebo group. Nevertheless, we believe that our statistical assessment is sufficiently robust to render our results useful for paediatric practice. As stated above, teething discomfort is a widespread condition during infancy, and paediatricians and parents can make use of the results of our study.

Conclusions

Within the limitations of the retrospective design and the absence of a placebo group, our study reports the efficacy and tolerability of Bonjela® in counteracting teething discomfort in infants. Its application significantly reduces such complaints.

Acknowledgements

We acknowledge the support of Dr. Carlo Fornaini, professor at the Dentistry Dept., University of Nice, for acting as Editor-in-Chief for this report.

References

1. Wake M, Hesketh K, Lucas J (2000) Teething and tooth eruption in infants: a cohort study. Pediatrics 106:1374–1379
2. Macknin ML, Piedmonte M, Jacobs J, Skibinski C (2000) Symptoms associated with infant teething: a prospective study. Pediatrics 105:747–752
3. Vaysse F, Noirrit E, Bailleul-Forestier I, Bah A, Bandon D (2010) Eruption and teething complications. Arch Pediatr 17:756–757
4. Hulland SA, Lucas JO, Wake MA, Hesketh KD (2000) Eruption of the primary dentition in human infants: a prospective descriptive study. Pediatr Dent 22:415–421
5. Cunha RF, Pugliesi DM, Garcia LD, Murata SS (2004) Systemic and local teething disturbances: prevalence in a clinic for infants. J Dent Child 71:24–26
6. Noor-Mohammed R, Basha S (2012) Teething disturbances; prevalence of objective manifestations in children under age 4 months to 36 months. Med Oral Patol Oral Cir Bucal 17:e491–e494
7. Dean E (2016) Teething. Nurs Stand 31:15
8. Markman L (2009) Teething: facts and fiction. Pediatr Rev 30:59–64
9. Leung A (1989) Teething. Am Fam Physician 39:131–134
10. McIntyre G, McIntyre G (2002) Teething troubles? Br Dent J 192:251–255
11. D'Ercole S, Nanussi A, Tieri M, Barattini DF, Tripodi D (2015) Hyaluronic acid-based medical device and oral disorders: can it be used in paediatric dentistry? J Biol Regul Homeost Agents 29:999–1005
12. Kim SK, Lee HS, Byeon KS (2010) The effect of hyaluronic acid on anti-inflammatory action in mouse. J Korean Assoc Oral Maxillofac Surg 36:16–22
13. Pistorius A, Martin M, Willershausen B, Rockmann P (2005) The clinical application of hyaluronic acid in gingivitis therapy. Quintessence Int 36:531–538
14. Rosu S, Barattini DF, Murina F, Gafencu M (2018) New medical device coating mouth gel for temporary relief of teething symptoms: a pilot randomised, open-label, controlled study. Minerva Pediatr (2018) Oct. 4th.
15. Kumar R, Singh AK, Gupta A, Bishayee A, Pandey AK (2019) Therapeutic potential of Aloe vera – a miracle gift of nature. Phytomedicine 60:152996

16. Mahabob N, Mohan J (2019) Preparation of mouthwash and gel from Rosa damascena Mill and evaluating its effectiveness – an in vivo analysis. J Pharm Bioallied Sci 11:S198–S202

17. Prudente AS, Sponchiado G, Mendes DAGB, Soley BS, Cabrini DA, Otuki MF (2017) Pre-clinical efficacy assessment of Malva sylvestris on chronic skin inflammation. Biomed Pharmacother 93:852–860

18. Braga FT, Santos AC, Bueno PC, Silveira RC, Santos CB, Bastos JK, Carvalho EC (2015) Use of Chamomilla recutita in the prevention and treatment of oral mucositis in patients undergoing hematopoietic stem cell transplantation: a randomized, controlled, phase II clinical trial. Cancer Nurs 38:322–329