Preventing facial pressure ulcers in patients under non-invasive mechanical ventilation: a randomised control trial

**Objective:** To comparatively assess the efficacy of four different therapeutic strategies to prevent the development of facial pressure ulcers (FPUs) related to the use of non-invasive mechanical ventilation (NIV) with oro-nasal masks in critically ill hospitalised patients.

**Method:** This randomised control trial was performed at the high dependency unit in the University General Hospital Gregorio Marañón in Madrid, Spain. Overall, 152 patients with acute respiratory failure were recruited. All patients were hospitalised and received NIV through oro-nasal masks. The Norton tool was used to evaluate the general risk of developing pressure ulcers (PUs). Subjects were divided into four groups, each of them receiving a different treatment. Tissue assessment and preventive care were performed by a member of the research team.

**Results:** The incidence of FPUs was significantly lower in the group receiving a solution of hyperoxygenated fatty acids (HOFA) when compared with each of the other therapeutic strategies: direct mask (p=0.055), adhesive thin dressing (p=0.03) and adhesive foam dressing (p=0.001).

**Conclusion:** The application of HOFA on the facial skin in contact with the oro-nasal masks showed the highest efficacy in the prevention of NIV-related FPUs.

**Declaration of interest:** The authors have no conflict of interest.
Background and rationale
The correct choice of the ventilatory interface is essential to obtain good outcomes with NIV. In general, the nasal mask is better tolerated, while the oro-nasal mask produces a faster reduction of the carbon dioxide partial pressure (pCO₂). The ideal ventilation mask must be distensible, comfortable, lightweight, easy to apply, latex-free, and available in or adaptable to different sizes; it must also provide low resistance to airflow and have the smallest possible dead space. The mask fixation, which should be simple, is generally done with Velcro ribbons, elastic strips and/or fixation harness.10–13

The incidence of subjective mask discomfort may be as high as 50%, but in most cases this can be treated by adjusting or changing the mask. In patients with chronic conditions, the main adverse effects of NIV are dry mouth, nasal congestion, gum pain, claustrophobia and the effects generated by air leaks; however, when NIV is used in acute patients, PUs on the skin in contact with the mask are the main adverse events.14,15 These adverse events become predictors of therapy failure.16

Evidence on NIV is profuse. Published literature about PUs is also abundant. However, there has been a paucity of publications combining these two subjects. This is may be due to the fact that, until now, research has focused on the prevention and treatment of PUs at more traditional locations, such as the sacrum and heels. Valtysson17 described the use of NIV as a therapy bearing the risk of producing suffering and pain during its use in the form of FPUs, and later on, in the form of scars disfiguring the face. Another study, by Schallom et al.,18 found a 20% incidence of NIV-related FPUs (NIV-R FPUs) in intensive care unit (ICU) patients ventilated with oro-nasal masks. However, they did not deal with the possible effect of preventive measures to avoid the development of NIV-R FPUs. A recently published article by Raurell Torreda et al.19 assessed how to optimise interventions in NIV. The authors followed 387 patients hospitalised mainly in critical care units. Skin nasal lesions were presented as adverse events and seemed to be directly correlated with the level of air leaks around the masks. The incidence of nasal skin lesions was 2.4%. The possible cause, as suggested by the authors, was the fact that nurses tended to press the mask tightly against the skin.

External pressure and medical device-related PUs
If we consider the increasing number of materials and clinical devices used with diagnostic or therapeutic purposes capable of producing external pressure, it would be reasonable to expect an increased number of medical device-related PUs in hospitalised patients.20–22 Many institutions have reduced the incidence of traditional PUs and therefore the significance of medical device-related PUs has become more apparent.20

The oro-nasal masks are the most commonly used interfaces at our HDU; despite being less well tolerated, their efficacy is higher in the management of acute problems.16 Initially, as non-invasive barometric ventilators compensate autonomously for small air leaks, our HDU used the lowest effective pressure on the mask’s fixation harness to prevent the development of NIV-R FPUs and, at the same time, increase the patient’s comfort by allowing small air leaks to encourage the tolerance of NIV. Nurses also applied different types of dressings on the most exposed areas, aiming to decrease the pressure exerted by the mask on the patient’s face.23

A study by Weng24 showed the potential protective effect of hydrocolloid and polyurethane dressings on NIV-R FPUs. However, Acorda25 described that foam dressings, even if not strongly adhesive, redistributed pressure better than hydrocolloid dressings. Our literature review on the subject found different studies showing large variability on the preventive measures, as well as highly dispersed results about the incidence of NIV-R FPUs.17,26–33

In a systematic review published in 2006 about care interventions in NIV, Blanca Gutierrez26 explained that the development of FPUs on the skin in contact with the mask is a subject not very commonly treated, and stated that ‘in such cases, the experience more than the evidence is in favour of using the appropriate mask size, avoiding applying the mask too tightly and using adhesive skin protectants over the pressure areas in order to maintain tissue integrity’.

In a descriptive study performed in 2009 at our HDU with patients undergoing NIV, the assessment of comfort showed that 50% of patients experienced pressure on the cheekbones and the nasal bridge, and 11% experienced pain. The authors highlighted a high variability in the prevention and treatment of PUs and found that iatrogenic lesions were underreported.23

Preventing and minimising costs of treatment
The fourth national study of PU prevalence in Spain showed an average prevalence of 7.87% [95% confidence interval (CI): 7.31–8.47%] in hospitals for adults; the average prevalence increased to 18% in the ICU.35 Soldevilla Agreda et al.36 presented in 2007 their work about the cost of treating PUs in hospitals. They found that the cost was directly linked to the severity of the lesion, ranging from 24 euros for a category I PU to 6802 euros for a category IV. The same study established that the total annual cost for treating PUs in Spain was approximately 461 million euros, which represents about 5% of the total expenditure in health care. Of this amount, 15% corresponded to the cost of dressings and other materials, 19% to nursing time and 45% to hospital stay linked to other concomitant diseases. A more recent systematic review by Demarré et al.37 is consistent with the same variability of costs, either for prevention or for treatment. The cost of prevention per patient per day ranged from 2.56 euros to 87.57 euros, while the cost of PU treatment was 1.71 euros to 470.49 euros (per patient per day). The total cost of treatment ranged...
Fig 1. The different phases of the randomised control trial from enrolment to analysis

Assessed for eligibility (n=220)

Randomised (n=171)

Excluded (n=49)
- Not meeting inclusion criteria (n=44)
- Facial tissue lesion (n=36)
- Facial deformity (n=8)
- Declined to participate (n=5)
- Other reasons (n=0)

ENROLMENT

Randomised (n=171)

Assessed for eligibility (n=220)

- Not meeting inclusion criteria (n=44)
- Facial tissue lesion (n=36)
- Facial deformity (n=8)
- Declined to participate (n=5)
- Other reasons (n=0)

Allocated

Group A: direct mask (n=44)
- Received allocated intervention (n=44)
- Did not receive allocated intervention (n=0)

Group B: adhesive thin dressing (ATD) (n=36)
- Received allocated intervention (n=36)
- Did not receive allocated intervention (n=0)

Group C: adhesive foam dressing (AFD) (n=46)
- Received allocated intervention (n=46)
- Did not receive allocated intervention (n=0)

Group D: hyperoxygenated fatty acids (HOFA) (n=45)
- Received allocated intervention (n=45)
- Did not receive allocated intervention (n=0)

ALLOCATION

Follow-up

Lost to follow-up (n=5)
- Transfer to another unit (n=3)
- Endotracheal intubation (n=1)
- Dead (n=0)
- Discontinued intervention (incomplete record >50%) (n=1)

Lost to follow-up (n=1)
- Transfer to another unit (n=1)
- Endotracheal intubation (n=0)
- Dead (n=0)
- Discontinued intervention (incomplete record >50%) (n=0)

Lost to follow-up (n=7)
- Transfer to another unit (n=4)
- Endotracheal intubation (n=0)
- Dead (n=1)
- Discontinued intervention (incomplete record >50%) (n=2)

Lost to follow-up (n=6)
- Transfer to another unit (n=2)
- Endotracheal intubation (n=0)
- Dead (n=3)
- Discontinued intervention (incomplete record >50%) (n=1)

FOLLOW-UP

Analysed (n=39)
- Excluded from analysis (n=0)

Analysed (n=35)
- Excluded from analysis (n=0)

Analysed (n=39)
- Excluded from analysis (n=0)

Analysed (n=39)
- Excluded from analysis (n=0)

ANALYSIS

from 15.10 euros to 69 472 euros, the cost being higher, as expected, for category IV PUs.

In their studies, Padula38 and Schuurman39 concluded it was more cost-effective to pay for prevention than for treatment of hospital-acquired PUs. Prevention must be based on methods that quantify risk factors and assist to determine the extent of tissue damage.40,41

There are general protocols for the prevention and treatment of PUs in our hospital, but these are not specifically targeting NIV-R FPUs. Instead, departments or wards using NIV choose to implement or not their own measures to prevent the development of FPUs.

NIV-R FPUs generate important costs to health-care systems and negatively impact the tolerance/acceptance of NIV. Variability in interventions induces a bigger usage of consumable goods, increases direct costs, makes it difficult to reach consensus about protocols of care, and produces a decreased perception of quality of care. As there is paucity in published evidence about the subject, this study has focused on finding evidence to support the creation of protocols of care aiming to prevent NIV-R FPUs, focusing on increasing safety and decreasing variability of care.

Methods

This study was designed as a randomised controlled trial (RCT) to assess four different clinical strategies for NIV-R FPU prevention. It was performed at the HDU, part of the Emergency and Critical Care Department of the UGHGM.

Patients with acute respiratory failure requiring NIV—regardless of the type of NIV employed—were recruited. All patients received ventilatory support through the use of oro-nasal masks. Recruited patients did not present any lesion on the skin supporting the respiratory interface. The inclusion criteria were:
- Adult patients (18 years or older)
- Absence of facial soft tissue injury
- Absence of facial anatomy structural deformity.
The exclusion criteria were:
- Patients not agreeing to participate and not signing the informed consent form
- Patients with facial soft tissue lesions
- Patients with any deformity of the facial anatomy.

Recruited patients or their legal representatives signed an informed consent form.

The study complied with the Declaration of Helsinki and the requirements of the Spanish law 15/1999, dated 13 December 1999, regarding confidentiality and data protection. The study protocol (PUPPVMNI_200910) was approved by the Clinical Research Ethics Committee of the UGHGM. The study was registered at the European Medicines Agency clinical trials database (EudraCT number 2015-004185-28) and the ClinicalTrials.gov database, under the number NCT02526862.

Population size
We calculated the population size by considering an effect difference of 15.8% that we obtained on a previous protocol of the proposed bigger trial.

Assuming a power (1-β) of 80% (with a type II error β=0.20) and a CI of 95% (α= 0.05) we estimated a total of 152 patients needed to be recruited. We decided to replace all withdrawals and drop-outs and to perform a data analysis by following a protocol (per-protocol).

Interventions
All patients were hospitalised in the HDU and received NIV through oro-nasal Respironics PerformaTrak full face masks (Philips). Tissue assessment and preventive care were performed by a member of the research team. We used the Norton tool42 to evaluate the general risk of developing PUs.

To avoid bias and confounding variables, we randomised subjects into four different groups (Fig 1) using specifically designed tables of random numbers. The interventions for each group were as follows:
- Group A (direct mask/control group): the oro-nasal mask was applied directly over the patient’s skin
- Group B (adhesive thin dressing (ATD)): the oro-nasal mask was applied over skin protected with adhesive thin polyurethane foam dressings (Allevyn Thin). The Allevyn Thin (Smith & Nephew) adhesive dressing consists of a layer of hydrophilic polyurethane matrix, and a semipermeable polyurethane film and a perforated polymeric wound contact layer. This inner layer is coated with a hypoallergenic acrylic adhesive
- Group C (adhesive foam dressing (AFD)): the oro-nasal mask was applied over skin protected with adhesive foam dressings (Askina Foam). Askina Foam (B.Braun) is a two-layered non-adherent dressing made from a breathable hydrophilic polyurethane foam layer and a thin semipermeable, transparent and protective polyurethane film, which is waterproof and bacteria-resistant
- Group D (hyperoxygenated fatty acids (HOFA)): the oro-nasal mask was applied over skin protected with a solution of HOFA, gently applied without rubbing on the chin, cheekbones, nasal bridge and forehead. Linovera (B.Braun) was chosen because it was the only HOFA commercially available with an anticontamination dispenser system, in a bottle offering UV protection, a leaflet describing its composition (linoleic acid 60–70%), and a flash point of 112°C. Fatty acids have flash points between 85°C and 120°C, meaning that they can be safely used in the clinical setting. The proposed mechanism for the HOFA efficacy may be the increase in the concentration of inflammatory mediators, such as nitric oxide and prostaglandins,43 resulting in an increased local tissue oxygenation44 which, combined with an increased keratinocyte renewal, appear to counteract the impact of pressure and friction forces.

All the medical devices used in the present study had the CE mark and were handled following the manufacturers’ instructions for use.

The preventive intervention for patients in groups B and C included placing dressings over the nasal bridge and cheekbones. We did not put them on the forehead because the mask used at the hospital includes a foam pad at the point of contact with the forehead. In order to avoid bias, all trial dressings were cut using the same standard procedure: in a circular way.

Table 1. Distribution by treatment group and gender

<table>
<thead>
<tr>
<th>Preventative method</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct mask</td>
<td>26</td>
<td>13</td>
<td>39</td>
<td>25.6%</td>
</tr>
<tr>
<td>ATD</td>
<td>24</td>
<td>11</td>
<td>35</td>
<td>23.2%</td>
</tr>
<tr>
<td>AFD</td>
<td>17</td>
<td>22</td>
<td>39</td>
<td>25.6%</td>
</tr>
<tr>
<td>HOFA</td>
<td>19</td>
<td>20</td>
<td>39</td>
<td>25.6%</td>
</tr>
<tr>
<td>Total</td>
<td>86</td>
<td>66</td>
<td>152</td>
<td>100%</td>
</tr>
</tbody>
</table>

ATD–adhesive thin dressing; AFD–adhesive foam dressing; HOFA–hyperoxygenated fatty acids

Table 2. Distribution by treatment group and hours during which patients received NIV

<table>
<thead>
<tr>
<th>Preventative method</th>
<th>Hours (average)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct mask</td>
<td>13.78</td>
<td>10.58</td>
</tr>
<tr>
<td>ATD</td>
<td>13.29</td>
<td>8.90</td>
</tr>
<tr>
<td>AFD</td>
<td>13.96</td>
<td>10.58</td>
</tr>
<tr>
<td>HOFA</td>
<td>16.75</td>
<td>10.72</td>
</tr>
<tr>
<td>Total</td>
<td>14.48</td>
<td>10.24</td>
</tr>
</tbody>
</table>

NIV–non-invasive ventilation; ATD–adhesive thin dressing; AFD–adhesive foam dressing; HOFA–hyperoxygenated fatty acids
Table 3. Development of PUs compared with age, score and NIV

<table>
<thead>
<tr>
<th></th>
<th>FPU developed</th>
<th>n</th>
<th>Average</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>74</td>
<td>74</td>
<td>77.95</td>
<td>9.41</td>
</tr>
<tr>
<td>No</td>
<td>78</td>
<td>78</td>
<td>77.67</td>
<td>9.80</td>
</tr>
<tr>
<td><strong>Norton score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>74</td>
<td>74</td>
<td>10.74</td>
<td>2.67</td>
</tr>
<tr>
<td>No</td>
<td>78</td>
<td>78</td>
<td>10.64</td>
<td>3.02</td>
</tr>
<tr>
<td><strong>Number of hours with NIV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>74</td>
<td>74</td>
<td>15.62</td>
<td>10.74</td>
</tr>
<tr>
<td>No</td>
<td>78</td>
<td>78</td>
<td>13.39</td>
<td>9.69</td>
</tr>
</tbody>
</table>

PU-pressure ulcer; FPU-facial pressure ulcer; NIV-non-invasive ventilation; SD-standard deviation

For all patients, the skin and dressing under the mask were assessed every 6 hours. Dressings were assessed for correct fixation and changed if considered necessary. The hydration status of the skin under the mask was evaluated for patients in group D, and if considered necessary, more HOFA solution was reapplied. Skin assessments were performed independently by two different evaluators using the GNEAUPP (Grupo Nacional para el Estudio y Asesoramiento en Úlceras por Presión y Heridas Crónicas) classification for PU staging.\(^1\) In case of discrepancy, the highest category was recorded.

Data collection
Collected data included socio-demographic data; Norton score at admission; location and staging of any skin tissue lesion present at admission; development of PU at the HDU; presence, location and staging of tissue lesions appearing between 5 and 10 hours after stopping the treatment with NIV; method of primary prevention employed; number of hours under NIV; use of vasoactive medications; and observations.

When the NIV was stopped for more than 5 hours, an assessment for PU staging was performed. The final assessment of the facial skin was always performed between the fifth and tenth hour after finalising the treatment with NIV. This waiting time is necessary to allow for any signs of pressure ischaemia to become apparent.

Efficacy measurement and statistical analysis
Treatment efficacy was measured by the incidence of PUs on the areas of skin in contact with the mask. We performed a general descriptive analysis, as well as a descriptive analysis for each of the study groups. This was followed by a homogeneity analysis of the four groups. For descriptive statistics analysis, the SPSS v.18 software package was used.

In order to establish statistically significant differences in the development of NIV-R FPUs, we performed a comparative analysis of data. Results were described based on average, standard deviation (SD) and quartiles in case of normal distribution; adding the median and interquartile range in case of asymmetric distribution.

Qualitative variables were evaluated in frequency and percentage. We used valid statistical tests for comparison. To estimate the magnitude effect, the absolute risk reduction (ARR) and the number needed to treat (NNT) were calculated.

Results
Recruitment started on 7 February 2012 and reached 152 patients on 17 August 2013. During this period, 220 patients were assessed for eligibility to participate in the trial; 171 of them were included and randomly assigned to each one of the four treatment groups (Fig 1). A total of 19 patients were lost to follow-up; 4 died before the end of the trial, and data recording was incomplete for 4 patients. As initially planned, we collected complete data sets for the purpose of this trial from a population of 152 patients (56.6% men; 43.4% women) (Table 1). Data analysis was performed following the per-protocol principle.

Because of the acute character of the situation before starting NIV, 150 patients received a Norton score of 1 (bed bound) for the item activity, as they needed to stay in bed. A Norton score of 12 or less was considered an indicator of high risk of developing a PU. The average Norton score of the total population was 10.69 (SD=2.85); considering the results by type of treatment, all groups showed Norton scores lower than 12 and higher than 10. For the total population, the parameter from the Norton scale showing the highest variability was the physical condition (very bad, poor, fair, good). The number of patients with ‘very bad’ or ‘poor’ scores was:

- 20 out of 39 patients in group A (direct mask)
- 19 out of 35 patients in group B (ATD)
- 19 out of 39 in group C (AFD)
- 25 out of 39 patients in group D (HOFA).

The average number of hours during which patients received NIV for the total population was 14.48. By groups, all averages were below this figure except the value for the HOFA group: 16.75 hours (Table 2). Using ANOVA tests, we analysed the variables of age and Norton score (Table 3) in the four groups to determine their influence in the results. We did not find any significant difference for age (p=0.337) or Norton score (p=0.368). The statistical analysis of data from the four groups did not find any significant difference related to the number of hours under NIV and the development of FPUs (p=0.179).

During this trial, 74 patients (48.68% of the total population) developed 87 FPUs. The nasal bridge was the anatomical structure most frequently affected (72 patients), followed by the cheekbones (12 patients). Only one patient developed a PU on the chin (in the ATD group). A total of 10 patients developed more than one FPU. Fig 2 shows the distribution (number) of PUs on the nasal bridge by category and treatment group. In total, 72 patients presented 74 PUs on the nasal bridge; two patients, one in the direct mask group and other in the AFD group, each developed each two different lesions. No nasal-bridge category IV PUs were present in any of...
the treatment groups. Patients in the HOFA group developed nasal bridge category I PUs only. Patients treated with HOFA did not develop PUs on the cheekbones; there was one case of a cheekbone PU in the control group, and patients receiving ATD and FD developed 6 and 5 cases, respectively. There were no PUs on the forehead of any patients.

The use of vasoactive medications is required in some critically ill patients, and they exert a quick action. They were used in 31 patients in our study (20.5% of the total population). We found a slightly higher incidence of FPUs in the group of patients receiving vasoactive medications when compared with patients not receiving them (54.8% versus 47.5%). The incidence of two or more FPUs on the same patient was 15.2% in the group with vasoactive medications and 12.7% in patients without it. Nevertheless, the statistical analysis about the use of vasoactive medications versus the incidence of FPUs did not show any significant relationship (p=0.452).

**HOFA versus other therapies**

We found that the HOFA group produced the best results (lower incidence of NIV-R FPUs) and decided to analyse the differences of FPU incidence in patients in the HOFA group versus the incidence of FPUs in each one of the other groups. Fig 3 shows the incidence of FPUs by treatment group, considered as the proportion of patients developing at least one NIV-R FPU during the observation period.

The incidence of PUs was significantly lower in the HOFA group when compared with each of the other therapeutic strategies: direct mask (p=0.055), adhesive thin dressing (p=0.03) and foam dressing (p<0.001).

Concerning the ARR, HOFA offered a higher level of protective effect when compared with the use of direct mask or the use of ATD, meaning that if 100 patients were treated, 21 would be prevented from developing NIV-R FPUs. This can also be expressed as the number needed to treat (NNT), thus, we need to preventively treat 5 patients with HOFA to avoid one NIV-R FPU (NNT=4.76).

The protective effect of HOFA seemed even bigger when compared with the use of AFD, as it would avoid 49 NIV-R FPUs for every 100 patients treated. Under such circumstances, the number of patients needing to be treated so as to avoid one NIV-R FPU would be only three (NNT=2.04). There were no adverse events related to the devices under investigation.

**Discussion**

There seems to be a wide consensus among scientific societies and health professionals on the fact that prevention is the most effective element to deal with PUs, and on that four areas require measures implementation: risk assessment, skin care, pressure reduction, and education. Preventing PUs is a subject in which health professionals have a significant responsibility, as it is estimated that 95% of PUs can be prevented.45

This clinical trial was motivated by the lack of consensus regarding care interventions to be implemented as a protocol to prevent the risk of NIV-R FPUs. NIV is increasingly used in the management of acute and chronic respiratory problems; therefore, there is a real need for establishing evidence-based interventions/protocols to increase patients’ comfort and prevent the development of tissue lesions.

In the current absence of a better tool, and following the recommendations from Pancorbo,46 we used the Norton scale to assess the risk of developing a PU.47 However, the Norton scale is not specific for FPUs, and the results from our study seem to confirm this. Patients in this trial typify the high-risk patient because of their evident immobility, the expectation of neural and endothelial control of blood flow being impaired by critical illnesses, making them more susceptible to ischaemic tissue damage,46 and the necessity of using an important number of medical devices for monitoring and therapeutic purposes. Thus, the need for tools specifically designed to assess the risk of medical device-related PU development is evident; and it seems clear that those tools are to be used jointly with the traditional PU risk-assessment tools (such as Norton and Waterlow).
A factor with a potential effect on the development of FPU is the priority given to care interventions in patients with acute respiratory failure. Facing an imminent risk of shock, health professionals focus on life-threatening physiological needs, while comfort is frequently considered secondary. However, depending on the intensity, it may take only 2–6 hours of excess pressure for the skin to develop a PU.

Our intervention protocol indicated the assessment of the skin under the mask every 6 hours, still, during common clinical practice the assessment could be done every 4 hours, coinciding with repositioning schedules. This observation is in line with current clinical practice and the results of a study by Manzano et al. in ICU patients under mechanical ventilation. The authors found that repositioning every 2 hours was no more effective than repositioning every 4 hours to prevent PUs and, instead, increased device-related adverse events and nursing workload. Workload in critical care units may affect negatively any PU preventive protocol; therefore, priority should be given to compliance, making sure that skin assessments are effectively made every 4 to 6 hours and preventive measures modified accordingly.

Efficacy in preventing NIV-related FPUs

The results of this study showed a significant superiority regarding the main outcome of the strategy using HOFA versus the absence of intervention (control), the use of ATD, and the use of AFD.

The results of this study do not support those reported by Weng et al. and Acorda about dressings’ efficacy in preventing NIV-R FPUs. In the paper by Weng et al. about the protective effect of hydrocolloid and polyurethane dressings on NIV-R FPUs, any differences in the control group versus the intervention groups may be the result of bias. The authors recognised some possible limitations related to the population size and the randomisation of patients. In the paper by Acorda the use of foam dressings to prevent PUs is recommended; however, the effect of foam dressings was not compared with the effect of alternative therapies.

Levy et al. assessed the protective effect of dressings on the development of heel ulcers and suggested that dressings’ preventive action was real and came from their ability to reduce/dissipate pressure and shear loads, but not all dressings provided the same level of protection. Multi-layered dressings seemed to redistribute forces better than monolayer dressings.

Whereas increased pressure and shear loads have been directly linked to the pathophysiology of PUs, and recent work by Levy et al. provided compelling evidence about this perspective, we need to acknowledge what authors such as Gefen and Wehls propose as a different cutting-edge approach: the concept of dynamic cytoskeleton, which plays an important role in supporting the plasma membrane and protecting the cellular integrity and functioning. Importantly, both approaches seem to be complementary and it is highly probable that new therapies for the prevention and management of PUs will be derived from them. This may be relevant to understand the mechanism of action of therapies not necessarily intended to physically reduce pressure, such as HOFA. Also, another important difference in risk factors between FPUs and PUs on other regions of the body is the necessity of adjusting the pressure exerted by the mask on the facial skin in order to avoid air leaks. Repositioning schedules help prevent the development of PUs over bony surfaces; however, pressure relief through body repositioning is not necessarily possible in NIV-R FPUs.

Group D in our study supported the use of HOFA to prevent the risk of tissue lesions related to the pressure exerted by the mask. Regarding the mechanism of action, from a cellular-level perspective, it has been proposed that HOFA efficacy could come from the increase in the concentration of inflammatory mediators, such as nitric oxide and prostaglandins, leading to an increased local tissue oxygenation, which, combined with an increased keratinocyte renewal, may help counteract the impact of pressure and friction forces.

Concentrations of oxygen provided during assisted ventilation can potentially be as high as 100%. Because the risk of combustion is high under such circumstances, some health professionals wrongly consider HOFA to be flammable, therefore carrying a risk of burns, and avoid using them concomitantly with oxygen, preferring instead pieces of adhesive dressings (foams, hydrocolloids, polyurethane) with sizes that may not be appropriate, and without necessarily considering that an unplanned superposition of layers of dressings between the skin and the mask may produce an opposite effect (for instance, an increase in pressure leading to the development of a FPU).

FPU incidence and vasoactive medications

Globally, we found an FPU incidence (48.7%) higher than the one reported by Schallom (20%) and Raurell-Torredà, but lower than the one reported by Valtysson (71.8%). Higher incidences may be explained by the critical condition of the patients, the increased risk related to the use of oro-nasal masks, and the expertise of clinicians assessing the skin.

Valtysson also reported an apparent relationship between the use of vasoactive medications and the development of NIV-R FPUs. Out of 35 patients who developed category II FPUs, 33 required treatment with vasoactive medications, while only 2 out of 75 patients who developed category I FPUs required vasoactive medications. Valtysson concluded that patients treated with vasoactive medications, because of circulatory and microcirculatory instability, were much more sensitive for pressure injury. In our study, the incidence of FPUs was slightly higher in patients receiving vasoactive medications, but no significant relationship was found between FPU development and vasoactive medications.
However, as the number of patients receiving vasoactive medications was only 20% of the total population, recorded data did not allow us to establish a final conclusion on this topic.

The results of this study allowed reinforcing our belief that all health-care interventions should be guided by the primary intention of optimising benefits while minimising risks. A first step must be the assessment of the purpose and the function of any medical device, as well as making sure that it is used following the manufacturer’s instructions.

Immediately after, it is important to verify that the device’s size is appropriate for the patient’s size, that it is correctly secured to avoid unnecessary rubbing against the skin, and that it is fitted with the correct level of pressure to guarantee correct functioning while avoiding excessive pressure on the underlying tissues.

The next step would be to implement protective measures over the skin, followed by putting in place a surveillance schedule, ideally every 4–6 hours, to assess the evolution of the skin, assess the efficacy of the protective measures by detecting any early sign of skin damage and continue or modify the preventive strategy as required.

This is in line with Makic’s recommendations and the nursing intervention NIC 3302, describing the nursing care activities related to NIV, which also recommends ensuring periods of pressure rest of 15 to 30 minutes every 4 to 6 hours.

No adverse events related to any of the study devices were identified during the observation period (local skin reactions without the intervention of pressure). It is important to clarify that FPUs can be considered adverse events under normal conditions. However, in the present trial they cannot be considered adverse events; the development of FPUs require the combination of multiple risk factors, and FPU incidence represents here the measurement variable for the primary end point, which expresses the capacity of some medical devices to prevent FPU development.

Limitations
There are some bio-physiological conditions capable of affecting tissue integrity, which are not considered as variables; these include the nutritional status and the use of vasoactive medications at different doses. With the study design, the randomisation and the population size statistically calculated, we tried to avoid potential confounding factors.

As the researchers were also part of the care team at the HDU, it was impossible to implement a blinded study. To mitigate this potential source of bias we employed independent double evaluations.

During our study, caregivers had the opportunity to cut the dressings to a predetermined shape. Whether this action introduced bias or not, is difficult to assess. However, we think that this factor needs to be carefully considered in future studies on the same subject.

We did not assess the nutritional profile of patients in our study; even if many clinicians recognise its importance in the development of PUs, we considered that the risk of bias could be mitigated by the statistical power and the population size.

We considered the possibility of a Hawthorne effect, such as caregivers modifying their behavior because they knew their actions were being scrutinised through during the clinical trial. This well-known phenomenon could have had an effect on the results; however, it does not invalidate the results or question their variations, as all four study arms were subjected to the same effect.

Further research would be required to establish the best assessment tool for FPU development risk, and the appropriateness of using different types of medical devices (such as adhesive dressings) and under which conditions, to prevent NIV-R FPUs.

Conclusion
The application of HOFA on the facial skin in contact with the oro-nasal masks showed the highest efficacy in the prevention of NIV-R FPUs. These results are encouraging enough to lead us to include permanently HOFA in our protocol for the prevention of FPUs in patients undergoing NIV. Assessment and care of the facial skin of patients receiving NIV must be performed at least every 4 to 6 hours.

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