Efficacy of a Ready-to-Drink Gelled Water and of a Thickening Powder in Patients with Oropharyngeal Dysphagia: a Crossover Randomized Study

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Abstract
Management of oropharyngeal dysphagia (OD) is mainly based on modifying liquid viscosity and solid consistency in order to preserve oral feeding while avoiding unsafe swallowing. Adding thickening powders (TP) to water is the most common practice in patients suffering from OD to liquids, but ready-to-use gelled waters (RGW) can also be proposed. The main objective of this study was to assess the efficacy of a RGW and a TP on swallowing in hospitalized patients with different OD etiologies. This open, crossover, multicenter trial recruited thirty hospitalized patients with OD to liquids, confirmed by positive 3-ounce water test or positive Practical Aspiration Screening Scheme test. The patient’s ability to swallow 120 g of a RGW (IDDSI level 4) and a drink prepared with TP (nectar viscosity; NTP, 291 cP, IDDSI level 2; or if necessary, honey; HTP, 769 cP, IDDSI level 3) was evaluated in a random order at 1- to 3-day intervals. The main criterion was the efficacy of each product, defined as the proportion of patients who successfully swallowed without immediate reflexive cough. The RGW and TP were successfully swallowed in respectively 93.3% (95% CI: 77.9–99.2) and 82.8% (95% CI: 64.2–94.2) of patients with different dysphagia etiologies (stroke, neurodegenerative diseases, or aging) and unable to swallow thin water. Taste and texture of both study products were well appreciated by patients, with a preference for the RGW over TP. Therefore, the use of these thickened products could be part of the therapeutic strategy for patients with OD to liquids.

Keywords Dysphagia · Swallowing · Thickened liquids · Viscosity · Thickening powder · Ready-to-drink gelled water

Introduction
Oropharyngeal dysphagia (OD), a prevalent condition recognized by the World Health Organization (WHO) in the International Classification of Diseases \cite{1}, is characterized by difficulties in swallowing liquids and/or solids that may lead to aspiration. OD must be rapidly diagnosed and managed in order to prevent related severe complications.
Videofluoroscopy (VFS) is considered the “gold standard” method to assess the effect of increased viscosity on swallowing [9] and is largely used to evaluate thickened drink. However, this method does not apply to RGW that are solid gelled waters, because stirring for the addition of contrast product needed for such evaluation would induce a modification of the texture and viscosity level of RGW. Similarly, viscosity measurement by rheology would destroy the gel structure and would modify its texture. Finally, considering that mastication and hydration processes of the bolus are not reproducible by technical evaluation [10], a clinical evaluation of the safety of products is required.

This is the first study to assess the effectiveness on swallowing of two commercial products, a RGW and a thickening powder (TP), in standard hospital practices. Therefore, the main objective of this study was to assess the efficacy of the consumption of an entire cup of RGW, or the same amount of thickened water (120ml), in hospitalized patients with different OD etiologies.

## Methods

### Patients

Patients with OD hospitalized in acute or rehabilitation hospitals in France, for whom aspiration was detected, were prospectively included. Inclusion criteria were age > 18 years, suffering from OD following neurological diseases (stroke or neurodegenerative diseases) or aging, positive 3-ounce water test (3oz WT) or positive Practical Aspiration Screening Scheme (PASS) test, and able of understanding and signing written consent after receiving study information. The PASS test combines the Clinical Predictive Scale of Aspiration (CPSA) and the 3oz WT in patients falling in the uncertain range of CPSA (between 14 and 28) [11]. The CPSA is a non-ingestion test consisting of a questionnaire with six clinical signs correlating with aspiration risk. The 3oz WT was performed for all the patients at inclusion and was considered positive when it evidenced coughing after ingestion of 90 ml of water [12]. Non-inclusion criteria were medical or surgical history which interfered with the participation to the study, intolerance to one or more components of the products, and diabetic patient. All participants provided written informed consent. The protocol (registration number: 2014-A01084-43) was approved by French authorities: the Agence Nationale de Sécurité du Médicament and the Comité de Protection des Personnes Sud-Ouest et Outre-Mer IV, Limoges, France. The trial was conducted according to the principles and rules of the Declaration of Helsinki and its subsequent amendments.

### Products and Design of the Study

Three grenadine-flavored thickened waters were studied: one RGW and two drinks prepared with TP at two different viscosities. Compositions of study products are detailed in Table 1. The RGW (Gelodiet, Delical, Lactalis Nutrition Santé, France) was a 120-g cup (IDDSI level 4). The two other drinks were prepared with a TP (Gelodiet, Delical, Lactalis Nutrition Santé, France) as followed: at room temperature, 8.4 g grenadine syrup was mixed with either 5.5 g of TP and mineral water (qsp 120 g) to obtain nectar viscosity (NTP, 291 cP, IDDSI level 2) or 6.9 g of TP to obtain honey viscosity (HTP, 769 cP, IDDSI level 3).

After positive 3oz WT at the inclusion visit, patients were randomized in a crossover, open study to assess the efficacy of swallowing of the products following the sequence “RGW then NTP” or “NTP then RGW.” Randomization was done by automatic list generation. The different tests were performed at 1- to 3-day intervals.

The patient’s ability to swallow 120 g of each product was evaluated. The product was considered effective if it did not induce an immediate reflexive cough or the...
inability to swallow leading to split out the bolus. If the NTP induced a reflexive cough, a subsequent test with the HTP was performed at the same visit. Total amount of liquid consumed and test duration were recorded. Patients stayed under medical observation for 1 h after ingestion of each study product. The main criterion of the study was the efficacy of each product, defined as the proportion of patients who successfully swallowed without immediate reflexive cough.

A satisfaction questionnaire was completed at the end of each intake test. Appreciation of taste and texture as well as global appreciation of each product was scored using a visual scale based on seven smiley levels as previously described [13]. Patients were also questioned about their intended consumption of each product and the amount of thickened/gelled water they would be ready to consume daily. Any adverse event occurring during the study was recorded, assessed for severity and related or not with product intake according to the investigator’s opinion.

### Results

Five centers with different specialties participated to the trial from September 2015 to September 2016: one Physical and Rehabilitation Medicine Service, two Geriatric Services, one Neurology Unit, and one Digestive and Nutritional Rehabilitation Service. The flow chart of the study is given in Fig. 1. Thirty hospitalized patients with OD were included in the study. Characteristics of the study population are presented in Table 2. CPSA was evaluated for 28 patients, and 86% of them were at potential risk of aspiration (score ≤ 28). All the patients had a positive 3oz WT at inclusion. Ninety-three percent of the patients had been placed on a thickened fluid recommendation prior to inclusion, and two patients (7%) were not orally hydrated (complementary enteral feeding).

RGW was tested by all patients (n=30) and TP by 29 patients because one patient refused to consume the product. Twenty-seven patients were assessed with the NTP in agreement with the protocol. The two patients who were not orally hydrated coughed after HTP, but one of them successfully swallowed RGW. Finally, RGW was successfully swallowed in 93.3% (95% CI: 77.9–99.2) of patients and TP in 82.8% (95% CI: 51x488]sn 475]induced a reflexive cough, a subsequent test with the HTP was performed at the same visit. Total amount of liquid consumed and test duration were recorded. Patients stayed under medical observation for 1 h after ingestion of each study product. The main criterion of the study was the efficacy of each product, defined as the proportion of patients who successfully swallowed without immediate reflexive cough.

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### Statistical Analysis

Statistical analyses were performed, using JMP® 13.0 from SAS Institute (Cary, USA). Quantitative variables were described by mean ± standard deviation (SD) and compared using the Student t-test for paired data or the non-parametric Wilcoxon test. The main criterion was efficacy of each product. The 95% confidence intervals were calculated for each proportion using the Clopper-Pearson method. Efficacies of the two products (RGW and TP) were compared a posteriori using a McNemar test. Results were considered significant when p-value <0.05.

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**Table 1** Products composition and viscosity for 120 g

|          | RGW | NTP       | HTP           |
|----------|-----|-----------|---------------|
| Energy (kcal) | 37  | 19(53*)   | 24(57*)       |
| Protein (g)  | 0.1 | 0.0       | 0.0           |
| Fat (g)      | 0   | 0         | 0             |
| Carbohydrates (g) | 8.5 | 4.4 (12.8*) | 5.5 (13.9*)   |
| Fibers (g)   | 1.2 | 0.7       | 0.9           |
| Sodium (mg)  | NS  | 9.3       | 11.6          |
| Calcium (mg) | 23  | 0         | 0             |
| Chlorine (mg) | 52  | 0         | 0             |
| Mean viscosity (cP) | NE | 291       | 769           |
| NDD viscosity range | NA | Nectar (51-350 cP) | Honey (351-1750 cP) |
| IDDSI level  | 4   | 2         | 3             |

*Values with syrup

RGW ready-to-drink gelled water, NTP nectar-like thickened powder, HTP honey-like thickened powder. NDD National Dysphagia Diet (7), IDDSI International Dysphagia Diet Standardization Initiative (8), NS not specified, NE not evaluable, NA not applicable
Body mass index (kg/m²) 25.1±4.3

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Clinical Predictive Scale of Aspiration, CPSA
Positive 3oz WT (%) 30 (100)
>28 (no risk) 14–28 (uncertain range) 14 (14)
<14 (risk of aspiration)

CPSA score 23.1 ± 5.6

Age distribution
○ ≤ 60 years 5 (17)
○ 60–80 years 13 (43)
○ ≥ 80 years 12 (40)

Age-related dysphagia
○ Stroke 20 (67)
○ Ischemic 18 (90)
○ Hemorrhagic 2 (10)

Neurodegenerative diseases
○ Parkinson’s disease 7 (23)
○ Autoimmune limbic encephalitis 1 (14)
○ Cerebella degeneration by genetic atrophy 1 (14)
○ Progressive supranuclear palsy 1 (14)
○ Multiple sclerosis 1 (14)

Age-related dysphagia 3 (10)

Table 2 Characteristics of the study population at inclusion

| Sex       | n (%) or mean ± SD |
|-----------|--------------------|
| Men       | 15 (50)            |
| Women     | 15 (50)            |
| Age (years) | 74.3 ± 13.5       |

○ CPSA score distribution
○ <14 (risk of aspiration) 2 (7)
○ 14-28 (uncertain range) 22 (79)
○ >28 (no risk) 4 (14)

Positive 3oz WT (%) 30 (100)

CPSA Clinical Predictive Scale of Aspiration, 3oz WT 3-ounce water test

64.2–94.2) of patients (Table 3). Only one non-serious adverse event was recorded related to the study product: difficulty to catch the breath during the test with RGW, resolved by a brief oxygen supply.

Results of the satisfaction questionnaire are presented in Table 4. Significant differences were observed between the two products for taste, texture, and global appreciation, indicating a preference for the RGW over TP (Table 4). However, no difference was observed for intended consumption of RGW or TP, with about 60% of patients who declared to be ready to consume each product daily (Table 4).

Discussion

This is the first study conducted using normal French hospital practices to treat dysphagic patients and based on the entire consumption of a glass of thickened water or a cup of ready to drink gelled water.

Our results showed that both products were effective to ameliorate swallowing in patients with OD from different etiologies. None of the 30 patients enrolled in this study was able to swallow thin liquid at inclusion, whereas 93% of them successfully swallowed RGW and 83% successfully swallowed TP. These results confirm that modifying liquid viscosity by adding thickening agents is an effective strategy for the management of OD.

Previous studies in patients suffering from OD showed an improvement of swallowing, defined as a reduced prevalence of penetration and aspiration evaluated by VFS or FEES (fiberoptic endoscopic evaluation of swallowing) [9]. Whatever the thickening agents used, thickened fluids were successfully swallowed by 50–100% of patients with OD [4–6, 9, 14, 15]. However, most of these studies were performed in patients including 20–60% who were still able to safely swallow thin liquids [4, 6, 9, 14, 15]. By contrast, in our study, all the patients demonstrated signs of aspiration and/or penetration on thin liquids and presented a reflexive cough after 90 ml water ingestion at inclusion. Only the study of Leder et al. [5] enrolled patients who exhibited aspiration with thin liquid on FEES and showed that 100% of them successfully swallowed both nectar-like and honey-like thickened liquids. However, only 5–7 ml bolus volumes were tested, whereas aspiration could potentially occur with larger volumes. Moreover, Miles et al. [16] showed a significant association between cough response to aspiration and viscosity and volume of drink intake, but some of their patients coughed when they aspirated thin fluids but silently aspirated thick fluids indicating that cough response could be poor indicator of aspiration. However, the inversed reaction was observed within 7% of their patients ingesting a 5ml bolus and 1.7% of them ingesting a 50 ml bolus. In our study, the ingested bolus was 120 ml. Indeed, increasing bolus volume was reported to significantly reduce the safety of swallow whatever the viscosity [9]. We choose to test a high quantity of drinks to be more representative of the common practice in hospital, and this may also reduce the risk of inobservance of silent aspiration.

Despite their different viscosities and their different thickener agents, efficacy was not statistically different between the 2 tested products. However, RGW (IDDSI level 4) was successfully swallowed in three patients who coughed after NTP (IDDSI level 2) and/or HTP (IDDSI level 3) ingestion. This observation is consistent with the previous results showing that prevalence of safe swallowing significantly increased in a bolus viscosity-dependent manner, with maximal therapeutic effect observed with spoon-thick viscosity [4, 9, 14]. However, spoon-thick viscosity with modified starch thickeners has been reported to increase the prevalence of oropharyngeal residue, which may result in post-swallow airway ingestion [14]. In our study, the TP was tested only at nectar or honey viscosities and not at spoon-thick viscosity. RGW was more viscous than TP according to the IDSSI classification, but the NDD classification is not applicable to RGW because rheological measurements are not possible on this product. Presence of oropharyngeal residue was not evaluated in our
study, but patients remained under medical examination for 1 h after the ingestion test, in order to identify potential post-swallow reactions.

Another important point in the management of OD is palatability of thickened fluids, because a good compliance is required to ensure an adequate level of hydration of patients. An aversion for thickened liquids is often described in patients with OD, who declared to prefer nectar viscosity over honey or spoon-thick viscosities [17]. Therefore, it is recommended to reach a proper level of safety with the minimum amount of thickeners possible [18]. In our study, both products were well appreciated (rated above average) by the patients, with a

Table 3  Efficacy of the study products on swallowing

|                                      | RGW (n=30)       | TP (n=29)       |
|--------------------------------------|------------------|-----------------|
| Total amount of product consumed, g (%) | 97.8 (82)        | 100.8 (84)      |
| Time needed to consume the study product, min (mean ± SD) | 5.6 ± 3.2        | 6.8 ±4.7        |
| Number of patients who coughed after ingestion | 2                | 5               |
| Efficacy (proportion of patients who successfully swallowed, %) | 93.3 (IC95 %: 81.7–99.9) | 82.8 (IC95 %: 64.2–94.2) |

*RGW ready-to-drink gelled water, TP thickened powder*
preference for RGW over TP. However, the RGW was specifically formulated to have optimal taste and texture, while TP-based drinks were obtained by mixing water, TP, and grenadine syrup, which may explain this difference. Around 60% of patients declared to be ready to consume RGW or TP daily, but most of them would be ready to consume less than 8 cups (i.e., 960 ml) per day, which is less than the recommended standards of fluid intake for hospitalized adults established at 1500 ml [19]. Previous studies showed that patients consuming pre-thickened drinks or drinks thickened with TP consumed less than their recommended daily fluid intake orally [20, 21]. Therefore, particular attention must be paid to avoid dehydration of dysphagic patients, and the use of thickened fluids needs to be completed by foods with high water content or use of non-oral supplementary routes [19, 21].

There are several limitations in this study. First, sample size of 30 patients was low and did not include patients suffering from head or neck cancer, while prevalence of OD is high in this population. Clinical evaluation of efficacy of product on swallowing was based on the presence or absence of a reflexive cough after ingestion, and “silent aspiration” was not evaluated in this study. VFS is the gold standard method to evaluate deglutition but is not applicable with pre-thickened drinks. Further evaluation with the use of FEES and additional clinical parameters (such as voice changes and measurement of oropharyngeal residue) would be needed to complete our results and better evaluate the efficacy of the 2 tested products. However, the efficacy as measured in the present study was an easy-to-measure non-invasive parameter that did not require specific material or trained staff and compatible with common hospital practice, but also that is realized with a high quantity of tested product to secure the cough response. All patients exhibited reflexive cough after water ingestion at inclusion, and our study showed that this specific symptom was significantly improved with thickened liquids.

### Conclusion

This study showed that a RGW and a TP were successfully swallowed in 93% and 83%, respectively, of hospitalized patients with different dysphagia etiologies and unable to swallow thin water. Therefore, the use of these thickened products could be part as the therapeutic strategy to improve patient safety and compliance as well as to contribute to the maintenance of adequate fluid intake to prevent dehydration.

### Abbreviations

3oz WT, 3-ounce water test; CPSA, Clinical Predictive Scale of Aspiration; FEES, fiberoptic endoscopic evaluation of swallowing; HTP, honey-like thickened powder; IDDSI, International Dysphagia Diet Standardization Initiative; NDD, National Dysphagia Diet; NTP, nectar-like thickened powder; RGW, ready-to-drink gelled water; TP, thickening powder; VFS, videofluoroscopy

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### Author Contribution

JYS, AT, RT, AO, LD, FT, CG, PF, PJ, and JCD make substantial contributions to acquisition, analysis, and interpretation of data. JCD participates in drafting the article. All authors participate in revising the article critically for important intellectual content. All authors give final approval of the version to be submitted and any revised version.

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This study was supported by the Lactalis group. The funding source had no influence in subjects’ recruitment, data collection, and analysis.

### Data Availability

The authors confirm that the data supporting the findings of this study are available within the article.

### Declarations

### Ethics Approval

The protocol (registration number: 2014-A01084-43) was approved by French authorities: the Agence Nationale de Sécurité du Médicament and the Comité de Protection des Personnes Sud-Ouest et Outre-Mer IV, Limoges, France. The trial was conducted according to the principles and rules of the Declaration of Helsinki and its subsequent amendments.
Informed Consent  All participants recruited were able to understand and sign written consent after receiving study information and provided written informed consent.

Conflict of Interest  Cécile Bonhomme, Etienne Hazart, and Charlotte Baudry are employees of the Lactalis Group. Jean-Claude Desport participated in 2017 at the AFDN congress invited by Lactalis and was supported for training by Nutricia, in 2018 and 2019. None of the other authors has conflicts of interest to declare.

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