

Syncope following Immunization Among Teenagers

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Coordinator: Good afternoon and thank you for standing by. All lines will be in a listen-only mode until the question and answer session. To ask your question, please press star 1. Today's conference is being recorded. If anyone has any objections you may disconnect at this time.

Now I'll turn the meeting over to your host for today, Ms. LeShaundra Cordier. You may begin.

LeShaundra Cordier: Good afternoon and welcome to today's COCA conference call, Syncope Following Immunization Among Teenagers.

We are very excited to have Dr. Jane Gidudu and Dr. Andrea Sutherland present on this call. Dr. Gidudu is the Acting Team Lead of the Surveillance and Public Health Response Team in the Immunization Safety Office here at the Centers for Disease Control and Prevention.

Dr. Andrea Sutherland is the Acting Chief of the Vaccine Safety Branch at the Food and Drug Administration.

We are using a PowerPoint presentation for part of this call that you should be able to access from our Web site. If you have not already downloaded the presentation, please go to emergency.cdc.gov/coca, click on the conference call information summaries and slide sets.

The PowerPoint can be found under the call in number and pass code.

After the activity the participants will be able to review the epidemiology, clinical aspects and prevention of syncope following immunization among teenagers, describe ACIP and AAP recommendations on prevention of syncopal injuries following immunizations among teenagers.

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CDC, our planners and presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services or commercial supporters.

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I will now turn the call over to Dr. Gidudu.

Jane Gidudu: All right, thank you. Hi everybody and thank you for joining me. I hope you can hear me wherever you are.

So I'm going to share some current information on syncope as an adverse event following immunization especially among teenagers.

We all know that this is a very dangerous group that needs to be taken care of. They have several issues going on in their lives. And the objectives of the talk as is clearly outlined are really two and they've already been told to you.

To review the epidemiology, clinical aspects and prevention of syncope following immunization among teenagers. And the second one is to describe the ACIP and AAP recommendations on prevention of syncopal injuries following immunizations among teenagers.

The main message is I hope you all have my slides. And I'm still on the first slide. The main message is syncope is a common post-immunization event particularly among adolescents.

Dramatic injury and convulsive syncope can occur with post-immunization syncope. The dramatic injuries can be very, very severe like skull fracture, cerebral hemorrhage and even death.

Prevention of this event is possible. Through a 15 minute observation time and awareness for pre-syncopal signs and symptoms and understanding of convulsive syncope or (anoxic) seizures is very, very important.

(This) published a recommended preventive measures VAERS which is a Vaccine Adverse Event Reporting System continues to receive reports of traumatic injury related to post-immunization syncope.

Healthcare providers, vaccine administrators, patients and their accompanying family and friends need to help prevent this tragic event.

So I want to - I you want you now to move onto this slide next I believe Slide 4 which is vasovagal syncope.

Vasovagal syncope is a transient loss of posture or tone and cautiousness with spontaneous recovery. This is typically due to bradycardia, vasodilation and hypertension resulting in decreased brain perfusion.

It may also be due to abnormal (sympathetic) reflexes and can be listed by a variety of stimuli in settings of fear or emotional distress.

It also cause of the medical procedures including vaccinations (sic). Emphasis here is that syncope is a transient symptom and not a disease. It's coded as syncope or syncope vasovagal using our medical dictionary for regulatory activities which is MedDRA we use for coding terms that is currently being used in VAERS.

Let's go to the next slide on general recommendations. The current general recommendations on immunization are the - by the Advisory Committee on the Immunization Practices ACIP and the American Academy of Pediatrics.

So the ACIP recommendation was published in MMWR. And it reads although syncopal episodes are uncommon and severe allergic reactions are rare, vaccine providers should strongly consider observing patients for 15 minutes after they are vaccinated.

If syncope results, patients should be observed until symptoms resolved.

The recommendation by the AAP which was published in (2006) it reads personnel should be aware of pre-syncopal manifestations and take appropriate measures to prevent injuries.

Having vaccine recipients set or lie down for 15 minutes after immunization could avert many syncope episodes and secondary injuries.

The next slide, the Vaccine Adverse Events Reporting System, VAERS that many of you may be aware of is a national passive surveillance system for monitoring adverse events following immunization.

It is jointly operated by CDC and FDA since November 1990. It largely focuses on post-vaccine surveillance for vaccines license in the US.

It receives over 20,000 reports. And like all spontaneous reports supporting systems it's subject to well described limitations including underreporting and reporting bias.

The next slide which is on published VAERS data on syncope, using some of the current literature on syncope I will highlight a few that include Barbara Slade's paper that was published two days ago in JAMA and was quoted a lot in the media including CBS Evening News on Tuesday evening indicates that the most frequent reported adverse event following HPV vaccine included syncope in a review of VAERS data between 2006 and December of 2008.

And then Jane Woo and others found that serious injuries with at least one fatality have occurred. (Brown) and others found that 89% of syncope occurred within 15 minutes of vaccine administration.

Also in an MMWR publication on VAERS data between 1990 and 2004 the total number of reports then was just over 3000 and 35% were among persons aged 18, 10 to 18-year-olds 14% of which resulted in hospitalization for injury or medical evaluation.

So the next slide which is on syncope associated with injuries in VAERS reports.

This slide shows an overview, an aerial review of syncope and VAERS between 2005 and 2007. The numbers could have been changed now. But basically this indicates that even with a small number of syncope cases here the number was 41, most of that - most were adolescents aged 11 to 18 years of age with 17% of them occurring in females. And this excluded 14 cases with unknown onset interval.

The onset of syncope after vaccination was 5 minutes in 49% of cases and occurred within 15 minutes in 80% of cases and 24% them it was considered serious.

And serious here includes cases which result in death, life-threatening illness, hospitalization or prolonged hospitalization or disability.

So let's go move onto the next slide which is the number of post-vaccination syncope episodes reported to VAERS. This slide indicates the number of post-vaccination syncope episodes reported to VAERS by (mass) and (dia) of reported between January 2002 to the end of last month 31st July this year.

It shows the cumulative number of cases over the years. And the arrow - arrows show when different vaccines were introduced into the US market.

MCV4 or Menactra was released in February of 2005. This was followed by Tdap in June of the same year 2005. HPV was licensed in 2006. And since then the story in this graph is very clear that there has been a big increase in reports on syncope following the HPV vaccine.

The pink bars shows females ages 11 to 18. Yellow bars show males 11 to 18. And the green bars show other persons outside this age group. As you can see, most of these cases seen are females.

So the next slide which is vaccines if you can move onto the next slide which is vaccine associated with syncope reports again, this slide shows vaccines associated with syncope reports between 2005 and 2007.

A comparison between one vaccine given which gave a total of 302 reports compared to the multiple vaccines given (concurrently) were 161 reports to VAERS.

The number indicates HPV alone contributed 52% of the cases and MCV4 5% and Tdap 4% in descending order. All these vaccines contributed to 60% of one vaccine given (alone) reports.

The next slide which is a table indicates a breakdown of syncope reports by sex, age groups and severity across two time periods. Two-thousand and two, 2004 is on the left column and 2005, 2009 is the column on the far right.

In the period 2000, 2004, 201 reports were seen. And the period 2005 to 2009 we received an almost - an increase of tenfold increase to 2000 reports.

Again, about 61% of the reports were female 11 to 18 - in the 11 to 18 years age group. And the most affected - were the most affected. And luckily the serious reports have stayed small at less than 6%.

Let's go to the next slide which is showing a real example of one of the cases that was sent in to VAERS.

A 13 year old girl fainted within 10 minutes of receiving HPV vaccine and MCV4. She fell backward, hit her head on a carpeted floor of the clinic and was admitted to the pediatric intensive care unit because of skull fractures and had a subarachnoid hemorrhage.

Let's go to the next slide. This slide, the VAERS system which is a spontaneous reporting system like many other spontaneous systems has some limitations.

We cannot collect syncope incident rates based on VAERS data. We use (numerate) data without good denominators. So then there is underreporting of adverse events. There's lack of age or sex specific vaccine doses administered. And VAERS MedDRA recording times may not reflect diagnosis accurately.

We cannot determine if syncope is related to a vaccine, targeted age group or both.

VAERS does not assess causality. It only generates signals for additional studies.

Let's move onto the next slide and such studies, additional studies as that I've just mentioned can be conducted in one of our systems here at CDC which is the Vaccine Safety Data Link. And here is a slide showing some of their data.

This slide shows syncope per 100 - per 1000 vaccine visit following Tdap Menactra and Varicella in ages 9 to 26.

Using this aggregated data this graph shows the overall increase in the rate of syncope across the calendar year on the growth listed here between 1996 up to the end of 2008 I believe.

So the next slide in my conclusions, since 2005 there is been an increase in VAERS syncope reports among females aged 11 to 18 years.

Most of them have been non-serious reports. Reports had been associated with vaccines recommended for adolescents. Similar in VSD rates for post-vaccination syncope are increasing over time.

We should encourage health-care providers to adhere both to ACIP and AAP recommendations.

Although syncope is uncommon, it can have serious yet preventable consequences. And CDC recommends that providers strongly consider observing patients for 15 minutes after they are vaccinated according to the ACIP recommendation or having vaccine recipients sit or lie down for 15 minutes after immunization.

And I want to thank my colleagues who helped me. They're all listed on this last slide. And I thank you for listening to me.

Hello?

Andrea Sutherland: Hi. This is Andrea Sutherland from FDA. And I'm the Acting Branch Chief for the Vaccine Safety Branch. And I wanted to thank (Jane) for a wonderful kind of summary of the background data and epidemiology and hope that everyone on the call finds that useful.

I think the main message that we wanted to get across on this call and the main discussion points and questions that we hope to field after we finish speaking is really how to prevent this adverse event from happening after teenage vaccination.

We here at FDA like at CDC we review these VAERS reports and passive reports of adverse events after vaccination on a daily basis. And on a daily basis we review reports of syncope occurring particularly among teenagers the most tragic of which are those reports are these reports of healthy teenagers going in for a vaccination and ending up with very serious traumatic injuries.

It's one of the adverse events that we know is triggered by vaccination as it is from by donation of blood and other procedures involving needles.

And at the same time we also know that there are measures that we can take to prevent the syncope itself or at least the adverse consequences that are happening afterwards.

So we really want that to be the main message. We've tried publishing MMWRs and doing other publications, other public health outreaches. But again, continuously on a daily basis we don't see a decrease in the number of these various syncope reports and particularly the traumatic injuries that we're seeing after adolescent vaccinations.

And as (Jane) pointed out this is a time of particular heightened interest in this because since 2005 we've greatly increased the number of vaccines to which adolescents are exposed. And therefore we've increase the risk for having this adverse event occurring after vaccination.

So again, those were the main messages of working together with you as representatives of healthcare providers and direct vaccine administrators, how we can prevent this from happening.

We again see the average age of onset of syncope is approximately 13 years of age with the peak prevalence in 15 to 16 year olds and then slightly higher in females.

Many of the serious post immunization trauma cases are occurring in teens. In fact the majority of them are occurring in teenagers.

And again this has implications for injury prevention guidelines, injury prevention practices and also has implications for if we start thinking about school or mass immunization programs which we might want to also touch upon given the upcoming H1N1 possible vaccine strategies.

Again we see this increase of VAERS reports of these cases of teenage syncope and trauma. A majority of them are occurring within 5 to 15 minutes. And actually the majority are occurring while the teenager is still in the immunization clinic or health care provider's office.

In fact the majority of injuries are happening when they're at the checkout counter making a follow-up appointment.

So the 15 minutes we need to discuss too. There's a wide variation of how people are understanding this 15 minutes of observation after immunization.

It really has to be close observation with either the patient, the parents or the accompanying parties being alerted to the possibility that syncope can occur, being educated about warning signs.

The majority of reports that we received where falls have been prevented and injuries have been prevented is when there's close attentive reaction by either an immediate healthcare provider who's next to the patient or the family member who recognizes the pre-syncope signs of pallor, sweating, dizziness, changes in visual changes and attends to that by lying the patient down or protecting them from a fall, even catching them from a fall.

The risk factors that we've identified in a review of VAERS reports include a personal history of vasovagal syncope, family history of vasovagal history, these pre-syncope signs that we described.

They can also - (so that's) pallor, dizziness, nausea, sweating, visual changes, fall from a high exam table. So patients are left on the exam table and left alone in the room or they're asked to change during - immediately after vaccination. Those are the times that we see a high rates of injury, walking to the waiting room and again waiting at the checkout counter.

Some syncope does seem to occur without warning. And those obviously are high risk for injury to occur.

There's some documented cases where the patients have received refused to wait. So the healthcare provider has advised them to wait 15 minutes and yet the patient themselves leaves or the family leaves prematurely.

The other risk factors we've identified are teenagers who haven't had sufficient hydration during the day or are on severe diets or haven't eaten during the day. And one can make the analogy to when people are giving blood often times we have cookies and orange juice to prevent the syncope from happening.

We had other cases that are reported in parking lots or while driving home. So the vaccine recipient is actually driving within minutes after - or within 5 minutes or 10 minutes after the vaccination.

And then there some other risk factors. The one that our data has shown is that if a teenager receives multiple vaccinations, meaning if they've received Tdap, Menactra and HPV at the same visit they have a higher risk of syncope and a higher risk of syncopal trauma, syncopal associated trauma.

The only - the other main point in addition to traumatic injury that we would like to discuss on today's call is something that's called convulsive syncope.

It was first described in 1950 by a French neurologist named (Gasteau) and has been well documented with EEGs particularly after blood donation after anesthesia and after other needle procedures.

But essentially if there's prolonged cerebral hyper perfusion or not enough oxygen is getting to the brain for more than 10 to 15 seconds, patients actually start having what seems to be seizure-like activities. They have atonic, clonic or jerking-like movements. They may even have urinary incontinence, tongue biting -- everything that stimulates simulates kind of an epileptic seizure.

And I think for many vaccine providers and healthcare providers this can be quite frightening.

We have had documented cases where patients are somewhat mismanaged during this convulsive syncope episode. They're propped up in wheelchairs for example to prevent further injury which really in the end only prolongs their hyper perfusion.

In addition we've seen other cases that were given Valium or excessive doses of Valium in order to control what would be an epileptic-like seizure but this is really convulsive syncope.

If you look at the etiology and actually the EEGs, these are two completely different phenomenons. It's again, the convulsive syncope is prolonged hyper perfusion of the brain. It's transient. It's benign and has no other sequelae whereas an epileptic like seizure has distinct patterns on the brainwave tracing or EEG and it's quite different in both its immediate treatment and long term consequences.

So that's something I think that often when we see the reports, it's often misunderstood by healthcare providers by many physicians who aren't aware of that phenomenon.

But we are seeing that particularly with teenage vaccinations and want to make people aware of that and field any questions that people have.

Recently we changed the Gardasil label and add it to the warnings and precautions section descriptions of post immunization syncope as well as convulsive syncope.

And this was really again to try to highlight to healthcare providers that vital information to prevent any injuries or adverse sequelae or mistreatment or misunderstanding of the situations.

So again we really emphasize there needs to be more education for patients, parents, healthcare providers about the potential consequences of syncope occurring after immunization.

Again, this is commonly seen in adolescence after vaccination. It's something that needs to be addressed in the patient education prior to vaccination.

We strongly urge that people follow through with the recommendations both by the ACIP as well as the American Academy of Pediatrics, American Academy of Family Practice all recommending close observation for those 15 minute post immunization. And this would apply for syncope as well actually for anaphylaxis. So it's a standard recommendation.

That 15 minutes actually has to be someone closely observing the patient and the patient not being asked to walk during that time.

And we realize this is a challenge having practiced medicine. We realize this is a challenge for busy practices. But we would love to engage with you today in a discussion of how we as the healthcare provider community can think of additional steps that we can take to prevent further injury or further convulsive syncope from happening.

So thanks. I think at this point we'll open up the floor to discussion and questions.

LeShaundra Cordier: Thank you so much for that presentation. It was incredibly informative.

We now open up the lines for question and answer session.

Coordinator: Thank you. At this time if you'd like to ask a question, please press star 1 and record your first and last name. You will be announced prior to asking a question. To withdraw your question press star 2.

Once again if you have a question, please press star 1 and record your first and last name. Your name is required in order to introduce your question. One moment please.

One moment for the first question.

Our first question.

Question: Hi. Yes I'm - I work in a pediatric clinic. And when the Gardasil information came out about syncope we changed our policy for that particular vaccine to have all of the women who received it to wait for 15 minutes.

However I - from what I'm hearing in this call, you're recommending it for any vaccination to any age. Is that correct?

Andrea Sutherland: The recommendations are for any vaccination for any age. What we're saying practically in VAERS reports -- and actually if you look at the literature on syncope rates in the epidemiology, we do see peaks in this adolescent period peaking at 15 to 16 years of age.

There is another peak that does occur in the elderly which is probably more cardiac related. But we do see those two peaks and we do see that reflected in VAERS reports.

What we found when we reviewed adolescent syncope cases, even though we have a higher proportion of reports for Gardasil, we are seeing it in all vaccines even if given independently.

So Tdap, Menactra, even things like typhoid, Hepatitis B, we have reports for all vaccines among adolescents.

So we would strongly encourage it just given the physiologic seemingly predisposition of adolescents to have this syncopal, post- immunization syncopal episode we would recommend it particularly for adolescents in all vaccines.

Jane Gidudu: Yes just also to add to that you're going to use your judgment because you may have a mix of populations. You want to prioritize the group that is (right) at the highest risk possible.

Question cont'd: Thank you. I just had one other part to that question. So is it partly - I understand that's partly a function of their age and their reactions to things.

So it is it also because they are more independently mobile and taller? I know that sounds strange but they fall from higher heights and maybe are more independently moving along without people with them as opposed to like school aged children?

Andrea Sutherland: There are many theories and I don't think anyone quite understands the full physiology of vasovagal syncope or the predisposing factors.

It seems based on the epidemiology it's a phenomenon that starts somewhere - the average age of onset's around 13 years of age just based on background epidemiology of syncope in general regardless of the cause.

There is some serious thinking that it's hormonally partly mediated. Essentially what happens is that you get anxious or you feel pain and you have an increase in heart rate and your body compensates by basically shutting down or lowering your blood pressure.

So it's this adverse reflex or neurologic reflex to the stimuli and for whatever reason seems to peak in this adolescent period and then taper off as people enter their early adulthood years.

So it's - the falling certainly I hear your point, but there seems to be something basically physiologically different about adolescents that predisposes them to syncope.

Question cont'd:: Okay. Thank you very much.

Coordinator: Our next question.

Question: Thank you. I just wanted to go back again to the CDC recommendation. Because I think we got mixed messages that are being given out there in the community, I want to just get - explore little more.

Can we get some consistency in messages? Because when we explored this issue we've gotten mixed messages from CDC saying that the waiting period was not a requirement.

And especially with some of these drive-through clinics that are happening, especially delivered by hospitals and other organizations, I think we're sending mixed messages to the public and to the practitioners on what is the right thing to do.

Andrea Sutherland: And what is the waiting period you're talking about?

Question cont'd: Post-vaccinations.

Andrea Sutherland: Now it is - I think we need to be consistent on these. The message here from CDC is at least 15 minutes. And you have any other difference in the timing of observation that is not 15 minutes?

Question cont'd: We've asked that question several times. Because of these drive-through clinics that are happening in communities, we've asked that question. And we've been told that it was not a CDC requirement for a specific waiting time.

So I think another communication out to providers is going to be necessary especially during the upcoming H1N1 and the seasonal flu season.

Jane Gidudu: Let me just be clear that it is not - it's not a requirement but a recommendation. I think the messaging from CDC is very clear these are recommendations because this is the same message that should go out to the people who are giving vaccines that it is not a requirement but a recommendation.

Coordinator: Are you done with your question?

Question cont'd: Yes. Thank you.

Coordinator: Thank you. One moment. You may ask your question.

Question: Yes my question regards if the CDC or ACIP will be making the recommendation then for seasonal flu and H1N1 not be given at the same time then because of this conclusion with the syncopal?

Jane Gidudu: I don't think we do have that recommendation yet from ACIP. It's not yet there. And we will share any - if you monitor the ACIP Web site all the recommendations that our current are posted as soon as possible.

Andrea Sutherland: And I just from the FDA's point I want to make that point clear, our studies did show if you receive multiple vaccinations you seem to have a higher risk for syncope or convulsive syncope.

But that doesn't translate into our not recommending vaccines be given concurrently. It's just I think alerts the physician that these patients will be at higher risk and needs closer attention.

Question cont'd: Okay thanks.

Coordinator: Thank you. Once again if you have a question please press star 1 and record your first and last name.

At this time I'm not showing any further questions.

LeShaundra Cordier: Okay. Well I want to thank our presenters for providing our listeners with this information. I'd also like to thank our participants for joining us today.

In case you didn't get the chance to ask your question, please send an email to COCA@cdc.gov. That's C-O-C-A@C-D-C.G-O-V.

Please be sure to note which presenter your question is for in your email request.

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You have a year to obtain continuing education for this call. All continuing education credits and contact hours for COCA conference calls are issued online through the CDC Training and Continuing Education Online System, www.2a.cdc.gov/tceonline/.

Thanks again for participating and have a wonderful day.

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