Hyperglycemia in liver transplantation: A frequent event or risk factor?

La hiperglucemia en el trasplante hepático. ¿Un evento frecuente o un factor de riesgo?

Hyperglycemia in hospitalized patients has frequently been associated with a higher risk for infections, longer hospital stay, and greater mortality.\(^1\)\(^2\) It is a frequent phenomenon in posttransplantation patients, and most likely is related to the exogenous and endogenous production of catecholamines due to surgery, immunosuppression, and in some cases, diabetes mellitus.\(^3\) Even though there are studies on patients with kidney transplant and with liver transplant (LT) showing that those presenting with perioperative and postoperative hyperglycemia\(^4\) -\(^5\) have a greater incidence of acute rejection and related complications, other groups have shown no benefit from carrying out a strict control of glycemia in the perioperative period of LT patients.\(^6\)

The study by Builes-Montaño et al.\(^7\) evaluates whether hyperglycemia during the first 48 h after LT is associated with a greater risk for infection, rejection, or longer hospital stay. It is a retrospective study that defines hyperglycemia as a value above 140 mg/dL and is measured in 3 different manners (as an isolated value, as a mean value, and as a time-weighted value). The authors concluded that hyperglycemia is a very frequent event in LT; 94% of the patients presented with some form of hyperglycemia during the first 48 post-transplantation hours and there was no greater risk for rejection, infection, or longer hospital stay. Unfortunately, the study has certain limitations due to its retrospective design. Of the 316 patients that underwent liver transplantation, more than half of them (152 patients) were excluded because of incomplete results or due to death within the first 48 h. This is striking, given that in the first 2 post-transplantation days, a glucose test is one of the most important studies for monitoring allograft function and detecting a delay or primary failure of the allograft when there is hypoglycemia.

Even with 3 different definitions of hyperglycemia, no significant difference was found in relation to complications. It is also worth mentioning that both this study’s definition of hyperglycemia (>140 mg/dL) and the mean glycemia of posttransplantation patients at the time of admission to the intensive care unit (ICU) of 182 ± 55 mg/dL, are figures that are below what other groups have regarded as hyperglycemia (> 200 mg/dl). Park et al. conducted the largest study on glycemic control in patients that underwent LT. They evaluated 680 patients and in the multivariate analysis found that hyperglycemia > 200 mg/dL was a risk factor for postoperative surgical site infections, although they focused exclusively on intraoperative hyperglycemia.\(^8\) Wallia et al. also demonstrated that a glycemia value > 200 mg/dL was a risk factor for acute rejection.\(^5\) It is possible that the value of 140 mg/dL as hyperglycemia used by Builes-Montaño et al. was low for detecting differences in relation to posttransplantation complications.

It is important to mention that when the authors compared the diabetic and nondiabetic patients, looking for differences, they found none, and the diabetic patients showed no greater risk for infection or differences in length of hospital stay.\(^7\) Doubtlessly, the diabetic patients that were able to undergo LT after having gone through the evaluation protocol, did not present with the chronic complications characteristic of diabetes mellitus, and thus the populations were quite comparable.

The information presented here is valuable. Nevertheless, due to the limitations inherent in a retrospective and observational study such as this, it is difficult to confirm that hyperglycemia does not represent a risk for a greater number of complications, as has been demonstrated in other types of populations, such as patients that present with cerebrovascular accident, acute myocardial infarction, or cardiac surgery.\(^9\)\(^10\) One would think that a prospective and randomized study in which glycemia is strictly controlled in...
one group of patients and not controlled in another would be a logical design, but results of such studies have also been ambiguous. In some reports on patients that underwent kidney transplantation and critically ill patients in the ICU, the risk for hypoglycemia appeared to be greater than the benefits of glycemic control, whereas in other reports specifically on LT, intensive insulin protocol use was shown to be safe and effective, but no advantages were found in relation to complications in patients with strict glucose monitoring.

Therefore, we can say that hyperglycemia is a frequent phenomenon in post-LT patients that apparently does not increase the risk for complications; most likely these present as a consequence of other factors, such as characteristics of the donor, surgical aspects, the perioperative management of anesthesia, the use of immunosuppressant drugs, and the degree of severity of the LT patient’s health status.

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References

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