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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Antimicrobial Products and Bacterial Resistance

ANTIMICROBIAL PRODUCTS AND BACTERIAL RESISTANCE

Cleanliness is next to godliness, that's the old adage, but in terms of household antimicrobial products, are they helpful or harmful? Welcome to the Clinician's Roundtable on ReachMD, the Channel for Medical Professionals.

I am your host, Dr. Lee Freedman and with me today is Dr. Allison Aiello from the Department of Epidemiology, the Center for Social Epidemiology and Population Health at the University of Michigan School of Public Health.

DR. LEE FREEDMAN:

Dr. Aiello, thank you so much for being with us.

DR. ALLISON AIELLO:

Thank you Dr. Freedman, I am happy to be here.

DR. LEE FREEDMAN:

To me, this is a very interesting topic because we always are told to wash our hands and to keep things clean, but I guess with some products, this may not be the best idea or could potentially be harmful.

DR. ALLISON AIELLO:

Right and that's a very good point. It's about the types of products. So, we know that, you know the concept of cleansing hands for reducing infections in the clinical setting has been around, you know since the early 19th Century. It started with the seminal studies by Dr. Ignaz Semmelweis where he showed that babies that were being delivered by students and physicians had higher mortality compared to the midwives and it turned out that the students and physicians were of course delivering the babies after they had been working on cadavers and he actually came up with an interesting intervention, which was to have the students and physicians dip their hands in chlorinated lime before they did the deliveries and that really reduced the mortality rates and got close to what it was in the midwives in his research and then there has been, you know many, many studies showing that in the clinical setting, handwashing is

very important, but there really haven't been as many studies done in the community setting and that's what I have really focused on and have been very interested in. So, the research that we see in the clinical setting, can we extrapolate that to the community setting in terms of preventing infectious, illnesses in the community setting and we know, as I mentioned, that, you know, handwashing in general is important, but really there has been very few studies looking at specifically different types of regimens of handwashing with different types of products and that's what I have been focusing on to try to get out what are the best methods for preventing infectious illnesses in the community setting and what is the benefits as well as the potential risks associated with some of the products that are available.

DR. LEE FREEDMAN:

Very interesting and so there definitely are differences between the ordinary soaps and things that are labeled antimicrobial?

DR. ALLISON AIELLO:

Yes, there are differences in terms of within those soaps; however, our studies show that the differences in terms of the impact on microbial flora on the hands as well as illnesses really doesn't show much of a difference when we are talking about some specific ingredients and that is the ingredient triclosan, which is an antimicrobial that's in many of the liquid soaps that are labeled as antibacterial and in a similar ingredient called triclocarban is in the bar soaps that are labeled as antibacterial that are available in the consumer setting and our studies on this ingredient, in particular which is quite prevalent in products in the consumer setting does not show a difference in terms of bacterial counts on the hands as well as reductions in infectious illnesses.

DR. LEE FREEDMAN:

So, those particular antimicrobials seem to be safe, either others that seem to perhaps pose a risk?

DR. ALLISON AIELLO:

Well, the triclosan is the one that we actually are concerned with in terms of posing a potential risk and so what we have identified are a number of studies, we did a large review, a number of studies that show that in the lab setting, the use of this ingredient triclosan for a range of bacterial species can lead to cross resistance with some antibiotics that are used for treating clinical infections. In addition, this ingredient triclosan can act as a substrate for multidrug efflux pumps, which allow bacteria to evade the triclosan ingredient as well as multiple different antibiotics that might be used to treat a clinical infection. So, these are some of the concerns. We have done some research looking at whether this is actually occurring at the population levels, so some epidemiological studies among people who were randomized using these antibacterial products compared to plain products and we didn't find that the use of the triclosan-containing hand soaps led to a big change over time in one year in levels of antibiotic resistance on the hands of the individuals who were using these products. However, our study, you know, was only a one-year period and these products have been around since the 1960s, so really there needs to be more research in this area and surveillance on the use of these types of products that contain triclosan and the impact on antibiotic resistance in the community setting.

DR. LEE FREEDMAN:

And the products that have that triclosan in them, are they clearly marked as antibacterial and we can see that triclosan is one of the active ingredients?

DR. ALLISON AIELLO:

Yes and so that's an important aspect. If it's labeled as antibacterial, then there is usually some kind of active ingredient in it and it would say in terms of the ingredient list that it has triclosan in it if it's a triclosan-containing product and most of the liquid soaps, there has been a study by Eli Perencevich, which was done a few years ago, that looked at the prevalence of these products in consumer products out there on the market. What they found was that it was in about 70% or so of the products, they found it was more than 75% of all liquid hand soaps contained triclosan and so that you have to really sort of look to see whether you are using a plain soap or a soap containing triclosan when you are looking out there on the market.

DR. LEE FREEDMAN:

So, it's very prevalent out there and at least at this point it's a theoretical concern, although in the one-year study, there was not a difference shown. Now, I have also seen this other agent, benzalkonium chloride, if I am pronouncing it correctly. Tell us about that and whether we need to be careful of that one?

DR. ALLISON AIELLO:

Okay, so benzalkonium chloride including quaternary ammonium compounds, it's a type of quaternary ammonium compound, is another ingredient that's mostly used in not so much skin preparations, although there are some sort of sanitizing wipes, for example, that are used on the skin that can have quaternary ammonium compounds in them like the benzalkonium chloride, but there is a lot of quaternary ammonium compounds in ingredients that are used as floor or surface cleaners, for example in the household, so there are really in these household-cleaning products in general and now the issue with those ingredients is there have been a few studies similar to triclosan showing that the quaternary ammonium compounds may also lead to antibiotic resistance and that's primarily through efflux pump and in general though there are a little bit more broad spectrum in terms of the way that they kill the bacteria compared to triclosan and they are thought to have this more generalized membrane damage to the bacteria. The exact specific mechanisms are still unclear, but in terms of cross resistance, it's not exactly clear whether it might be from plasmid-mediated efflux, that's what some studies have suggested and then there is also in the Staph isolates, there are actual resistance determinants called qacA, B, and C determinants, which are genetic factors that allow the bacteria to evade the quaternary ammonium compound.

DR. LEE FREEDMAN:

If you are just joining us, I am Dr. Lee Freedman, your host and I am discussing the benefits and possible harms of household antimicrobial products with Dr. Allison Aiello from The Center For Social Epidemiology and Public Health at the University of Michigan School of Public Health.

So, Dr. Aiello, because of a wider mechanism of action, the question of resistance seems to be a little less acute than with this BCK?

DR. ALLISON AIELLO:

Yeah, well, I think there is just really not enough literature out there to assess whether there is an issue. As I mentioned, it does have this ability to turn on these efflux pumps in bacteria and we actually recently conducted an epidemiological study using the same data where we examined the effects of triclosan on resistance and we found that there was no difference between people who use the quaternary ammonium compounds or benzalkonium chloride also as it's also known and so the use of those products and resistance; however, we did find that the odds of antibiotic resistance amongst bacteria with high minimum inhibitory concentrations which are

basically an indicator of whether the organism is more resistant to the benzalkonium chloride or not. We found that that was associated with antibiotic resistance. So, for all bacterial species that we looked at, at the end of the 1-year period of the study, there was a higher association between the qac MICs and the antibiotic resistance.

DR. LEE FREEDMAN:

So, the MICs did seem to go up. It makes me think about the hospital setting. Are these the same antimicrobials that we would see used in the hospital and are there some implications in terms of gram-negative infections in nosocomial things we see?

DR. ALLISON AIELLO:

This is an interesting question and it hasn't been very well studied in terms of the hospital setting and we know triclosan, for example, there is some of use of it in the hospital setting, but in general, the amount that's used in the hospital setting is actually quite higher than what you see in the community setting. The consumer levels are about 0.2% to 0.45% and that at the clinical level, it's greater than 0.45% to 2% and so now the difference in those concentrations is important because it's similar to an antibiotic when you sort of lower levels that allow the bacteria to thrive, that's when we might see problems with antibiotic resistance, but triclosan in general is not used that often in the clinical setting in US. It has been used for patients in the UK and hospitals in UK, but not so much in US. In terms of benzalkonium chloride, that's a very good question and I think there needs to be studies in terms of the types of ingredients that are being used in some of the hygiene within the hospitals, what are being used to clean the floors and surfaces for example and there should be studies looking at the use of those ingredients and the potential for antibiotic resistance.

DR. LEE FREEDMAN:

Very interesting and that makes me think of how we do use antibiotics and how the high-dose short courses in to try to eliminate the possibly slightly resistant bacteria who could thrive in a lower concentration setting. Are there some positives? Should we tell our patients, hey stay away from these antimicrobials, they don't help at all and there is a theoretical reason they could be harmful or there are some positives with these products?

DR. ALLISON AIELLO:

In terms of the community setting, we were talking about generally healthy individuals, that's what most of our studies have been and the available literature among generally healthy individuals. It appears that plain soap and water work well to reduce infectious illnesses and that there is no added benefit when we are using the ingredients like triclosan, for example to reducing infectious illnesses as well as bacterial counts on the hands. Now, in terms of the quaternary ammonium compounds, which I mentioned are in a lot of the household cleaners, it's still unclear. I don't think there are enough studies to say whether there is a benefit and whether people are using them appropriately in the household, so one of the important aspects would be to find out whether people are diluting them or are they using them at the use concentration that is prescribed on the product bottles. So, that's an important aspect because that could, you know, if we are talking again about the low levels, we want to make sure that the concentration is high enough that it actually can kill the microbes that are there on the surface or of concern, but you know, in general, if we are talking about sort of a generally healthy household, soap and water works just fine, but if, for example, you are preparing a chicken and you may be concerned about salmonella or if you have an ill person in the household, that's when you would want to turn to ingredients that may be more powerful that would allow you to kill potentially pathogenic microbes in the household, but in general, soap and water, as I mentioned, is a good alternative to work with given that some of these other products like triclosan, for example, don't show a benefit and then with the quaternary ammonium compounds, you know, I think there needs to be more research on that in terms of the household products to examine the effectiveness and exactly how well they do for reducing transmission of infectious illnesses in the households.

DR. LEE FREEDMAN:

And I imagine there may not be data on this, but if we flip that home situation around where you have somebody who is immunocompromised in the home, either on cancer chemotherapy or some other immunocompromised state, might there be a theoretical reason to avoid the BCK and triclosan?

DR. ALLISON AIELLO:

Because of the issues of resistance that worked here suggesting possibly?

DR. LEE FREEDMAN:

Right, right.

DR. ALLISON AIELLO:

Well, I mean I don't think there is enough research to assess that. You know, we know that hand hygiene as an infection control is very important for individuals who are immunocompromised and so I don't think at this point we can say whether the risks outweigh the benefits in that case because there need to be studies to see if these products are indeed more efficacious for individuals who are specialized population such as immunocompromised aged individuals, for example, that may be more susceptible. So, I don't think we can make that decision at this point in terms of what might be a greater risk or a benefit in terms of those populations because we just don't have a study that have examined that, but there are alternatives too that are quite effective that are more broad spectrum that, you know, we know we haven't seen issues with resistance for example like the alcohol-based hand sanitizers where we see that they are very effective in killing a good range of bacteria and viruses and there haven't been those risks suggested at this time.

DR. LEE FREEDMAN:

Well, I want to thank Dr. Allison Aiello from the Department of Epidemiology at the University of Michigan School of Public Health. This has been the Clinician's Roundtable on ReachMD, the Channel for Medical Professionals. Thank you for listening.