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ORIGINAL ARTICLE

Evaluation of the treatment used in cases of acute viral bronchiolitis diagnosed in the pediatric emergency room

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Abstract

Introduction: Bronchiolitis is a viral disease that occurs in infants and is an important cause of hospitalization in this group. It has a benign course. The only treatment that is proven to be effective is supportive. **Objectives:** To evaluate the frequency of pharmacological and non-pharmacological treatments used in patients who received bronchiolitis diagnosis in the Emergency room (ER) in the last five years, bronchiolitis evolution in these patients and develop a treatment protocol for bronchiolitis patients. **Methods:** Longitudinal retrospective study including children diagnosed with bronchiolitis in the ER from January 1, 2014 to December 31, 2018. Patients were compared for age, month of year in which they sought the ER, clinical characteristics before and after initial approach, need for ventilatory assistance, and outcome. **Results:** We analyzed 614 children; 58.3% were male; mean age was 5.21 months; there was a concentration of cases between April and July; Complication was described in 18.24% of patients. First therapeutic choice was inhaled bronchodilator (60.6%). All treatments were related to a statistically significant reduction in wheezing. Treatments that showed the highest improvement rates in infant respiratory pattern were nasal washing with SF0.9% and oxygen therapy. **Conclusion:** Evolution in bronchiolitis patients mainly depends on how the organism reacts to infection. No treatment demonstrated efficacy in changing bronchiolitis outcome, although transitory clinical improvement. Drug usage seems to be associated with greater physician concern due to greater severity in these children. Thus, a protocol needs to be created for treating a patient with bronchiolitis which reduces unnecessary interventions.

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INTRODUCTION

Acute viral bronchiolitis (AVB) is the most common cause of lower respiratory tract infection in young infants[1] and an important cause of hospitalization[2]. It is a seasonal disease with a benign course in healthy infants but a few cases have unfavorable evolution[3].

In the United States, incidence rate was 11 cases per 100 children of less than one year old[1,4]. In Brazil, the hospitalization rate was 2.1%. In respiratory syncytial virus infection (RSV) cases, 2.7% were admitted to the intensive care unit (ICU), 1.5% required mechanical ventilatory support, and death occurred in 0.2%[5].

RSV is the most common cause of AVB. Other pathogens such rhinovirus and adenovirus can also cause bronchiolitis[1,3]. RSV infection peaks during cooler and rainy seasons[7,8].

Pathophysiologically, the virus damages the lower airway mucosa, causing edema, eventual necrosis and mucus plugs. Thus, there is airway obstruction and varying degrees of lobar collapse[4]. Smooth muscle contraction is another potential mechanism of airway obstruction. Consequently, pulmonary hyperinflation, ventilation/perfusion mismatch and increased dead space occur, causing hypercapnia and hypoxemia[3].

It is usually a self-limited, benign, well-defined disease with low fever and a runny nose for three to five days, progressing to dry cough, tachypnea and/or respiratory distress, wheezing and/or crackling on respiratory auscultation. Apnea may occur in young infants[3]. Severe cases predominate in males due to gender differences in immunologic maturation and airway development[9]. The main risk factors for an unfavorable course of AVB are infants younger than three months, premature born less than thirty-four weeks, immunodeficiency, heart, and chronic lung diseases[3].

Home treatment is indicated in most cases, but those under two months old, with apnea, respiratory rate (RR) >70irpm, oxygen saturation (SpO_2) <92%, cyanosis, respiratory distress, altered level of consciousness and inadequate water intake should be hospitalized[3,8].

Scores help identify cases that can evolve with severity, including respiratory distress assessment instrument (RDAI). Pediatric early warning score (PEWS) is generally used the most in pediatric practice[5]. They document clinical severity of the patient and should be performed throughout the child's evolution together with other severity measures, to better define therapeutic strategies[5,12].

The diagnosis of AVB is clinical, and complementary exams such as X-rays and hemogram can be used to investigate complications or differential diagnoses[3]. The virus can be identified by aspiration of secretion from the nasopharynx and oropharynx[13].

AVB treatment can be controversial with several therapeutic proposals, reflecting a lack of clear evidence for a single effective treatment. Many interventions have failed to show relevant consistent effects[14].

Initial conduct is focused on general measures, such as monitoring, temperature control and maintaining calmness in the child, which causes a decrease in swirling of the pulmonary airflow. Studies suggest intermittent oxygenation monitoring[14].

Nasal irrigation with 0.9% saline is indicated as well as gentle aspiration of secretions[1]. In addition, oral, intravenous or nasogastric tube hydration due to increased insensible losses because of fever, tachypnea, respiratory effort and low water intake is essential[13]. Oxygen is indicated when SpO_2<92% or there is increased respiratory effort[3]. It should be administered through a nasal catheter, a Venturi mask, a non-rebreather mask or high-flow nasal cannula[3,15]. Patients with respiratory failure must be coupled to non-invasive or mechanical ventilation[3]. As for respiratory physiotherapy, there is no data showing a benefit in relation to oxygen[14].

Short-acting bronchodilator inhalers are not recommended, although some studies have shown improvements in clinical score. Their use in AVB has been indiscriminate, perhaps due to the similarity to asthma[14,16]. In the case of patients who have experienced a wheezing episode prior to AVB, a therapeutic test with a bronchodilator is suggested with subsequent maintenance if there is clinical improvement. Inhaled epinephrine should also not be routinely used in AVB treatment as there is no overwhelming evidence about its use[14].

Hypertonic saline 3%, used in hospitalized children for demonstrating transient clinical improvement and reducing hospital stay, did not have the same efficacy when used in the emergency situation[14]. The use of systemic corticosteroids in children with AVB is prohibited, as there is no data on safety or side effects[1,14].

The unnecessary use of antibiotics occurs due to health professional concern because of the presence of fever, difficulty in differentiating between atelectasis and pneumonia by radiography image, or fear of not detecting secondary bacterial infection. Their use does not improve duration of symptoms; they do not decrease the time and need for hospitalization or the use of oxygen[1]. Antibiotics are therefore not recommended except in concomitant bacterial infection[14]. Specific antivirals, such as ribavirin, are poorly studied and not recommended due to their high cost[17].

Clinical management of AVB is still a challenge[1]. It is a disease that has few proven interventions and generates enough discomfort for the patient, family, and also for professionals. It is therefore common that pharmacological therapy is used without evidence in an attempt to improve the patient symptoms and reduce length of stay and unfavorable outcomes.

OBJECTIVES

1. To evaluate the frequency of pharmacological and non-pharmacological treatments used in patients who were diagnosed with AVB.
2. To evaluate the etiology, clinical features, and evolution (hospital discharge, admission to the ward, pediatric ICU or death) of AVB in these patients.

3. Develop a treatment protocol for patients diagnosed with AVB based on international recommendations.

METHODS

This was a retrospective longitudinal study of children with AVB cared for at *Hospital das Clínicas de Botucatu* pediatric Emergency Room (ER) between January 1, 2014 and December 31, 2018.

All infants who had the first episode of wheezing associated with a viral infection were included in the study. Patients, who were diagnosed with AVB, even with a previous episode, were also included.

Patients were compared regarding age, month of diagnosis, clinical characteristics before and after initial approach (heart rate, respiratory rate, O_2 saturation, presence of wheezing on pulmonary auscultation and presence of any degree of respiratory distress), need for ventilatory assistance (nasal cannula, high flow nasal, mask and mechanic ventilation), and outcome (need for hospitalization and complications).

The intensity of respiratory distress was subjectively defined as mild, moderate or severe subdiaphragmatic and/or intercostal retractions.

The following initial approaches were evaluated: 1) no intervention; 2) nasal irrigation with 0.9% saline; 3) inhaled fenoterol; 4) inhaled fenoterol + nasal irrigation with 0.9% saline; 5) inhaled 0.9% saline; and 6) oxygen therapy alone (nasal cannula, high-flow nasal, mask and mechanic ventilation).

Pharmacological treatment was defined as the use of inhaled bronchodilators, systemic corticosteroids, inhaled hypertonic saline, oxygen therapy, antibiotics, and oseltamivir. Non-pharmacological is inhaled and nasal irrigation with 0.9% saline. No intervention is only imaging and laboratory tests were performed.

Complications was atelectasis (image suggestive of X-rays described in the medical records) and secondary bacterial infection when antibiotics were introduced during the patient's evolution.

The PEWS score was used in the formulation of the protocol because it is more objective and easier to apply.

The study was approved by the ethics committee of *Faculdade de Medicina de Botucatu* (CAAE: 16651919.0.0000.5411).

Data were taken from the electronic medical records, which caused limitations the study due to a lack of some information.

Descriptive statistical analysis of the data was performed, with frequencies and percentages for qualitative variables and mean, median, standard deviation, minimum and maximum values for quantitative variables.

The chi-square test or, when necessary, Fisher's exact test were performed to check associations between complications and explanatory variables of interest and between treatment and explanatory variables. Where necessary, a proportion test was performed after the chi-square test to verify statistical differences between the variables.

For continuous variables, a data normality test was performed to check data symmetry for continuous variables. The t-Student test was used on variables with symmetrical distribution to check differences between pre- and post-moments within each treatment, and an adjusted generalized linear model and gamma distribution were used when variables presented asymmetric distribution.

Results were considered significant when $p<0.05$.

RESULTS AND DISCUSSION

In total, 614 children with AVB were analyzed, 358 (58.3%) were male which is in accordance with other literature[9].

Mean age was 5.21 months, in agreement with reviewed articles[1,4], ranging from zero to 29 months. The average time of symptoms when seeking the ER was 4.11 days, ranging from zero to 45 days (1 case), the latter with several visits to the unit.

Cases were concentrated between April and July (63.19%), peaking in May and June (38.6%), demonstrating a seasonality also described in literature[1,3], repeating each year of the study, as seen in Graph 2.

A majority, 65.64% required hospitalization in a ward or ICU (12.9%), differing from literature. Average hospitalization in developed countries is 3%[4]. In a Brazilian study, hospitalization rate was 2.1%. Of those infected by RSV, 2.7% received ICU support[5]. Such data in our study can be explained by greater health team caution in patient observations or mild cases went undiagnosed. Average length of stay was 5.58 days, ranging from 1 day to 21 days, and ICU stay was 5.25 days, ranging from 2 days to 15 days.

A total of 360 patients (58%) required O_2. Principi et al (2016)[22] reported that 64% of patients needed O_2. Thus, our value for this variable is similar to literature. Average time on oxygen was 2.9 days, ranging from 2 hours to 20 days.

Most patients who required O_2 used nasal catheter (80.80%), demonstrating benign AVB evolution, matching literature[3]. Less than 1% of our patients used a high-flow nasal cannula, due to the lack of equipment in our service, even though it considerably improves patient respiratory distress[3]. Not having the device during this study period may have contributed to the high hospitalization rate in our series.

Of the 366 tested for Influenza in this study, only 6 (1.64%) were positive. This low detection rate may be due to some patients having been vaccinated, but there was no such description in their medical records. Of these, 5 (83.34%) were hospitalized for between 1 and 14 days (average 6.40 days). The hospitalization rate found in this study, despite the small number of patients, is much higher than that found in literature. This may be due to low testing rates for this type of virus. All hospitalized Influenza patients required O_2, for an average of 5.2 days. Complications appeared in 2 (33.34%). None needed intensive care unit (ICU). All 5 hospitalized patients received oseltamivir in the first 48 hours of hospitalization, which may explain the absence of ICU admission for these patients.

Of the 373 tested for RSV, 190 (50.94%) were positive. This is lower than literature, which reports about 80% positive RSV cases[3]. This difference can be explained by the low testing rate during this period (60.7% of patients). Of all those with positive RSV, 180 (95.78%) were hospitalized for an average of 6.46 days. Of these, 33 (17.26%) needed ICU. In the RSV patients, 170 (89.47%) required O_2 and complications appeared in 59 (31.05%).

It is important to note that our service only has kits to identify Influenza and RSV viruses and that these are in short supply during times of greater demand.

Out of all patients, 18.24% had some type of complication (atelectasis or secondary infection) with an average age of 4.98 months. The mean symptoms time for these patients when seeking ER was 3.88 days. Average hospital stay was 9.02 days and O_2 use was 7.46 days. Of those admitted to the ICU, the majority (75%) presented some type of complication.

None of the patients diagnosed in this period died, which is consistent with literature that reports a very low mortality rate in AVB[3,5].

At the time of the study, 57 patients (9.5%) received no intervention. Nasal irrigation with 0.9% saline was given to 90 patients (15%); inhaled fenoterol to 305 patients (51.17%); inhaled fenoterol + nasal irrigation with 0.9% saline to 57 patients (9.5%); inhaled 0.9% saline to 34 patients (5.5%); and oxygen therapy alone to 55 patients (9.19%). It should be taken into account that analysis of oxygen therapy in group 6 was performed as an isolated therapy, with the use of nasal catheter, Venturi mask, non-rebreather mask, NIV, and MV as required by the patient.

The majority (69.8%) of patients received some type of drug as first therapeutic choice, especially via inhaled bronchodilator (60.6%). In Table 1, we see that patients who received a drug (3, 4, and 6) were those who presented most respiratory distress at pre-treatment physical examination, especially those who were more tachypneic and hypoxemic. Taking Table 1, we can assume that there is a tendency to use more drugs when the patient shows some sign of severity.

The average length of hospital stay was longer in group 4 (6.2 days), but with no statistically significant difference between groups, either in terms of length of stay or O_2 usage time.

Table 2 shows that when patients are kept under observation, they evolve with improved HR and RR after admission to the ER, probably because the child has a mild form of the disease. Besides, they are calm and comfortable in the accompanying person's lap, leading to less airflow swirling, improving respiratory performance and reducing effort, tachypnea and tachycardia.

After nasal irrigation, we observed an improvement in RR, which can be explained by the removal of secretions obstructing the infant's airway, who have predominantly nasal breathing. This data reinforces literature regarding the usefulness of this simple measure[2,3].

After nebulization with fenoterol, there was an improvement in HR, RR, and SpO_2. Literature has shown that inhaled bronchodilator improves clinical scores, as found in our study, but in a transient manner[3]. In this case, we are evaluating patient response shortly after treatment and we do not have clinical data to verify whether there was sustained improvement.

The drop in patient HR and RR can be explained by improvement in breathing pattern. However, it must be considered that this decrease in HR demonstrated in statistical terms, may not have biological significance.

There were improvements in HR, RR, and SpO_2 after treatment 4 (inhaled fenoterol + nasal irrigation with 0.9% saline) and treatment 2 (nasal irrigation). As infants are nasal breathers, their breathing pattern significantly improves when removing nasal secretion, as they become more comfortable and less irritated, and oxygenate better with an increase in SpO_2. In this case, HR can improve due to improved respiratory effort, independent of bronchodilator use.

There was an improvement in HR, RR, and SpO_2 values after treatment 5 but without statistical significance, which can be explained by the small sample.

In treatment 6, we found improvement in SpO_2 and RR. Improved SpO_2 with oxygen therapy is simply explained by the provision of greater FiO_2, with a consequent improvement in tachypnea.

All treatments showed a statistically significant improvement in wheezing on auscultation.

Table 1. Comparison of clinical data of patients according to treatment given.

	Dyspnea	Wheeze	RR≥60	SpO_2<90%
TREATMENT 1	24.5%	52.6%	47.3%	8.7%
TREATMENT 2	40%	45.5%	35.5%	8.8%
TREATMENT 3	45.5%	75.4%	36%	14.7%
TREATMENT 4	52.6%	78.9%	36.8%	10.5%
TREATMENT 5	41.1%	79.4%	23.5%	5.8%
TREATMENT 6	61.8%	42.2%	54.5%	20%

Notes: RR = Respiratory rate; SpO_2 = Oxygen saturation; Treatments = 1) no intervention; 2) nasal irrigation with 0.9% saline; 3) inhaled fenoterol; 4) inhaled fenoterol + nasal irrigation with 0.9% saline; 5) inhaled 0.9% saline; 6) oxygen therapy alone.

Table 2. Comparison between HR, RR, and SpO2 averages before and after patient observation (treatment 1).

	Pre	Post	*p*
HR	145.6 (SD: 19.8)	135.4 (SD: 18.0)	0.0261
RR	56.9 (SD: 11.8)	45.9 (SD: 11.3)	<0.0001
SpO_2 (%)	95.0 (SD: 2.7)	94.0 (SD: 4.1)	0.1507

Notes: HR = Heart rate; RR = Respiratory rate; SpO_2 = Oxygen saturation; N=57.

When analyzing this table, we noticed that all therapeutic measures improved patient respiratory auscultation, mainly treatments 1 and 2. Probably the fact that the infant is kept calm and comfortable in the accompanying person's lap, reduces respiratory flow swirling, making it easier for the air to reach the alveoli, reducing auscultation wheezing. The same can happen when performing nasal irrigation, because when upper airway secretion is removed, breathing pattern improves. This suggests that the improvement in wheezing is due more to mechanical aspects (such as child comfort and airway positioning) than pharmacological aspects.

There was less reduction in wheezing in those who received oxygen only, as this acts more on hypoxemia than airway obstruction, and in those who were nebulized with fenoterol, reinforcing the fact that airway obstruction is not caused by bronchial hyperactivity[4].

Analyzing improvement in respiratory distress for each group, we noticed that treatments 1 and 5 showed better results than treatments 2, 3, 4, and 6 (Table 10).

In Table 10, we noticed that group 3 had proportionally more hospitalizations, ventilatory assistance and complications. Groups 1 and 5 had the lowest proportionally in these variables. Evidently, this study does not allow us to establish a cause-and-effect relationship between initial treatment and these outcomes, also severity at initial presentation may have directly influenced choice of therapy in the ER.

Table 3. Comparison between HR, RR, and SpO_2 averages before and nasal irrigation with 0.9% saline (treatment 2).

	Pré-	Pós-	*p*
HR	144.4 (SD: 18.4)	139.0 (SD: 15.7)	0.1547
RR	54.3 (SD: 12.0)	49.5 (SD: 11.2)	0.0125
SpO_2 (%)	94.4 (SD: 3.7)	94.7 (SD: 3.4)	0.6041

Notes: HR = Heart rate; RR = Respiratory rate; SpO2 = Oxygen saturation; N=90.

Table 4. Comparação entre as médias de FC, FR e SpO_2 antes e depois da nebulização com fenoterol (Tratamento 3):

	Pre	Post	*p*
HR	146.2 (SD: 18.5)	139.9 (SD: 18.6)	0.0023
RR	55.9 (SD: 11.9)	47.6 (SD: 11.3)	<0.0001
SpO_2 (%)	94.7 (SD: 3.0)	96.0 (SD: 2.9)	<0.0001

Notes: HR = Heart rate; RR = Respiratory rate; SpO_2 = Oxygen saturation; N=305.

Table 5. Comparison between HR, RR, and SpO_2 averages before and after nebulization with fenoterol and nasal irrigation with 0.9% saline (treatment 4).

	Pre	Post	*p*
FC	145,5 (DP: 18,7)	135,1 (DP: 15,9)	0,0250
FR	54,0 (DP: 15,2)	47,6 (DP: 11,5)	0,0301
SpO_2 (%)	94,3 (DP: 6,3)	96,7 (DP: 2,2)	0,0410

FC: Frequência Cardíaca, FR: Frequência Respiratória, SpO_2: Saturação de Oxigênio; N = 57

Table 6. Comparison between HR, RR, and SpO2 averages before and after nebulization with 0.9% saline (treatment 5).

	Pre	Post	*p*
FC	141,8 (DP: 19,5)	135,1 (DP: 19,5)	0,3368
FR	52,3 (DP: 11,1)	46,2 (DP: 11,5)	0,0508
SpO_2 (%)	93,7 (DP: 3,0)	95,0 (DP: 3,7)	0,1657

FC: Frequência Cardíaca, FR: Frequência Respiratória, SpO_2: Saturação de Oxigênio; N = 34.

Table 7. Comparison between HR, RR, and SpO_2 averages before and after placing the patient on oxygen only (treatment 6).

	Pre	Post	*p*
HR	142.3 (SD: 21.1)	136.0 (SD: 23.4)	0.3412
RR	55.0 (SD: 12.0)	47.3 (SD: 10.9)	0.0063
SpO_2 (%)	92.0 (SD: 3.9)	97.8 (SD: 2.6)	0.0478

Notes: HR = Heart rate; RR = Respiratory rate; SpO_2 = Oxygen saturation; N=55.

Table 8. Comparison between frequency (and percentage) of patients who had wheezing on respiratory auscultation before and after initial treatment.

	1	2	3	4	5	6
Wheeze + pre	30 (61.22%)	41 (50.62%)	229 (78.14%)	44 (78.57%)	28 (84.85%)	28 (58.33%)
Wheeze + post	9 (24.32%)	11 (16.42%)	131 (51.76%)	18 (34.62%)	15 (55.56%)	16 (30.77%)
Δ	21 (70% improvement)	30 (73% improvement)	98 (42.79% improvement)	26 (59.09% improvement)	13 (46.42% improvement))	12 (42.85% improvement)
p	0.0007	< 0.0001	< 0.0001	< 0.0001	0.0122	0.0055

Notes: Treatments: 1) no intervention; 2) nasal irrigation with 0.9% saline; 3) inhaled fenoterol; 4) inhaled fenoterol + nasal irrigation with 0.9% saline; 5) inhaled 0.9% saline; and 6) oxygen therapy alone.

Table 9. Comparison between frequency (and percentage) of patients who had respiratory distress (RD) before and after initial treatment.

	1	2	3	4	5	6
RD + pre	14 (25.45%)	36 (40.45%)	136 (45.95%)	28 (49.12%)	14 (40.63%)	34 (62.96%)
RD + post	5 (10.64%)	12 (14.12%)	96 (34.04%)	15 (26.32%)	7 (21.88%)	14 (26.42%)
Δ	9 (64.28% improvement)	24 (66.67% improvement)	40 (29.41% improvement)	13 (46.42% improvement)	7 (50% improvement)	20 (55.55% improvement)
p	0.0554	0.0001	0.0035	0.0120	0.0765	0.0001

Notes: Treatments: 1) no intervention; 2) nasal irrigation with 0.9% saline; 3) inhaled fenoterol; 4) inhaled fenoterol + nasal irrigation with 0.9% saline; 5) inhaled 0.9% saline; and 6) oxygen therapy alone.

Table 10. Comparison between the frequency (and percentage) of patients requiring hospitalization, use of oxygen and complications according to initial treatment used.

	1	2	3	4	5	6	*p*
Hospitalization	26 (45.61%)[a]	48 (53.33%)[b]	205 (67.21%)[c]	43 (75.44%)[b]	20 (58.82%)[a]	52 (94.55%)[b]	< 0.0001
O_2 support	24 (42.11%)[a]	43 (47.78%)[b]	178 (58.36%)[c]	38 (66.67%)[ab]	17 (50.00%)[a]	54 (100.00%)[b]	< 0.0001
Complications	7 (12.28%)[a]	13 (14.44%)[ab]	40 (13.11%)[d]	18 (31.58%)[bc]	7 (20.59%)[a]	26 (50.00%)[cd]	< 0.0001

Notes: Treatments: 1) no intervention; 2) nasal irrigation with 0.9% saline; 3) inhaled fenoterol; 4) inhaled fenoterol + nasal irrigation with 0.9% saline; 5) inhaled 0.9% saline; and 6) oxygen therapy alone; Values with the same letter were considered to have no statistical difference.

The highest hospitalization rate occurred in those who received treatments 3, 4 and 6. As already discussed (Table 1), those arriving with more serious symptoms were those who received the most pharmacological therapy. The fact that they are the most serious, justifies them being in most need of hospitalization. In addition, when HR, RR, and SpO_2 were analyzed before and after nebulization with fenoterol (Table 4), we saw improvement in all parameters, but more than half of these patients were hospitalized, which supports literature, in that improvement in clinical scores is transient and the use of bronchodilators does not reduce the need for hospitalization[3]. The need for O_2 is a criterion for admission, which justifies that more than 90% of patients who received O_2 supplementation were hospitalized.

There were only 3 records in the electronic medical record of children who received systemic corticosteroids as their first therapy, making the statistical analysis of this data unfeasible. No patient received antibiotics in the ER, so it will be necessary to expand this study to analyze the impact of these medications on AVB evolution.

AVB is a disease that often has a benign course and no treatment has proven effective in changing its outcome, as hospitalization and complications. General measures, such as patient reassurance, hydration, nasal washing, and O_2 supplementation are important in improving breathing pattern and bringing more comfort. The use of drugs seems to be associated unsustainable clinical improvement, besides the greater physician concern due to severity in these children. Thus, the

creation of a protocol that can be used in any health service, as suggested below, unifies the measures to be taken when caring for a patient with AVB, thus reducing unnecessary interventions. The use of clinical scores contributes to objectifying clinical evaluation of patients and to having more concrete data regarding their evolution according to treatment.

The team that provides care in the ER must be trained to apply the suggested protocol (Figure 1) for better results and patient care.

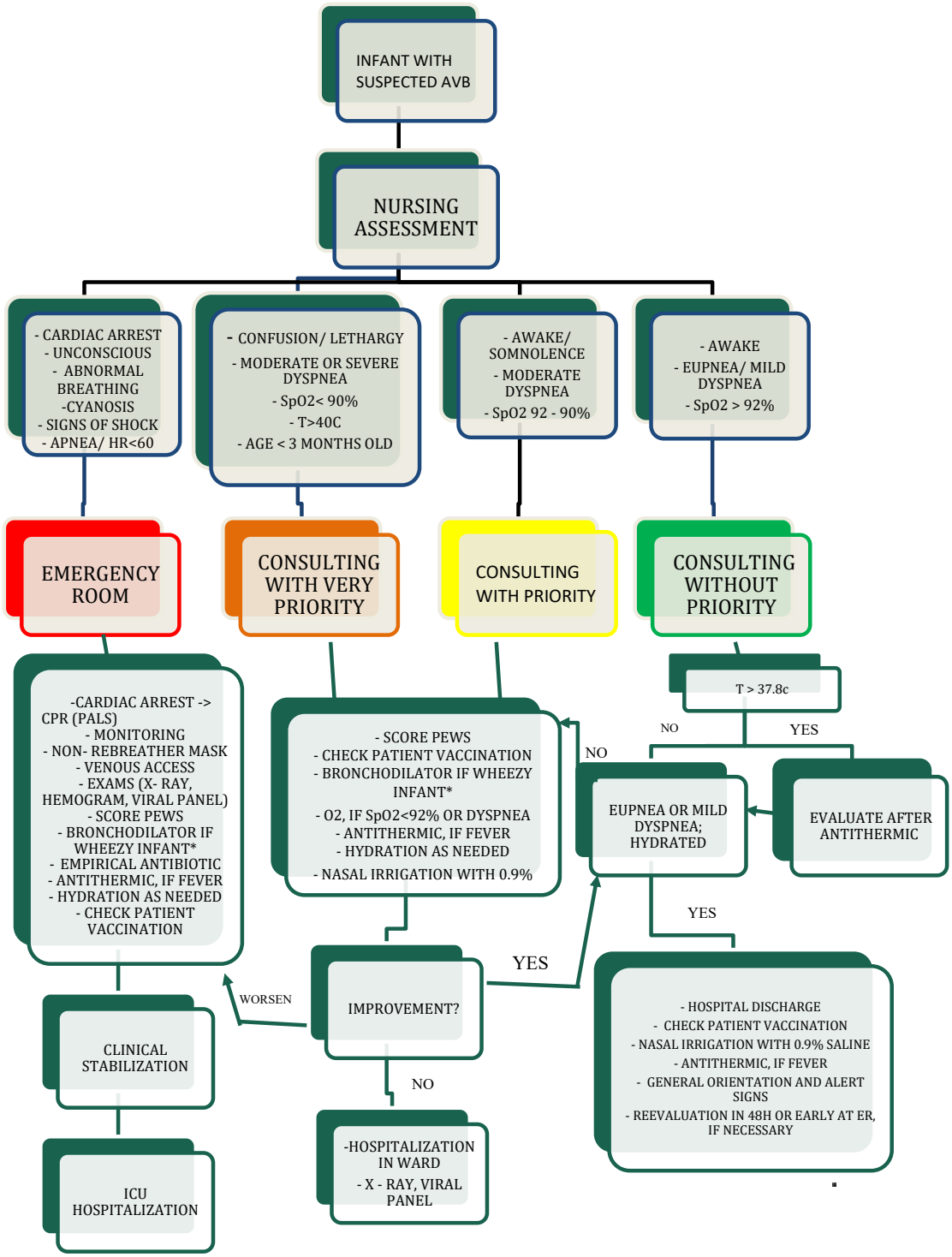


Figure 1. Suggested protocol. Notes: Patient with previous history of wheezing: perform therapeutic test with short acting B2.

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