Introduction

Acute bronchiolitis is one of the most prevalent diseases in infants [21]. Young age is a risk factor for severity and hospital admission [3]. More than 20 000 bronchiolitis infants were admitted in French hospitals during the 2017-2018 bronchiolitis season. In 2009, the hospitalization rate was 35.6 per 1000 French infants, with 13% requiring mechanical ventilation support [3]. Indeed, respiratory distress is one of the main symptoms of this disease, as a consequence of upper and lower airway obstruction with secretions or lower airways and alveolar inflammation. As a result, children presenting with bronchiolitis may present with feeding difficulties, which are frequent indications for admission. In severe bronchiolitis, these may even lead to underfeeding, faltering growth and dehydration. Poor oral intake with no nutritional support has been shown to be associated with longer hospital stays [35].

Surprisingly, nutritional support strategies for acute bronchiolitis have been inadequately studied. Practices are often based on common sense and experience. This consists of an increase of the number of feeds per day, combined with decreasing the amount of volume per feed, and/or of nasal suctioning prior to breast/bottle feeding and/or of formula thickening, as recommended in the European French speaking bronchiolitis guidelines published in 2001 [32]. Furthermore, these guidelines state that infants with acute bronchiolitis may require enteral nutrition via a naso-gastric tube, or parenteral nutrition. A group from the western French region has updated the bronchiolitis guidelines in 2013 [33] and proposed a nutritional strategy based on the Wang modified severity score (mainly based on respiratory markers). Low Wang scores allowed for oral feeding, moderate scores for naso-gastric enteral feeding and high scores for intravenous hydration with close monitoring of serum sodium levels (hyponatremia) because of the risk of syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Swiss guidelines similarly have highlighted the high risk of hyponatremia [1]. However, these nutritional support guidelines remain vague, while the benefit (or absence of) of other treatments are far much detailed (use of salbutamol, adrenalin, hypertonic saline nebulization; chest physiotherapy; antibiotics), based on plethora of literature.

Bronchiolitis nutritional practices in European French speaking countries have not yet been examined, nor has their compliance with existing guidelines. Recent emphasis on the hyponatremia risk in bronchiolitis infants may impact on the nutritional strategy, regarding the hydration/nutrition route (intravenous versus enteral) and regarding solution types (iso- versus hypo-tonic fluids). Indeed, hyponatremia (caused by both anti-diuretic

hormone secretion and renin-angiotensin-aldosterone system activation [16]) is also worsened by the use of intravenous hypotonic solution [19].

In this study, we aimed to describe nutritional practices among general paediatrics units in European French speaking countries (especially focusing on enteral versus parenteral route use, on formula and solution type use, and on nutritional goals), to assess their compliance with international nutritional bronchiolitis guidelines, and to locate national guidance around bronchiolitis management across the World.

Material and methods

A 23-item cross-sectional survey was constructed by the NutriSIP (the French speaking paediatric intensive care nutrition group) members (as no validated pre-existing tool matching our objectives existed) with all closed ended questions. The survey was pilot-tested on 6 physicians to assess clarity of questions and establish face validity, and was modified slightly. The survey items were selected as they corresponded to the main nutritional issues identified by the NutriSIP, in order to assess nutritional care of young infants presenting with acute bronchiolitis: advice given to parents for at home nutritional support, in hospital nutritional management, preferred methods for enteral nutrition, and preferred methods for intravenous fluid management. The focus was on acute bronchiolitis, excluding infants with chronic respiratory failure, congenital heart disease or history of prematurity. Infants presenting with asthma were outside the scope of the survey. Young infants were defined as children younger than 3 months of age.

This survey is presented in supplemental digital content 1 in its original French version which was sent to invited responders (an English translation is provided in supplemental digital content 2). The electronic survey was disseminated online in spring 2018 via Survey-Monkey® software (San Mateo, California, USA) within the NutriSIP network. Every paediatric unit of local or university hospitals, admitting young infants presenting with acute bronchiolitis, was contacted to participate to the survey, in 6 different areas of French-speaking western Europe countries (Belgium, France and Switzerland), corresponding to the recruitment area of university paediatric intensive care units (PICUs) where a NutriSIP member is working: Auvergne-Rhône-Alpes area, Languedoc-Roussillon area, French Grand-Ouest area, Provence-Côte d'Azur area, and French speaking parts of Belgium and Switzerland. In each unit, one only physician working in a general paediatric ward or a paediatric emergency department was asked to answer the survey (intermediate care and PICU physicians were excluded

from the survey). The survey was accompanied by an information letter with instructions clarifying the setting and how to answer the questionnaire, insisting on the fact that answers should describe local current practices rather than ideal practices (see supplemental digital content 1 and 2). We aimed for a response rate at 70%, so two reminder e-mails were sent in case of no response.

Ethical approval was obtained for the study (Hospices Civils de Lyon ethical committee 18/07/2017).

In addition to the survey, a focused documentary search and analysis of international bronchiolitis guidelines were conducted (published either in English, French, German, Spanish, Portuguese, Dutch, Swedish, Norwegian, Danish, or Italian), on Pubmed and Google Scholar (using Mesh terms: "bronchiolitis, "nutrition", and using the filter "consensus development conference") from 2000 to 2018. NutriSIP members contacted physicians involved in bronchiolitis management worldwide through their personal networks, in order to access national guidelines stored on national platforms or published in national non-referenced journals or websites.

Statistical analysis

Data are expressed as mean and standard deviation (SD) for normally distributed continuous variables, or as median and inter-quartiles (IQR) for non-normally distributed variables and frequency and proportions for categorical variables. The country where responders were working (i.e. Belgium, France, or Switzerland) was considered as a factor which we hypothesized could impact nutritional practices and was analysed using chi-square or Fisher's exact test for categorical variables. Statistical significance threshold was set at 5%. Statistical analyses were conducted using IBM SPSS® Statistics version 24.0 (IBM® Armonk, NY, USA).

Results

Ninety-three (66% response rate) physicians working in general paediatric and/or paediatric emergency wards completed the online survey, out of the 141 physicians (one only per unit) that were contacted (16 from Belgium, 73 from France, 4 from Switzerland: the list of responding centres is displayed in the acknowledgment section). Ninety seven percent of them were paediatricians, with 67% working in a local hospital and 33% in university hospitals; physicians had been working in paediatric wards for a median of 14 years (IQR 7-20) and the median number of beds in the unit was 20 (IQR 15-27). Survey completion ratio was high, with missing data rare (<4%).

Main results are presented in tables 1 to 4. (Detailed results are presented in supplemental digital content 2). 1-*Regarding home discharge nutritional information*, written documentation was given to parents in less than 25% of the units, and an increase number of feeds a day with pre-feed nasal suctioning was advised by about 80% physicians (Table 1). 2-*Regarding enteral versus parenteral choice strategy*, enteral nutrition was withheld at admission in 24% of the centres, and in case of severe forms of bronchiolitis in 65.6%. This aimed to reduce respiratory workload for 87.8% of the responders (Table 2). 3-*Regarding enteral nutrition*, usual milk (breast feeding was favoured by a vast majority of physicians) was administered by bolus method in 72% of the units. Nurses and parents were more reluctant to perform naso-gastric tube insertion (42.1% and 38.6% respectively), compared to physicians (12.1%; $p<0.00$) (Table 3). 4-*Regarding parenteral management*, isotonic fluids were used in 13.4% of the units, while easy availability of intravenous (IV) fluid solution was the major factor influencing the physicians' prescription. About one fourth admitted insufficient knowledge about hyponatremia risk and pathophysiology (Table 4).

The use of isotonic IV solution was more frequent in Belgium and Switzerland, compared with France but the difference was not significant. No other differences were found between countries.

The guideline search found Western Europe guidelines (n=13), and other developed country guidelines (n=8). Detailed nutritional care was not part of the guidelines in half of the countries. In others, nutritional support guidance provided varied widely depending on the country, as presented in Supplemental material 3. Oral feeding ability was a common criterion for hospitalisation, but thresholds (if mentioned) varied by country. Clear guidance around enteral or parenteral support was available in 6 (29%) in favour of enteral nutrition in 5 (80%) and indication when to withhold enteral nutrition poorly detailed. Type of fluid solutions to be used in case of intravenous hydration (isotonic solution) were clearly detailed in 5 (24%), and hyponatremia occurrence risk was mentioned in 12 (57%). Scarcity of and inconsistency between international guidelines did not allow for practices/guidelines concordance analysis.

Discussion

A wide range of practices was found regarding the assessment and management of nutritional care for acute bronchiolitis in young infants, among general paediatric physicians. Practices and reasons for the withholding of oral and enteral nutrition were not consistent. An awareness of hyponatremia occurrence risk was present, but its

pathophysiology and relation to hypotonic solution infusion was insufficiently known. Most international guidelines were vague about nutrition care.

Prescribing practices for enteral or parenteral hydration and nutrition were not consistent amongst physicians. This could partly be explained by the paucity of details regarding nutritional management found in the guidelines [1, 33]. Previous studies which assessed physicians' compliance with bronchiolitis guidelines, found that change in physicians' practices prior to and after guideline publication varied depending on the education program proposed at the same time, but limited data regarding nutritional support or hydration was collected [2, 4]. Dissemination of and incorporation of guidelines into daily clinical practice remain challenging.

Parental advice for home nutritional management and in-hospital management of moderate forms of bronchiolitis were not consistent amongst physicians, apart from the importance to perform nasal suctioning prior to oral feeding, and to increase the number of feeds a day whilst maintaining a normal daily total amount of feeds. Formula thickening was also proposed, as per Khoshoo et al. study [14]. Most international guidelines refer to the child's capacity to sustain adequate feeding and hydration as a disease severity indicator and potential criteria for hospital admission. However, the precise threshold (from guidelines and in our survey) is rarely set. It is also a commonly recommended criterion for hospital discharge. These are consensual recommendations and practices but are mainly based on experience and common sense, rather than on evidence.

For hospital care, physicians differed regarding their use of oral, enteral and parenteral hydration/nutrition. Oral and enteral support was favoured, but not in all centres, and IV management was often proposed in severe bronchiolitis. The main reason to withhold oral nutrition was its impact on respiratory work load, as described by Pinnington et al. [28], and to prevent aspiration [13]. More surprisingly, this was also a reason to withhold enteral tube feeding in one third of the units, even when no sucking /swallowing effort was involved. Similarly, half of the physicians mentioned that withholding enteral nutrition could prevent the impact of gastric overdistention on ventilation, but continuous feeding which may limit this side effect compared to bolus feeding, was prescribed by less than 25%. Finally, withholding feeds to keep an empty stomach was also mentioned as a reason in anticipation of the potential need for intubation to prevent aspiration. Yet, the very low rate of intubation required in bronchiolitis should question this perceived fear. Indeed, recent reviews of bronchiolitis hospital admissions found that 6.7% to 16.0% of hospitalized infants required PICU admission for respiratory support, but only 1.2% to 4.1% required intubation [26, 27]. In most international guidelines, nutrition management is described vaguely, especially regarding the optimal feeding method to implement (oral, versus

enteral, versus intravenous) and regarding the type of feeds to administer. When mentioned, breast milk remains the recommended formula. Oral/enteral feeding is generally recommended as a first line nutritional strategy, but often no clear benefit is highlighted in the guidelines in comparison to IV fluids. Yet, studies conducted in bronchiolitis infants have compared IV and enteral hydration and nutrition showing no significant difference on tolerance. Oakley et al. found no difference in length of stay and side effects while comparing gastric tube hydration (oral hydration solution) and intravenous hydration (hypotonic solution); however, the success rate of gastric tube insertion was higher than peripheral venous catheter insertion, and gastric hydration was also cost-saving [23–25]. Srinivasan et al. also found similar rates of aspiration while comparing IV hydration to gastric hydration [31]. Kugelman et al. compared IV hydration (hypotonic fluid) to gastric nutrition (breast milk or infant formula) and found no difference in outcomes [15]. There is ongoing debate around the optimal respiratory support method [8, 20], but nasal high flow and non-invasive ventilation does not seem to impact feeding tolerance: in infants receiving high flow nasal cannula support, feed related complications (emesis and respiratory distress) were not dependent on feeding/hydration mode [29, 30]. Finally, while enteral nutrition may be associated with respiratory failure progression in adults on non-invasive ventilation, complications related to enteral feeding in children were rare [17]. Unfortunately, the impact on nutritional status was not assessed as an outcome in these studies comparing intravenous to enteral routes. Enteral nutrition may be safer than originally thought by physicians.

When IV hydration was used, only 13% of surveyed physicians prescribed isotonic solutions. More than 40% of physicians were not aware of the hyponatremia risk in bronchiolitis infants. In various studies, hyponatremia was present at PICU admission in 16 to 22% of infants with bronchiolitis (this rate may increase to 57% depending on the measurement technique), and was associated with severity of illness and length of stay [10, 18, 22]. Lavagno et al. have recently published a reappraisal of the pathophysiology of hyponatremia occurring in children with acute respiratory infections [16]. Hyponatremia is more likely to be the consequence of a volume dependent activation of the renin-angiotensin-aldosterone system, combined with an appropriate anti diuretic hormone secretion which may also be inappropriately triggered by a volume independent stimulus. Guidelines referring to “SIADH related hyponatremia” may not reflect its true pathophysiology and lead to inappropriate fluid/sodium management. However, bronchiolitis related hyponatremia may be worsened by the use of IV hypotonic solutions [19]: Hanna et al. found that 3 out of 4 infants admitted to PICU with hyponatremic seizures had received hypotonic IV solutions prior to admission [9]. Moreover, only half of the bronchiolitis guidelines available highlighted this hyponatremia risk despite the plethora of literature on the topic [7, 34], and French,

Belgian and Swiss guidelines remain vague on the harm caused by hypotonic solutions [1, 32, 33]. Isotonic solution use should be standard practice [19, 34]. However, a majority of physicians based their choice on the availability of ready-to-use solutions. The absence of a ready-to-use isotonic solution designed for infants (containing sufficient amount of glucose, e.g. 'Glucose 5% - NaCl 0.9%') with a French marketing authorization may prevent physicians prescribing such a solution. Belgian and Swiss physicians were more likely to use these isotonic solutions, as these are available in their respective countries. Finally, it would also be useful to include hyponatremia as an outcome in the future studies assessing enteral nutrition support to confirm their safety regarding this issue.

As for energy targets, the vast majority of physicians surveyed stated that they prescribed or advised normal total amounts of feeds per day. No recommendations could be found worldwide to guide clinicians. A recent study which assessed resting energy expenditure (REE) by indirect calorimetry in infants (2- to 11-month-old), presenting with mild bronchiolitis (no oxygen requirements) found that most children were hyper or hypo metabolic [6]. Schofield equations failed to accurately predict REE. No data were presented regarding more severely ill infants. This makes the adaptation of feeds to energy requirements challenging. Finally, one study conducted in critically ill bronchiolitis infants has suggested that higher intakes of energy and protein improved anabolism, but no impact on clinical outcomes was assessed [5]. Yet, dyspnoea and bronchiolitis have been shown to be associated with increased risk for weight loss during admission in an intermediate care unit [11]. The impact on outcome of each specific macronutrient (i.e. proteins, lipids, carbohydrates) is poorly studied in the literature, and the questionnaire sent to clinicians did not intend to highlight this issue. Therefore, it is urgent to appropriately determine the optimal nutritional strategy in this setting. Finally, breast milk was favoured by most responders. Immunologic benefits of breast feeding to prevent bronchiolitis have been highlighted by Kaur et al.[12]; maintaining breast feeding may also have beneficial impact on total intakes and immune response to viral aggression.

This study has some limitations, inherent to its design. Responders may give answers reflecting their own beliefs rather than their local team practices; subjectivity of responses is present in survey design and may introduce a bias in the result interpretation; no previous validated survey to assess nutritional practices in bronchiolitis infants was found in the literature, which did not allow increasing responder objectivity. Questions based on short clinical cases describing at a precise time point the respiratory status and children' feeding capability did not take into account the rapid changes that bronchiolitis patients experience, which may limit the interpretation of answers. This is often reflected in guidelines that focus on static rather than dynamic parameters to guide

patients' care. The survey was not designed to outline a generic management profile of each responding unit, which did not allow comparing centres; the absence of clinical data collection did not allow comparing practices to clinical outcomes. The survey did not assess clinicians' practices regarding quantitative aspects of hydration, which may also play a significant role in hyponatremia occurrence. The limited number of answers from Belgium and Switzerland compared to France did not allow comparing practices between these countries appropriately. Analysis of concordance of practices with guidelines was not possible due to recommendations being inconsistent and not detailed enough regarding nutrition management of bronchiolitis.

Conclusion

There is an urgent need to update bronchiolitis recommendations and to include a detailed hydration and nutrition support strategy, based on the available evidence, especially regarding hydration issues. Paediatric isotonic solutions should be available in all units (and in all countries), and used when oral/enteral nutrition is not indicated. Further research is required to provide robust evidence regarding nutrition optimal practices in this setting (energy and protein goals, optimal feeding routes and feed types, etc.). More active and effective dissemination of available guidelines is crucial, with suggested implementation strategies and re-assessment of these practices is required regularly to assess the impact of this guidance.

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