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INFECTION PREVENTION: SSI PREVENTION AND GLUCOSE CONTROL

Hello. This is Patch Dellinger from the University of Washington, and I'm going to talk with you just now about preventing surgical-site infections, with an emphasis on glucose control. And I first got interested in this a number of years ago when I reviewed this paper from Vanderbilt, showing a dramatic increase in surgical-site infections for any cardiac surgery patient who developed a glucose above 200 at any time during the first 48 hours after the operation.

And when the authors did some multi-variant analyses, they showed that there was not an increased risk for a high A1C or for a preoperative hyperglycemia. But there was a definite increased risk for any patient who had a post-op glucose greater than 200 milligrams percent within 48 hours. And this was more likely to happen, and therefore, there was increased risk for patients with either diagnosed or undiagnosed diabetes.

But the thing that really caught my eye about this study was that 47% of all the hyperglycemic episodes occurred in non-diabetic patients. Now diabetic patients were more likely to become hyperglycemic. 48% of diabetic patients became hyperglycemic, whereas only 12% of non-diabetic patients became hyperglycemic. But whether you were diabetic or not diabetic, hyperglycemia doubled the risk of surgical site infections.

Now these similar data are available from other investigators. And these data come from Portland, Oregon, where Zur and colleagues, again, in a similar manner, correlated highest glucose in the first two days after operation with infection risk. And you can see that even a glucose above 150 appeared to be associated with increased risk, and certainly the higher the glucose the higher the surgical site infection risk. Now their cardiac surgical group there, led by Tony Furnari, recorded the rate of infection in their diabetic patients. And we see here in the upper line the infection rate for diabetic patients, compared to the lower line, with the infection rate for non-diabetic patients. And between 1987 and 1991 Furnari and his group worked very hard to control glucose in diabetic patients using subcutaneous insulin. And you can see that they didn't have a lot of luck.

In 1991 they began using continuous insulin infusion, abbreviated as CII here, and with aggressive use of this, they brought the diabetic infection rate down so that within four years it was equal to the non-diabetics, and in one year, even lower than what they saw in their diabetic patients. They also showed in a similar manner, a reduction in the mortality rate for their diabetic patients as they got better and better control of glucose. And Tony Furnari has suggested that what he thinks is important is what he calls "3BG." That is the average of every blood glucose measured, almost every one to two hours over the first two days following operations. And what he had shown is that, with the use of an aggressive continuous insulin infusion rate, they were able to bring the average 3BG level down to a level under 150, although you can see that for individual patients there's quite a spread. Each of these pink dots indicates the 3BG on a single patient.

In this study, Swen [ph] and colleagues looked at glucose levels and infection in cabbage patients, and what we see here is in the green bars no infection, any infection, or mediastinitis. And the level of these

bars shows the average glucose level on the day of operation, the second day, and the third day. And you can see in each case the patients with the most severe infections had higher blood glucose levels.

So now SCIP only mandates glucose control for cardiac surgery. Does that mean that glucose control is only important for cardiac surgical patients? To me that doesn't make any sense. It seems to me that the host impairment that is caused by high blood sugars, and particularly, probably one of the most important things is that white cells have difficulty ingesting and killing bacteria in the presence of high blood glucose. I can't believe that a white cell knows whether it's an mediastinotomy wound or a laparotomy wound or another type of surgical incision. And so it doesn't make sense to me that this would only apply to cardiac surgery.

Well here are data from vascular surgery done in the Netherlands, and you see that there is a very similar relationship of increasing blood glucose levels and increasing infection rates. Here is a study that comes from Brigham and Women's Hospital using data from their NSQIP database. And they looked at any postoperative infection, including pneumonia, surgical site infection, urinary tract infections, or sepsis. And they looked at postoperative glucose levels, age, race, diabetes, ASA score, whether the operation was emergent, how long it took. They did a multivariable analysis and showed that any postoperative glucose above 180 had a doubled risk of postoperative infection. And for every glucose increase of 40 the odds ratio increased by 90%.

This graph shows the rate of observed infection correlated with postoperative glucose levels. Vueler Compt [ph] in Mexico looked at 260 patients having mastectomy and showed that any glucose above 150 in the recovery room, operating room, or the first 24 hours, had an increased risk of infection almost three-fold higher than patients who did not show hyperglycemia. Ota [ph], looking at GI surgery in the United States, again showed similar results, with increasing glucose levels associated with increased infection rates.

Frisch, looking at postoperative glucose and morality in non-cardiac surgery, showed that hyperglycemia in non-diabetic patients was actually more dangerous and caused a higher rate of increased mortality than hyperglycemia in diabetics. We can speculate about why this might be, but perhaps diabetic bodies are more used to experiencing hyperglycemia.

Umperez [ph] and colleagues at Emery looked at two different methods of trying to control glucose in surgical patients. They compared basil-bolus with sliding scale insulin administration. In basal-bolus patients, the patients got half of their daily dose as a glargine long-acting injection, and then every six hours they got additional sliding-scale insulin as need; whereas the sliding-scale group got sliding scale only. You can see that the mean daily glucose was almost 20 points lower in the basal-bolus group, and there were fewer readings above 140, and this resulted in an infection rate that was three times lower in the patients with a management strategy that gave them a lower average blood glucose level.

Kowe [ph], reporting in 2011 on diabetics having gastrectomy for cancer, again, targeted their patients to get either 80 to 110 or 180 to 200 and found a significant reduction in wound infections and intra-abdominal infections, and any post operative complication in the group of patients with more aggressive glucose control. And the Umperez study and this study by Kowe were both prospective randomized studies. Kowe shows here in the improved rate of glucose control and insulin resistance in the patients getting more aggressive treatment and shows the different levels of glucose control that they were able to achieve in the first few postoperative days.

Nurovic [ph], in patients having total knee or hip arthroplasty, looked at almost 2,000 patients with 100 infections, and looked at body mass index, operative duration, knee versus hip operations, and comorbidity score, and with a multivariable analysis again showed increasing infection rates with increasing blood glucose levels after controlling for all of the other risk factors noted previously.

They showed that on postoperative day one there was -- so the last slide I showed you was any fasting blood glucose on any day. This show it is results on the first postoperative day. So one of the things about glucose is that it seems the influence infection rate even beyond the day of operation, either for as long as two days post-op.

Perna [ph] looked at hemoglobin A1C versus glucose as a risk factor for surgical site infection in patients have gastric bypass. And they looked at patients with A1C levels below 6.5, between 6.5 to 7.9, or 8 and above. What they found was that the hemoglobin A1C was not a significant predictor of infection rate if you controlled for glucose levels. Any glucose level increase by 20 milligrams percent resulted in a 27% increase in the rate of surgical site infections. And the mean glucose level was more significant than any level above 200 or hemoglobin A1C.

In the State of Washington we have a collaborative called “SCOAP,” or “Surgical Care Outcome Assessment Program,” which records data on perioperative measurements, including blood glucose, and on the experience of postoperative infection, as well as other complications. What we did is look at over 11,000 patients having either a bariatric operation or a colectomy, and we looked at those who had a high blood sugar above 180, that was 3,300 patients, compared to those who did not, 8,200 patients, either on the day of operation or on post-op day one or two.

One of the things we noticed was that 30% of all the patients with a blood glucose above 180 were not diabetic; although it was more likely to happen in diabetic patients. We also looked at whether insulin was used. What we showed was that for all patients any blood glucose above 180 was associated with an increased infection rate, and this was true both for bariatric patients and for colectomy patients. And you would expect, there were higher rates of infections in colon patients than in bariatric patients.

When we looked at diabetic patients we see the same type of increased risk, with increased blood glucose. But if you look at this and then you look at non-diabetic patients, the difference between patients who were hyperglycemic and not hyperglycemic, the differences are actually greater. Here are the non-diabetic patients. Here are the diabetic patients. So, again, we showed in our State of Washington data that the side effects of high blood sugar or the increased risk of infection seems to be more significant in non-diabetic patients. And we’re used to thinking about controlling blood glucose in diabetic patients, but what I’m here to tell you is that we need to worry about this in non-diabetic patients as well. And 30% of all the high blood sugar in our Washington data occurred in non-diabetic patients.

Now if you look at patients, only patients who had blood glucose above 180, we see, looking at an odds ratio here, that patients not being treated with insulin had a 50% increased risk of infection with a blood sugar above 180. But if those patients were being treated with insulin, as we see here, the odds ratio actually went down, so there was not an increased risk of infection. So this shows us that attempting to control blood glucose with insulin is valuable, even if we don’t get the glucose as well controlled as we would like. And this was true here for operative re-intervention as well, where treating with insulin was beneficial even if we didn’t keep the blood sugar as low as we would have liked. And the same type of

result was seen for mortality risk after colectomy and bariatric surgery, where treating hyperglycemia with insulin was beneficial in reducing the mortality.

Now why is hyperglycemia so important for these patients? We know that the non-enzymatic glycosylation of proteins partially inactivates some of our antibodies, particularly the IGG. It decreases complement activation. It increases collagenase activity, which impairs wound healing, and it impairs leukocyte function by delaying chemotaxis, impairing phagocytosis, and decreasing the ability of the white cells to kill the bacteria that they have ingested.

We also know from data in the endocrinology literature that hyperglycemia impairs ischemic preconditions for the myocardium, reduces collateral blood flow, may help induce myocyte death, and seems to have other effects on blood pressure, cardiac rhythms, and platelet abnormalities, an explanation for why better control of blood glucose appears to be beneficial, even in reducing mortality rate in cardiac surgery, as illustrated by Tony Furnari, and in patients having colectomy and bariatric surgery, as illustrated from the State of Washington data.

There is also information from the American Association of Clinical Endocrinologists that insulin administration appears to inhibit lipolysis and elevated free fatty acids, which are associated with poor outcomes, including cardiac arrhythmias. Insulin inhibits inflammatory growth factors, and stimulates endothelial nitric oxide synthase, as well as inhibiting proinflammatory cytokines, adhesion molecule, and chemokines, all of which are beneficial to our patients.

So glucose control has proven importance for risk of surgical site infections in cardiac surgery, in general surgery, in colorectal surgery, in vascular surgery, in breast surgery, in hepatobiliary surgery, in orthopedic surgery, and in trauma surgery. There are good observational studies in all of these areas. Regardless of the diagnosis of diabetes or not, hyperglycemia increases morbidity, mortality, and length of stay for our patients.

Levetan, examining the management of unrecognized diabetes in hospitalized patients, looked at over a thousand consecutive inpatients and found that a third of all surgical patients with a glucose above 200 did not have a prior history of diabetes, and that over a third of medical patients with glucose above 200 did not have a prior history of diabetes, and that these patients had a mean peak glucose of 299, many of them with more two determinations above 200. So there's a lot of unrecognized diabetes that is not getting aggressive treatment in our hospitals.

The last thing I want to demonstrate here is an abstract that I actually found on the Web only last week. This comes from an abstract that is published on the Web before the paper, Kieran and colleagues at the Cleveland Clinic are going to be presenting at the American Surgical Association this April there experience in following glucose in non-diabetic patients have colectomy. They found that one-third of the patients never had a glucose above 125, which means that two-thirds of their patients did have glucose levels above 125, and, in fact, 14%, or one in seven patients, had blood glucose levels above 200 milligrams percent. And when they looked at surgical site infections, sepsis, reoperation, and mortality, all of these were statistically significantly increased with increasing levels of blood glucose, which you see graphed here.

So we have mortality, sepsis, surgical site infections, and reoperations, and every one of these increases with increasing postoperative blood glucose at any time during the hospitalization following a colectomy;

further evidence that we need to be checking the glucose on our non-diabetic patients and controlling it for them just as we do for our diabetic patients.

Now the exact best level of glucose control in the perioperative period has not been well established. What we can say from the data I have reviewed is that high glucose levels unequivocally increase the risk of surgical site infection and other perioperative infections. But tight glucose control in the perioperative period is tricky, and hypoglycemia definitely increases the risk of morbidity and mortality. That means that for a successful glucose control program you have to have carefully worked out plans and algorithms for how this will be managed. And there are a number of programs available on the Web, which I will show in a minute.

But sometimes people object to the use of an insulin drip on patient with elevated blood glucose. They say, “Oh, patients are adequately controlled with subcutaneous and sliding scale.” But the papers I have shown you so far this is not the case. Or they worry that patients will become hypoglycemic. And what I can tell you is that the careful attention to properly constructed algorithms can achieve reduction in high blood sugars without achieving hypoglycemia. And we have data from my own medical center, collected by our anesthesia team, showing that if blood glucose is regularly checked in the operating room, and if the algorithms are carefully followed, hypoglycemia does not occur, and hyperglycemia can be largely avoided. Tony Furnari has similar data for the cardiac surgery group in Portland, Oregon.

A complaint is sometimes made that it takes too much nursing time to check blood glucose levels. There’s no question that it takes nursing time to check blood glucose levels. There’s also no question that doing that and controlling blood glucose reduces infection, reduces hospital length of stay, reduces readmission, and will benefit the patients in the hospital in the end. Some people say you can do it in an ICU but not on the floor. I can tell you we’ve been doing it on our surgery wards at the University of Washington Medical Center for the last 15 years, and we’ve been doing it successfully. In fact, episodes of hypoglycemia in my hospital are more common in patients getting subcutaneous insulin than intravenous insulin, because once you give subqu insulin you cannot take it back, whereas if the blood sugar starts to go down with an IV drip, you just turn it off.

You do not need an endocrine consult for every patient getting an insulin infusion but you do need endocrine input, nursing input, pharmacy input, anesthesia input, and surgery input for developing the protocols and the algorithms that you will use in your hospital. People argue non-diabetics don’t need this. I hope I have convinced you that that is clearly not the case.

The American College of Endocrinology had a consensus development conference and pointed out that the use of standard protocols developed by multidisciplinary teams can be associated with improved glycemic control and lower rates of hypoglycemia, but you need to have specific guidelines on how to manage these patients. On this slide we see websites which take you to the protocol that was used in the Umperez [ph] trial for basal bolus insulin in surgical patients, and there are full details of how that was done there. And at the bottom we have the Society of Hospital Medicine Glycemic Control Resource Room, which contains links to multiple different insulin infusion protocols present at the website given there below.

Here I have indicated the actual rabbit two protocols for basal bolus insulin, which is available on that website. And here, this goes for a number of different pages, and I’ll go through this quickly, because you can get it, if you want, on the website. And then here we have the algorithms and the preprinted order

form, which is used at the University of Washington, telling who should get an IV insulin infusion protocol. And as I said, this can be used both in our intensive care unit and in our surgery and medicine wards, and this also is available online.

And here we have the protocol for blood glucose monitoring, which is done every hour until blood sugars are in goal range for four hours, and then it can be decreased to every two hours. And we have the instructions for notifying the provider in case glucose levels are going out of range. And then we see a decision tree, looking at which algorithm to use, and we have actually a total of eight algorithms, and you move up or down on the different algorithms depending on how well the blood sugar is being controlled. And we see here our algorithms one, two, three, and four. We start naïve patients on algorithm one, but we move up the tree as we find that we are not getting adequate blood sugar control. And, in fact, we end up with having eight algorithms. But the high-dose infusion algorithms is only used after documented failure to achieve glucose control on one of the lowest four, and we see here the full range of algorithms.

I know at the rate I've gone through them here you won't be able to easily take this information down, but on the other hand, this type of information is available on the websites that I gave you. And if you want to institute something like this in your medical center, again, you're going to want to have a collaborative team involving endocrinology, anesthesiology, pharmacy, surgery, and nursing to work together and put together something that will be effective in your medical center.

So with that, I'll stop and thank you for your attention and hope that you're all seeing better blood sugar control in all of the surgical patients in your hospital in the coming years. Thank you again for your attention.