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Full Length Research Paper

Efficacy and mechanism of nasal irrigation with a hand pump against influenza and non-Influenza viral upper respiratory tract infection

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To investigate if nasal irrigation could impact the severity and duration of viral URTI. 22 patients with new onset non-influenza URTI were randomized to Control (Control, N=12) or Nasal Irrigation Group [NI-Flu (-), N=10], and 8 patients with new onset influenza URTI were assigned to Nasal Irrigation Group [NI-Flu (+), N=8]. Patients in control were treated with standard of care, those in Nasal Irrigation Groups performed nasal irrigation three times a day. URTI scores were determined at Day 1, 4 and 8 visits. Influenza virus antigen and soluble intercellular adhesion molecule -1 in nasal secretions were measured at each visit. Clinical symptoms and signs of URTI were significantly improved for patients in both Nasal Irrigation Groups as compared to Control on Day 4 and 8. Patients with positive influenza virus antigen initially become negative on Day 4 and 8 after daily nasal irrigation. Soluble intercellular adhesion molecule -1 concentration in nasal secretion was significantly reduced on Day 4 and 8 in the Nasal Irrigation Groups as compared to Control. Nasal irrigation 3 times a day reduced the severity and shortened the duration of viral URTI, probably in part by removing viruses and inflammatory mediators from and inhibiting viral replication in the nasal cavities.

Key words: Influenza, viral infection, influenza virus antigen, nasal irrigation, anti-backwash, soluble intercellular adhesion molecule -1.

INTRODUCTION

Influenza and non-influenza upper respiratory tract infections (URTI) remain the most common human illness (Fendrick et al., 2003; Nichols et al., 2008) and cost the US economy about 112 billion dollars annually (Birnbaum et al., 2002). While influenza is a great threat to humankind due to its easy transmission and rapid antigen change that renders vaccine and drugs less effective, non-influenza virus infection (common cold), largely caused by rhinoviruses, coronaviruses, parainfluenza viruses, etc., also represents a global health challenge due to the lack of effective drugs and vaccines against a diversity of more than 200 different common viruses. Therefore, a safe and effective therapy for influenza as well as non-influenza induced URTI is very much needed.

It is evidenced that the severity of viral URTI symptoms is directly related to the virus titer in nasal secretions (Couch, 1996). The antiviral effects of drugs and vaccines are to eliminate viruses as reflected by a reduced viral titer. Since viruses causing URTI replicate locally in the nasal

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Abbreviations: sICAM-1, Soluble intercellular adhesion molecule -1; **URTI,** upper respiratory tract infection; **NI,** nasal irrigation.

avities, physically removing the viruses and/or disrupting their replication environment may have significant therapeutic effect. Recently, it has been proven that nasal irrigation is useful in management of URTI (Passàli et al., 2005; Wang et al., 2009).

Currently, there are several types of nasal irrigator devices available in the market, and perhaps neti pots are the most well-known and have been used for nasal irrigation over thousand years. Recently, squeeze bottle nasal irrigator device is increasingly popular because of low cost and easy to use. Different from Neti pots which deliver solution to nasal cavities by gravity, squeeze bottle nasal irrigators deliver solution to nasal cavities by positive pressure supplied by manually squeezing the reservoir bottle. A recent study of nasal irrigation devices was performed regarding their efficacy and found that based on spray pattern and ability to penetrate the nasal cavities, brand and design of nasal irrigators profoundly affect parts of the nose and sinuses that are irrigated. With isolated rhinitis symptoms, irrigators that target the nasal mucosa are ideal, whereas excessive sinus penetration that is typical in certain brands may not be either useful or tolerable. A recent study conducted by Abadie et al. (2011) suggested that a Neti Pot or NasalCare heavy irrigators both had excellent nasal penetration yet did not have excessive sinus penetration.

It has been demonstrated that soluble intercellular adhesion molecule 1 (sICAM-1) reflects the presence of minimally invasive inflammation, which implicates the development of URTI. The lymphoepithelial cells lining up the nasal cavities are rich in the rhinovirus receptor ICAM-1 (Greve, 1989; Staunton, 1990; Winther 1997; Whiteman, 2003). It has been reported that the level of ICAM-1 expression by epithelial cells plays a critical role in the process of viral binding, whole-cell infection, and inflammatory events (Bianco, 1998; Colden-Stanfield, 1993; Malefyt, 1993; Whiteman, 2003). An appropriate nasal irrigation was reported to reduce the concentration of sICAM-1 in the nasal secretion of patients with nasal allergy (Li et al., 2009).

The aim of this study was to examine whether nasal irrigation could be used to effectively treat viral URTI, and further to determine its possible mechanism of action. We hypothesize that an appropriate nasal irrigation can shorten the duration and reduce the severity of viral URTI, reduce the presence of viruses, and decrease the concentration of sICAM-1 in nasal secretions obtained from patients with viral URTI.

MATERIALS AND METHODS

This was a controlled, clinical and laboratory observers blinded three-group comparison study. The study was approved by the Ethic Committee of the Third Affiliated Hospital of Shanghai Jiaotong University School of Medicine. The potential participants were workers from a large company whose employees normally come to the Third Affiliated Hospital for any treatment. Patient inclusion criteria included: (1) 18 to 55 years of age, 2) new onset symptoms (<2 days), 3) in good general health without known or suspected immunodeficiency conditions, other respiratory illness such as COPD, asthma, chronic rhinosinusitis, 4) not immunized with an influenza vaccine in the previous 60 days; 5) mentally competent.

When a patient visited the physician because of having URTI symptoms and signs, he or she was asked to read and sign an informed consent form before participating in the observational clinical study if he or she met the inclusion criteria. All participants clinically diagnosed with viral URTI were tested for influenza antigen. Influenza virus antigen negative patients were randomized to either Control or Nasal irrigation group [NI-Flu (-)], while influenza virus antigen positive patients were asked to perform nasal irrigation [NI-Flu (+)]. All participants were required to complete their daily symptom diary, and to have the Day 4 and 8 clinical follow up visits after the Day 1 evaluation and completing the treatment assignment. Nasal irrigation during the 8-day observational period was performed three times a day in the morning, at noontime and in the evening (at about 7 am, 1 pm and 8 pm) by the patients in the nasal irrigation groups. Patients in the Control were treated with an institutional standard of care which consists of acetaminophen 500 mg, P.O TID, PRN, GanMaoLing (Chinese herb medicine) 1 pack, PO, TID × 7 days, QingKaiLing (Chinese herb medicine), 1 pack, PO, TID × 7 days. The single-observing physician who performed clinical evaluation was blind to the patient's study assignment. Likewise, laboratory technicians were blind to the patient's assignment.

The nasal irrigation system used in this study was an imported Class 2 medical device approved by the Chinese State Food and Drug Administration (NasalCare® Nasal Rinse Starter Kit, TechWorld Corp, USA) and purchased from the Hospital Pharmacy of the Third Affiliated Hospital of Jiaotong University School of Medicine. The diagram of the irrigator was shown in Figure 1.

URTI symptoms and signs (sneezing, nasal congestion, rhinorrhea, color of nasal mucus and congestion of nasal mucosa) were evaluated and scored using a modified Jackson Scale (Jackson, 1960) (Table 1) by the same examining physician with endoscopy at each visit. By adding up the points assigned to each of the five URTI symptoms and signs, a URTI score from 0 to 15 was obtained. The higher the URTI score, the more severe the illness was. The URTI score for each patient, and the median, mean and standard deviations for each group were calculated. The duration of influenza and non-influenza URTI were the period from the first visit (day 1) of URTI to the day on which there were no observable symptoms and signs by the examining physician, and the URTI score was less than 3.

Another parameter used to assess the severity and to determine the duration of URTI was the URTI symptom score (0 = symptom-free, 1=mild, 2=moderate and 3=severe), which was recorded by patients in their illness dairies. When the symptom score recorded by the patient was ≤ 1, the episode ended. Median and mean URTI symptom scores for each group were calculated and used to compare control and nasal irrigation groups.

The inflammatory score of the nasal cavity was evaluated with endoscopy and graded at each office visit by the same otolaryngologist blind to the patient's study assignment.

The following criteria were used by the examining physician to determine the inflammatory score of the nasal cavities: 0=all examined surface area of the nasal cavities having normal color, no visible vascular congestion or edema and secretion; 1=less than 25% of the observed surface area of the nasal cavities being mildly to moderately congested, edematous, and covered with significant amount of secretion; 2=the majority of the observed surface area of the nasal cavities being moderately to severely congested, edematous, and covered with more secretion; 3=virtually all the examined surface area of the nasal cavities being severely congested, edematous, and covered with inflammatory secretion.

Nasal wash specimens (secretions) were collected from each patient at each clinic visit using the standard clinical procedure. Briefly, 10 ml saline (5 ml per nostril) was instilled into the nasal

Figure 1. NasalCare nasal irrigator equipped with an air valve and a liquid valve. This diagram shows the NasalCare nasal irrigator used in the current clinical study. The irrigator has two one-way valves. When the user manually squeezes the bottle (shown in part), the liquid valve opens and the air valve closes. Hence, the irrigation solution flows into nasal cavities under positive pressure. When the user releases the squeezing pressure, the liquid valve closes (preventing backflow) and the air valve opens (preventing negative pressure inside the bottle).

cavity with the patient's head extended. After 5 s, the saline was expelled through the nose into a cup, with recovery of 6 to 8 ml. An aliquot (2 ml) was frozen at –80°C for laboratory analyses. sICAM-1 was measured in duplicate using commercially available ELISA kits (Shanghai Bluegene Biotech Company) according to the manufacturer's instructions. The detection limit was 3 ng/ml of nasal secretion. An aliquot of nasal wash was used for influenza antigen detection using a commercially available kit (Beijing Ascle

Table 1. Modified Jackson Scale for evaluating symptoms and signs of URTI.

Sneezing	Nasal congestion
0=Absent	0=Absent
1=1-4 per day	1=Little, does not cause disturbance
2=5-10 per day	2=Oral breathing most of the day
3=11+ per day	3=Does not breathe through the nose/ interferes with sleep, olfaction, or voice
Rhinorrhea	**Color of nasal mucus**
0=Absent	0=Normal
1= Cleaning nose 1-4 times a day	1= Watery
2= Cleaning nose 5-10 times a day	2= White mucus
3= Constant cleaning	3= Yellow purulent
Congestion of nasal mucosa	
0=Absent	
1= mild congestion of nasal mucosa	
2= moderate congestion of nasal mucosa	
3= Acute congestion of nasal mucosa	

URTI score is derived from by adding all the numeric assigned to each of the five URTI symptoms and signs.

Table 2. Median and mean scores of URTI symptoms and signs for each study group at each visit.

Groups	Day 1	Day 4	Day 8
Control, n=12	10, 10.6 ± 0.2	13, 12.8 ± 0.2	9, 8.9 ± 0.1
NI Flu(-), n=10	11, 10.2 ± 0.3	3, 2.8 ± 0.2 [a]	0, 0.0 ± 0.0 [a]
NI Flu(+), n=8	13, 12.4 ± 0.3	5, 3.1 ± 0.3 [a]	0, 1.8 ± 0.3 [a]

[a] Significant different from the Control group ($P < 0.01$). The median scores were counted based on the ranked ordinal, and mean score of URTI symptoms and signs for each study group was the numeric mean of the scores of URTI symptoms and signs of all patients in the group.

Bioengineering Company, Flu A-Ag Rapid Test Kit for Dot ELISA). Briefly, a drop of the nasal wash was added onto the test strip (An anti- flu A nuclear antigen monoclonal antibody and control antibody along with necessary enzyme and reagents are immobilized in the test strip), and the result was checked 15 min later, with the presence of pink-purple color as positive. The sensitivity and specificity of the test were 96.77 and 90.41%, respectively.

Statistical analysis

Data were expressed as median, mean ± standard error of the mean when appropriate. Statistical evaluations using ANOVA, t-test or Mann-Whitney-Wilcoxon (MWW) test (de Winter, 2010) were performed for the appropriate data, and $p<0.05$ was accepted as statistically significant.

RESULTS

A total of 30 patients (22 women and 8 men) with clinical viral URTI were enrolled into the study. The mean age was 40 years with a range of 23 to 54 years. Twenty two (22) patients with non-influenza UTRI were randomly enrolled into Control Group (N=12) or Nasal Irrigation Group [NI-Flu (-), N=10]. Eight (8) patients tested positive for Influenza virus A antigen were enrolled into the Nasal Irrigation Group [NI-Flu (+), N=8]. All patients had URTI symptoms for less than 48 h, and 7/12 (58%), 7/10(70%) and 5/8 (62.5%) of the patients in the control, NI-Flu(-) and NI-flu(+), respectively) had URTI symptoms for less than 24 h before enrolled into the study. Patients in each group had similar age distribution. All patients completed their daily symptom diaries and follow-up visits on Day 4 and 8. Nasal secretion specimens were obtained from all patients during each office visit for laboratory analyses.

URTI severity

At the Day 1, 4 and 8 office visits, each patient's symptoms and signs of viral infection were observed and recorded by the examining physician who did not know the patient's treatment assignment. The median and mean URTI scores for patients in each group were not significantly different at the Day 1 visit (Table 2). Figure 2 showed the nasal cavity photos of patients from the Control and NI-Flu (-) groups at each office visit, to demonstrate the changes of URTI severity at each office visit. The results of median and mean symptom scores for

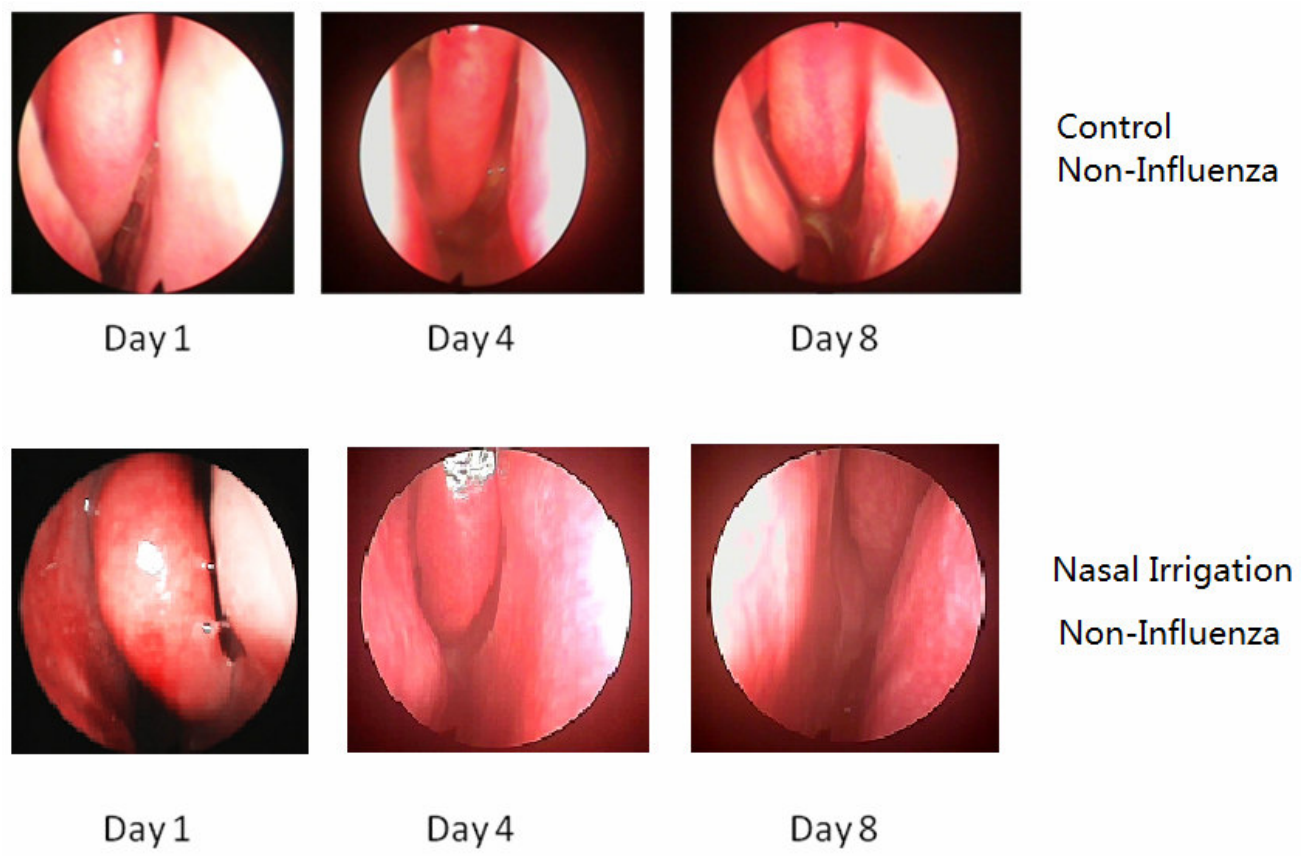

Figure 2.. Inflammation status of Nasal cavities of two patients at three different time points. Those photos showed the nasal cavities taken from two patients with non-influenza URTI, one from Control and one from the Nasal Irrigation group at each office visit. Significant inflammation of the nasal mucus membrane and significant amount of thick secretions were clearly present in both patients at day 1 visit. Nasal cavity inflammation had little or no improvement on Day 4 and only moderate improvement on Day 8 for the patient in the Control group. The inflammation was significantly improved on Day 4 and basically completely resolved on Day 8 for the patient in the nasal irrigation group.

each group based on patients' symptom diaries were shown in Figure 3. For patients in the Control group, their median and mean URTI symptom scores slowly but steadily increased from Day 1 to 5, and then gradually declined. At the end of the study (Day 8), they still had at least one URTI symptom or sign. In contrast, for patients who performed nasal irrigation three times a day in both nasal irrigation groups, their illness was not worsening further (Figure 3). Their URTI symptom scores quickly decreased on a daily basis. On Day 3, the reduction of URTI symptoms scores for patients in the nasal irrigation groups became significant as compared to Control ($P < 0.05$). On Day 4 and thereafter, URTI symptom scores for patients in both nasal irrigation groups were further reduced to a more significantly lower level as compared to that of the Control ($P < 0.01$).

URTI duration

All patients in the Control Group on Day 8 had at least one symptom or sign of URTI and therefore, their durations of URTI were eight days or longer (Figure 3). The median durations of the URTI episodes for patients in each group were ≥ 8, 3.5 and 5.5 days, respectively, for the Control Group, NI-Flu(-) and NI-Flu(+) Groups. The mean durations of the URTI episodes for patients in each group were ≥ 8, 4.2 and 5.8 days, respectively, for the Control Group, NI-Flu(-) and NI-Flu(+) Group (Figure 3). The median 4.5 days or mean 3.8 days shortened duration of URTI for the NI-Flu (-) group was statistically significant ($p < 0.05$) as compared to the Control. Although there was no influenza(+) control group in this study, the median 2.5-day or mean 2.2-day shortened duration observed in patients with influenza(+) who performed nasal irrigation was statistically significant ($p<0.05$) as compared to patients with influenza(-) URTI in the Control Group.

The URTI illness status of each patient was verified by the same physician at Day 4 and 8 office visit. The otolaryngologist-observed status of inflammation or inflammation score of the nasal cavities of patients is shown in Table 3. The inflammation score was not different on Day 1 among the three groups. However, patients in the NI-Flu (-) and NI-Flu (+) Group had a significantly lower inflammation score on Day 4 and 8 than

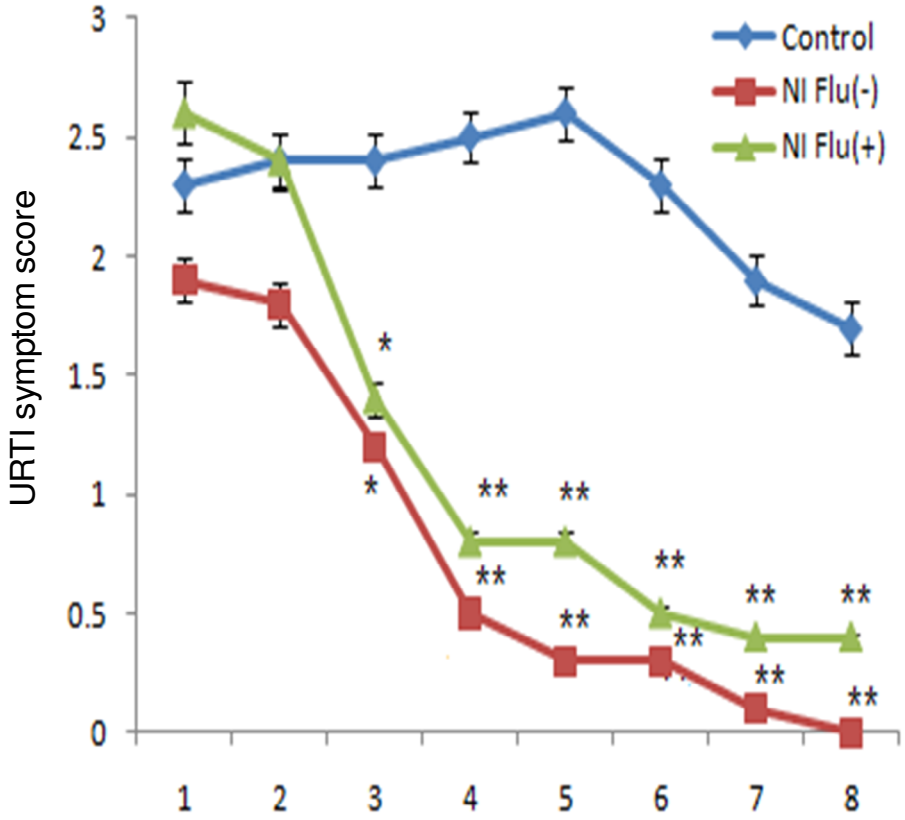

Figure 3. Changes of URTI symptom scores over time. This is the plot of the patient recorded daily URTI symptom scales (Y) against time (X, day) after URTI onset. The patients' URTI symptom scores in the Control group (Blue-Ball) had no improvement or even became slightly worse from Day 1 to Day 5 of UTRI onset, and then gradually decreased moderately thereafter. In contrast, patient URTI symptom scores in both nasal irrigation groups, influenza negative patients [NI-flu(-), Red-square] or influenza positive patients [NI-flu(+), Green-triangle] were dramatically reduced starting from Day 3, and the scores decreased to zero and 1.8 at Day 8 for patients in the influenza negative group and influenza positive group, respectively. The URTI symptom score improvements starting from day 3 in both nasal irrigation groups were statistically significant as compared to the Control, *<0.05, ** P<0.01.

those in the Control (p<0.01).

Removing viruses

At the office visit on Day 1, eight patients were tested positive for Influenza virus A antigen. After performing nasal irrigation three times a day for three days, all patients were tested negative for Influenza virus A antigen in their nasal secretions at the Day 4 office visit.

Removing sICAM-1

The concentrations of sICAM-1 in nasal secretions collected during the office visits of Day 1, 4 and 8 were analyzed and presented in Figure 4. The sICAM-1 concentrations of URTI patients in all three groups were not significantly different on Day 1, although these patients positive for Influenza virus A antigen had a slightly higher value. However, sICAM-1 concentrations in the nasal secretions of the patients in the nasal irrigation groups were significantly lower than that of the Control Group at Day 4 and 8 visits (P < 0.01). The sICAM-1 concentrations were not different between the two nasal irrigation groups at any visit.

DISCUSSION

Upper respiratory tract infections (URTIs) caused by influenza and non-influenza viruses are one of the most common forms of human diseases for all ages and a great burden to the healthcare system and the economy (Birnbaum et al., 2002). Though there are vaccines against influenza viruses, it is often difficult to predict or

Table 3. Median and mean inflammation scores of the nasal cavities of patients in different groups at each visit.

Groups	Day 1	Day 4	Day 8
Control, n=12	3, 2.50 ± 0.04	3, 3.00 ± 0.00	2, 2.25 ± 0.04
NI Flu(-), n=10	3, 2.60 ± 0.05	1, 0.50 ± 0.05 [a]	0, 0.00 ± 0.00 [a]
NI Flu(+), n=8	3, 2.63 ± 0.07	1, 0.88 ± 0.04 [a]	0, 0.38 ± 0.37 [a]

[a] Significant different from the Control group ($P < 0.01$).The median inflammation scores of the nasal cavities of patients were counted based on the ranked ordinal. The mean inflammation score for each study group was the numeric mean of the inflammation scores of all patients in the group.

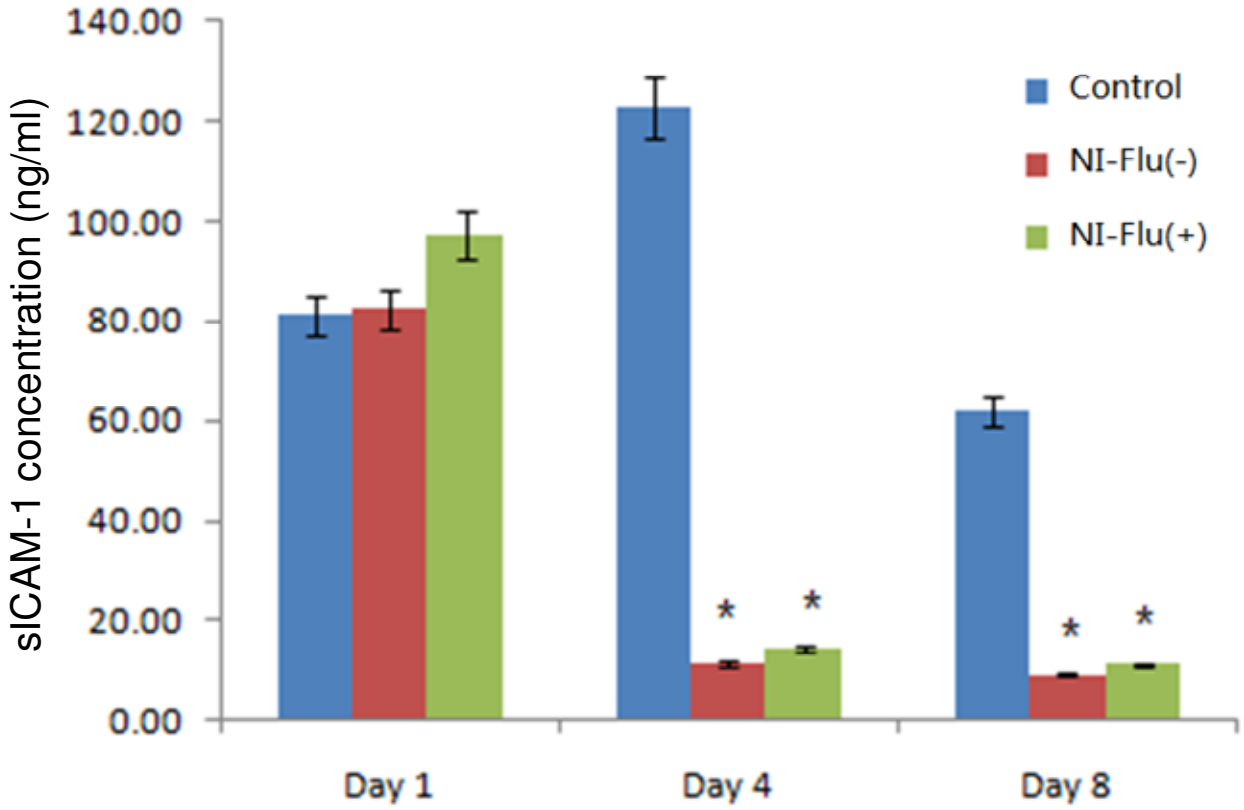

Figure 4. sICAM-1 concentration in nasal secretions of the patients with viral URTI at three different time points. This is the histogram of the sICAM-1 concentrations detected in the nasal secretions of patients from Control (Blue), influenza negative nasal irrigation group NI-Flu (-) (Red), and influenza positive NI-Flu (+) Nasal irrigation group (Green) at Day 1, 4 and 8 visits. At Day 1 visit, there was no difference in the sICAM-1 concentration in the nasal secretions among the three groups. The sICAM-1 concentrations were dramatically reduced in the nasal secretions of patients in the two nasal irrigation groups on Day 4 and further reduced on Day 8 as compared to that on Day 1, while its concentration in the patients of the Control group did not decrease but rather increased on Day 4, then decreased on Day 8 as compared to that on Day 1. The concentrations of sICAm-1 in the nasal secretions of patients in NI-Flu(-) and NI-Flu (+) groups were significantly lower than that of the control group at Day 4 and Day 8 visits, both $p<0.05$.

forecast which strain of Influenza viruses will dominate during the next season because they mutate frequently.

As there are more than 200 different rhinoviruses that can cause viral URTI, it makes vaccination difficult if not possible. Because there are no specific effective anti-virus medications for viral URTIs, treatments of viral URTI are mainly symptomatic with anti–pyretics, anti-histamines, decongestants, steroids or a combination.

Nasal irrigation is not new, and indeed it has been used as a personal hygiene practice for over one thousand years. Modern studies have demonstrated that nasal irrigation is safe and beneficial without significant side effects (Papsin et al., 2003; Rabago et al., 2002). Nasal irrigation is an effective adjunctive therapy for many common upper respiratory illnesses such as cold and chronic sinusitis (Tomooka et al., 2000; Rabago et al., 2002A; Slapak et al., 2008; Rabago et al., 2009). One of the major advantages of nasal irrigation is non-pharmaceutical and therefore it avoids the side effects of drugs, or potential adverse interactions among

drugs.

Nasal irrigation can be performed easily with a wide range of different devices from simple ones such as syringe to more sophisticated ones such as electricity-powered nasal irrigator. Currently, Neti Pot and squeeze bottle type nasal irrigators are the most commonly used devices for nasal irrigation. NasalCare nasal irrigator, a squeeze bottle type nasal irrigator was used in the current study. It has one unique and important figure which distinguishes it from other squeeze bottle type nasal irrigators as claimed by the inventor/manufacturer (Product information sheet). As shown in Figure 1, this nasal irrigator has two one-way valves, a liquid valve, and an air valve. The one-way liquid valve allows solution to flow out from the reservoir bottle when the bottle is squeezed or pressed, and prevents any fluid from outside returning into the bottle when squeezing on the bottle is stopped. The one-way air valve prevents air flowing out from the bottle when squeezing is applied on the bottle, and allows air to flow in to the bottle to rebalance the pressure inside the bottle quickly when squeezing on the bottle is stopped. By working together, the two one-way valves prevent backflow. Backflow can cause contamination of the solution in the bottle and may result in sinus re-infection (Welch et al., 2009; Keen et al., 2010). Because it does not have back flow problem, the investigators in the study felt that NasalCare nasal irrigator was the appropriate nasal irrigator device to be used in the study.

In this study, the results clearly showed that the median and mean URTI scores measured with the Jackson scale, and the median and mean inflammation scores of the nasal cavities for patients with either non-influenza or influenza URTI in the nasal irrigation groups were significantly lower than that for patients in the control. Furthermore, sICAM-1 concentrations in the nasal secretions from patients in both nasal irrigation groups were significantly lower than those from patients in the control. Therefore this study clearly demonstrated that nasal irrigation effectively improved URTI symptoms and shortened URTI durations based on patients reported symptoms (symptom scores), physician's observation and examination (URTI Scores), and laboratory tests (influenza antigen, sICAM-1 concentration). The duration of URTI was shortened by approximately 4 days and 2 days, respectively for patients with non-influenza and influenza URTI with nasal irrigation, which is significant as compared to the control.

It is well known that the symptoms and signs of viral URTI will usually become worse in the first few days, then gradually subside and be completely resolved about 7 to 10 day after onset for most patients. In this study, we did not further observe these patients after Day 8 visit, since it is hard to differentiate if the disappearance of URTI symptoms and signs were due to any treatment effects. It is obvious that when these patients performed nasal irrigation, their patterns of pathogenesis and their disease courses were significantly changed. With nasal irrigation, these patients' symptoms and signs were not worsening at Day 2, and the severity was quickly reduced thereafter. Those patients in the Control group, however, had the typical disease progression and regression. At Day 8 visit, all patients in the Control group had at least one symptom, although the overall severity was declined. This observation was similar to what was reported in a previous study (Rosenfeld, 2007). A number of symptoms of rhinovirus infection could continue for more than 14 days without an effective treatment. In the future, a large scale study may be conducted to further characterize the changed disease course and determine how many total sick days could be reduced with nasal irrigation.

One possible mechanism of the protective action offered by nasal irrigation is by reducing virus titers in the nasal and nasopharyngeal cavities to such a low degree that there were not enough viruses present to cause a full bloom clinical infection. This is supported by the findings in this study that there were no detectable influenza viruses in the nasal secretions from the patients with influenza URTI after 4 days of nasal irrigation.

It is evidenced that the severity of URTI symptoms is directly related to the virus titer in nasal secretions (Couch, 1996). Moreover, persons who have a later onset URTI tend to exhibit a slower increase in virus titer in their nasal secretions and tend to remain clinically free of symptoms (Douglas et al., 1966). For rhinovirus, the incubation period of virus shedding into nasal secretions is 1 to 4 days. Viral titers then reach peak for 2 to 4 days, and remain detectable for 3 weeks (Douglas et al., 1966). The 50% human infectious dose (HID_{50}) varies depending on the type of rhinoviruses, the specific part of the respiratory tract, and the background level of anti-rhinovirus antibody in the human body (Douglas et al., 1966). It is well accepted that the less viruses in the infected area, the less severe of the infection. Therefore, physical removal of viruses can reduce the severity of viral infection. This study confirmed that nasal irrigation effectively removed influenza viruses from nasal secretion. Hence, it reduced the severity and shortened the duration of the viral infection.

Another possible mechanism that nasal irrigation reduced the severity of viral URTI is by removing inflammatory mediators such as histamine, prostaglandins, and leukotriens contained in nasal mucus, creating a hostile environment for viral replication (Winther et al., 2002; Michael et al., 2003; Hull et al., 2007; Georgitis, 1994; DiLorenzo et al., 2001).

Though the above mentioned inflammatory mediators were not directly measured in this study, sICAM, an important molecule that is related to viral infection in the upper respiratory airway was measured and significantly reduced in the nasal secretions from patients in the nasal irrigation groups.

ICAM-1 has two distinct forms, the membrane-bound form (mICAM-1), and the soluble form (sICAM-1).

mICAM-1 is a cell surface glycoprotein, and a major human rhinovirus receptor (Greve et at., 1989). It facilitates viral infection and is up-regulated during viral infection (Whitman et al., 2003). It also plays a critical role in recruitment of immune effector cells. On the other hand, sICAM-1 can bind to virus and prevents virus adherence to epithelial cells. Therefore, sICAM-1 provides some protection against viral infection (Whitman et al., 2003; Witkowska, 2004). It seems that by removing sICAM-1 from nasal secretion, nasal irrigation is not beneficial if not detrimental to viral URTI.

However, the present study clearly demonstrated that nasal irrigation reduced the severity and the duration of viral URTI. This discrepancy may be explained as sICAM-1 may play only a limited role in fighting viral infection, while other inflammatory mediators such as histamine, prostaglandins, and leukotriens may be the major contributors to the severity and duration viral URTI beside virus itself.

Based on the results of this study that nasal irrigation could significantly reduce the symptoms and shorten the duration of viral URTI possibly by reducing or eliminating viruses and inflammatory mediators in the nasal cavities, the authors postulate that nasal irrigation at least once a day during common cold season could effectively remove those newly acquired viruses in the forms of droplets and/or aerosols originated from carriers of cold viruses and therefore might be an effective means of preventing upper respiratory tract infections. This hypothesis warrants a new clinical study with a large study population.

In this study, there were no influenza positive patients included in the Control. The reason for that was due to limited qualified influenza positive patients during that particular study period. The lack of influenza positive patients in the Control made evaluation on how effective nasal irrigation is in shortening the duration of flu symptoms and in eliminating influenza viruses in the nasal cavities less convincing. However, there are reports in literature that flu symptoms lasted about 11 days and flu patients shed the virus for about 6 days on average without antiviral treatment (Lin et al., 2004; Ling et al., 2010). Therefore, nasal irrigation clearly shortened the duration of flu symptoms and flu virus shedding as compared to the reports in literature. Another limitation of this study was a relatively small sample size, which may make the study results less reliable and therefore reduces the power of interpretation of the results. Hence, further study in a large patient population with an appropriate control group will be helpful for the medical community to reach a consensus.

Conclusion

This study has demonstrated that nasal irrigation with a squeeze bottle nasal irrigator is effective in reducing the severity and the duration of viral URTIs. This is in alignment with previous reports that nasal irrigation was effective for the treatment of URTIs in children and adults. Furthermore, nasal irrigation works by removing viruses and inflammatory mediators in the nasal mucus. The authors conclude that nasal irrigation with a squeeze bottle equipped with dual-valves is a safe, effective, and a non-pharmaceutical method of treating viral URTIs.

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