Evaluation of the Efficacy and Safety of “PureHands” in Hand Hygiene: A Prospective, Randomized, Double Blind, Placebo-Controlled, Phase III Clinical Trial.

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ABSTRACT

PureHands is an alcohol-based polyherbal hand sanitizer, and this study was planned to evaluate the clinical efficacy and safety of PureHands in ensuring hand hygiene in HCWs, in hospital settings.

This study was a double blind, randomized, and placebo controlled, phase III clinical trial, conducted with adherence to the “GCP” guidelines. A total of 16 HCWs, without any signs of abrasion/s, wound/s or infection/s on the skin of hand were included in the study. The 1st group used PureHands, while the 2nd group used placebo for ensuring hand hygiene. On the 1st day of the study, 2 swabs were taken with sterile cotton swab sticks from all the HCWs, which were inoculated and cultured. 5 ml of PureHands gel was squeezed out on the palms of the HCWs, which they were asked to rub thoroughly, and briskly on their palms, back of the hands and fingernails until dry. Subsequently, 2 swab samples were taken after 3, 10 and 30 minutes, and the samples were cultured. The CFUs of microorganisms were counted using a predefined score scale. All the HCWs were advised to use PureHands at least 5 times-a-day from the 2nd day to the 7th day. On the 3rd, 5th and 7th day, 2 samples from each person were cultured for microbial growth. Subsequently, all the HCWs were advised not to use PureHands for the next 2 days and on the 10th day, 2 more samples were taken from each of the HCW's hands. The predefined primary efficacy end points were reduction in the absolute microbiological count as reflected in CFUs. The predefined secondary safety end points were absence of adverse reactions, compliance to the drug therapy and reduction in the total residual microbial counts on the 3rd, 5th and 7th day. All the analyses were conducted on an intent-to-treat basis.

This study observed a highly significant reduction in the mean number of the CFUs in the PureHands group, as compared to the placebo group. There were no clinically significant adverse reactions and the overall compliance was excellent. These potent antimicrobial properties of Purehands might be due to the synergistic action of its ingredients, which have been well studied by various researchers. Therefore, it may be concluded that PureHands is clinically effective and safe to be used by HCWs for hand hygiene, in health-care settings.(The Ind. Pract. 2005; 58(5):275-282)

ABBREVIATIONS: HCW - Healthcare worker, GCP - Good clinical practice, CFU - Colony forming unit, NS - Nonsignificant, HS - Highly significant, S - Significant

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INTRODUCTION

“...As I have noted, women who delivered on the street contracted childbed fever at a significantly lower rate than those who delivered in the hospital.”

- Dr. Ignaz Semmelweis

Although Dr. Semmelweis documented and reported his results to his colleagues, very few doctors were willing to believe that they were spreading diseases to their patients; today, Dr. Semmelweis is referred to as the “Father of Infection Control”!

Nosocomial infections are a major public health issue, responsible for a major chunk of morbidity and mortality. Nosocomial infections are the result of high prevalence of pathogens, compromised hosts, and an efficient infection transmission mechanism. Opportunistic (S. aureus, E. coli and Pseudomonas species), and multi-drug resistant (Vancomycin-resistant etherichia coli and Vancomycin-resistant staphylococcus aureus) bacteria, alongwith certain fungi (P. versicolor, Tinea, C. albicans, A. fumigatus, and C. neoformans) cause a spectrum of nosocomial infections, ranging from minor superficial skin infections to life-threatening systemic infections. Antimicrobial resistance is becoming a factor in virtually all nosocomial infections, and physicians are concerned that several bacterial infections soon may be untreatable.

The hands of HCWs are the primary mode of transmission of these pathogens to patients, and “hand hygiene” is the single most important, simplest, and least expensive means of preventing nosocomial infections. Unfortunately, poor hand-hygiene practices are observed due to lack of knowledge, and awareness about risks, misconceptions, non-availability of hand-hygiene facilities, understaffing and patient overcrowding.

Clinical evaluation of efficacy of a hand wash, although seemingly simple, is quite complex, due to multifactorial influences such as the intrinsic resistance of microorganisms, the number of microorganisms, the amount of presence of organic material, concentration, pH, and stability of hand wash, contact time and temperature at the time of exposure, and hydration of skin. PureHands is an alcohol-based polyherbal hand sanitizer, and contains the extracts of Coriandrum sativum, Citrus limon, Azadirachta indica, Vetiveria zizanioides, and Coleus vettiveroides in ethyl alcohol (60% w/w). This study was planned to evaluate the clinical efficacy and safety of PureHands in ensuring hand hygiene in HCWs, in hospital settings.

STUDY DESIGN

This study was a prospective, double blind, randomized, and placebo-controlled, phase III clinical trial involving 16 HCWs, and was conducted during August 2004, at Department of Microbiology, Patna Medical College and Hospital, Patna, India, with adherence to the “GCP guidelines”, and was approved by the “Institutional Ethics Committee”.

MATERIAL AND METHODS

Inclusion and exclusion criteria

A total of 16 HCWs (4 doctors, 4 nurses, 4 ward boys and 4 laboratory technicians), without any signs of abrasion/s, wound/s or infection/s on the skin of hand were included in the study. Healthcare workers with any visible signs of abrasion, wound or infection on the skin of the hand, and those who were unwilling to give informed consent were excluded from the study.

Study procedure

Informed written consent was obtained from all the HCWs. All the enrolled HCWs were randomly divided into 2 groups, and after stratification, double blinding was done. The 1st group used PureHands, while the 2nd group used placebo for ensuring hand hygiene.

On the 1st day of the study, 2 swabs were taken (from both the hands: ventral and dorsal surface, including nails and fingers) with sterile cotton swab sticks from all the HCWs, which were inoculated and cultured.
in different media (MacConkey’s and blood agar). Approximately 5 ml of PureHands gel was squeezed out on the palms of the HCWs, which they were asked to rub thoroughly, and briskly on their palms, back of the hands and fingernails until dry. Subsequently, 2 swabs samples were taken after 3, 10 and 30 minutes, and the samples were cultured. The petri dishes were incubated at 37°C for 48 hours, and the smears prepared from the culture or colony were stained using Gram’s stain and were examined microscopically. The CFUs of microorganisms were counted and were assigned a score scale as follows: <10 CFUs=0, 11-100 CFUs=1, 101-500 CFUs =2, and >501 CFUs=3.

All the HCWs were advised to use PureHands at least 5 times-a-day from the 2nd to the 7th day. On the 3rd, 5th and 7th day, 2 samples from each person were cultured for microbial growth. Subsequently, all the HCWs were advised not to use PureHands for the next 2 days and on the 10th day, 2 more samples were taken from each of the HCW’s hands. At each follow-up visit (day 3, 5, 7 and 10), the investigators recorded any information about adverse events, and local examination of the hands was done.

**Primary and secondary end points**

The predefined primary efficacy end points were reduction in the absolute microbiological count as reflected in the CFUs. The predefined secondary safety end points were absence of adverse reactions (burning sensation, skin rash, local irritation, overall compliance to the drug therapy and erythema), and reduction in the total residual microbial count on the 3rd, 5th and 7th day.

**Analysis of data**

All the analyses were conducted on an intent-to-treat basis. Statistical analysis was performed using “Repeated Measures ANOVA Test”, followed by “Dunnett’s Multiple Comparison Test”. The minimum level of significance was fixed at 99% confidence limit, and a 2-sided p value of < 0.001 was considered as significant.

**RESULTS**

A total of 16 HCWs were enrolled in the study and each group had 8 HCWs (2 doctors, 2 nurses, 2 ward boys and 2 laboratory technicians).

*Staphylococcus aureus* and *Enterococcus faecalis* were the commonest isolated microorganism, and a few CFUs of *Escherichia coli*, *Klebsiella species* and *Pseudomonas aeruginosa* were detected. There was a highly significant reduction in the mean score of the CFUs of *Staphylococcus aureus* (Table 1 and Figure 1) and *Enterococcus faecalis* (Table 2 and Figure 2) as compared to the placebo group, after 3, 10 and 30 minutes on the 1st day, and also, on the 3rd, 5th and 7th day. There was no statistically significant difference in CFU count in both the groups, on the 10th day.

There were no clinically significant adverse reactions either reported by the HCWs or observed by the investigators, during the entire study period, and the overall compliance to the drug was excellent.

**DISCUSSION**

The microbial flora found on the hands of HCW can be divided as “transient flora” and “resident flora”. Transient flora, which colonizes the superficial layers of the skin, which is acquired by HCWs during direct contact, is more amenable to removal by routine handwashing. Resident flora, which is attached to the deeper layers of the skin, is more resistant to removal, and is less likely to be associated with nosocomial infections. There are 2 common routes for transmission of nosocomial infections, namely contact route (direct and indirect), and airborne droplet route. The risk factors for nosocomial infections include extreme age (elderly and neonates), immunodeficiency, serious disease, certain medications (high-dose corticosteroids, oral contraceptives and certain antibiotics), mechanical ventilation, intravascular catheters, neutropenia, hemodialysis, and intrauterine contraception.

Methods of prevention of nosocomial infections include implementation of
### Table 1
Effect of PureHands and placebo on number of *S. aureus* CFUs

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 7</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 Min.</td>
<td>3 Min.</td>
<td>10 Min.</td>
<td>30 Min.</td>
<td></td>
</tr>
<tr>
<td><strong>PureHands</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>2.875 ± 0.125</td>
<td>0.250 ± 0.164</td>
<td>1.125 ± 0.295</td>
<td>0.500 ± 0.378</td>
<td>0.750 ± 0.313</td>
</tr>
<tr>
<td>SEM</td>
<td>2.250</td>
<td>0.875</td>
<td>1.500</td>
<td>0.839</td>
<td>0.350</td>
</tr>
<tr>
<td>Lower 95% CI</td>
<td>2.438</td>
<td>-0.323</td>
<td>0.0926</td>
<td>-0.8225</td>
<td>-0.347</td>
</tr>
<tr>
<td>Upper 95% CI</td>
<td>3.312</td>
<td>0.823</td>
<td>2.157</td>
<td>1.822</td>
<td>1.847</td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>2.625</td>
<td>2.375</td>
<td>2.500</td>
<td>2.125</td>
<td>2.625</td>
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<tr>
<td>SEM</td>
<td>0.183</td>
<td>0.183</td>
<td>0.267</td>
<td>0.350</td>
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<td>1.735</td>
<td>1.565</td>
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<td>Upper 95% CI</td>
<td>3.265</td>
<td>3.015</td>
<td>3.435</td>
<td>3.351</td>
<td>3.265</td>
</tr>
</tbody>
</table>

**Figure 1: Effect of PureHands and placebo on the number of *S. aureus* CFUs**

F=8.088, p<0.001; HS (Two-Way Repeated Measure ANOVA Test Statistics)
Table 2
Effect of PureHands and placebo on number of E. faecalis CFUs

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 7</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 Min.</td>
<td>3 Min.</td>
<td>10 Min.</td>
<td>30 Min.</td>
<td>Day 3</td>
</tr>
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<td>PureHands</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean</td>
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<td>0.625</td>
<td>0.000</td>
<td>0.000</td>
<td>0.125</td>
</tr>
<tr>
<td>SEM</td>
<td>± 0.350</td>
<td>± 0.183</td>
<td>± 0.000</td>
<td>± 0.000</td>
<td>± 0.125</td>
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<td>Lower 95% CI</td>
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<td>0.000</td>
<td>0.000</td>
<td>-0.312</td>
</tr>
<tr>
<td>Upper 95% CI</td>
<td>2.351</td>
<td>1.265</td>
<td>0.000</td>
<td>0.000</td>
<td>0.562</td>
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<tr>
<td>Placebo</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
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<td>0.875</td>
<td>1.000</td>
<td>1.250</td>
<td>1.375</td>
</tr>
<tr>
<td>SEM</td>
<td>± 0.378</td>
<td>± 0.350</td>
<td>± 0.378</td>
<td>± 0.491</td>
<td>± 0.461</td>
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<tr>
<td>Lower 95% CI</td>
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<td>-0.351</td>
<td>-0.323</td>
<td>-0.468</td>
<td>-0.236</td>
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<tr>
<td>Upper 95% CI</td>
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<td>2.322</td>
<td>2.968</td>
<td>2.986</td>
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</table>

Figure 2: Effect of PureHands and placebo on the number of E. faecalis CFUs

F=5.54, p<0.001; HS (Two-Way Repeated Measure ANOVA Test Statistics)
changes in hospital staff activities (hand washing - especially between attending different patients, avoiding hand contact with eyes or oral area, and hospital staff education), changes in the patient environment (isolation of patient, education of visitors - to avoid certain types of touching, washing of hands, and avoidance of ill visitors), and changes in hospital environment (sterilization of equipment, air filtration systems, and appropriate vaccination).

Currently available options for hand hygiene include chlorhexidine, chloroxylenol, hexachlorophene, iodine, quaternary ammonium compounds, and triclosan. Chlorhexidine’s antimicrobial activity is slower than that of alcohols, and has less activity against certain pathogens (gram-negative bacilli, and nonenveloped viruses - rotavirus, adenovirus, and enteroviruses). Chloroxylenol has less activity against gram-negative bacteria, mycobacteria, and viruses. Hexachlorophene has modest activity. The antimicrobial activity of iodosphors is affected by pH, temperature, exposure time, concentration of total available iodine, and the presence of other compounds (organic and inorganic). In concentrations used in antiseptics, iodosphors are not sporicidal, and have poor persistent activity. Quaternary ammonium compounds (alkyl benzalkonium chlorides, benzethonium chloride, cetrimide, and cetlypyridium chloride) are bactericidal and fungicidal agents. Triclosan is bacteriostatic agent, and lacks activity against gram-negative bacilli.

This study observed a significant reduction in the mean number of the CFUs in the PureHands group, as compared to the placebo group. There were no clinically significant adverse reactions, and the overall compliance was excellent. These potent antimicrobial properties of PureHands might be due to the synergistic action of its ingredients, which have been well studied by various researchers.


The ingredients of PureHands have strong antiviral action. Azadirachta indica inhibits vaccinia virus, chikungunya virus, measles virus, and Group-B coxsackie viruses. Citrus limon inhibits rabies virus. Ethyl alcohol has better virucidal activity, and alcohol-based hand rubs are approximately 100 times more effective against viruses than any form of hand washing. Ethyl alcohol inhibits adenovirus, coronavirus, coxsackievirus, cytomegalovirus, Epstein-Barr virus, hepatitis virus, herpes simplex virus, human immunodeficiency virus, human T-cell lymphoma virus, influenza virus, measles virus, mumps virus, Norwalk virus, papilloma virus, parainfluenza virus, poliovirus, respiratory syncytial virus, rhinovirus, rotavirus, rubella virus and varicella-zoster virus.
The laboratory and clinical evidence, and ease of use support the use of alcohol-based hand rubs amongst HCWs. The alcohol-based hand rub is less likely to cause skin problems and saves resources and is associated with better adherence. The occasional drawback of alcohol-based hand rubs is the dryness of skin; however, this study did not observe the same, which might be due to the presence of *Coleus vettiveroides* and *Vetiveria zizanioides*, which are potent emollients and act as moisturizing and soothing agents.

**CONCLUSION**

PureHands is an alcohol-based polyherbal hand sanitizer, and this study was planned to evaluate the clinical efficacy and safety of PureHands in ensuring hand hygiene in HCWs, in hospital settings.

This study observed a significant reduction in the mean number of the CFUs in the PureHands group, as compared to the placebo group. There were no clinically significant adverse reactions, and the overall compliance was excellent. These potent antimicrobial properties of PureHands might be due to the synergistic action of its ingredients, which have been well studied by various researchers. Therefore, it may be concluded that PureHands is clinically effective and safe to be used by HCWs for hand hygiene, in health-care settings.

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