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Controversy between Obesity and Complications in Thromboembolic Disease, Series of Cases of Fuenlabrada University Hospital in Tinzaparine Treatment

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Abstract

Thromboembolic disease is the second leading cause of death in cancer patients (mostly, in the first year from diagnosis). The needing for anticoagulation with low molecular weight heparin (LMWH) in patients who are at high risk for complications (risk of bleeding in digestive tumors, brain tumors ...) require us to be more aware of their evolution. In addition, presenting venous thromboembolic disease (VTE) is usually an exclusion criterion in clinical trials so we do not know what happens with the combination of new drugs. Our objective is to study in a sample of 31 patients diagnosed with VTE, whether incidence of complications such as re-thrombosis or bleeding is higher in patients treated with tinzaparin (LMWH) depending on BMI.

Keywords: Obesity; Disease; Bioavailability

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Introduction and Objectives

Introduction

Venous thromboembolic disease (VTE) is present in up to 20% of oncology patients, presenting a lower recurrence in patients treated with low molecular weight heparin (LMWH) than with antivitamin K drugs (10-17% *vs.* 6-9%).

LMWH has a bioavailability close to 100% after subcutaneous administration. Compared with unfractionated heparins, they have fewer interactions. However, they offer doubts about the doses when the pharmacokinetic parameters are altered (as in the elderly, renal failure and obese) since the data in the literature are very scarce because they are excluded from the majority of clinical trials. It may be useful in these cases to monitor AntiXa activity [1,2].

Objectives

To describe the incidence of complications and recurrences in patients with extreme weights within a cohort of 31 patients treated with tinzaparin.

Material and Methods

31 patients were treated with therapeutic doses of tinzaparin (LMWH) after diagnosis of pulmonary thromboembolism (PE), catheter thrombosis and/or deep venous thrombosis (DVT). We analyzed complications and re-thrombosis according to the body mass index (BMI), dividing it into 3 groups (BMI 20-25, 25-30 and >30).

Results

Among 31 patients, 6 (19.4%) had BMI 20-25, 12 (38.7%) BMI 25-30, 8 (25.8%) BMI> 30 and 5 (16.1%) values lost.

Analyzing the distribution by frequency order from major to minor and type of primary tumor was lung, breast, colon, ovary and head and neck. According to tumor stage, more than 80% presented metastatic disease. Regarding to the histology, more than a half (16/31) were adenocarcinomas. As for the relationship with overweight, of the 8 patients with BMI>30, 4 were lung tumors (out of 9 total lung). Among the complications associated with obesity, there is a belief of a highest rate of rebleeding, so the controversy arises when adjusting doses (it is believed that the dose should not be increased more than 80 kg). In our case we described 2 severe bleedings (1 cerebral hemorrhage and 1 digestive bleeding both in colon tumors), in a patient with BMI 25-30 and the

other unknown BMI. They did not present thrombopenia or anemia secondary to treatment, but occurred within several cardiovascular risk factors. No patient underwent surgery in the previous or subsequent months, so they did not undergo surgical prophylaxis for VTE.

As for the rethrombosis (which is another complication that is thought to occur more frequently in obese patients), of the 4 cases (12.9%) that we described, 2 had BMI 25-30, 1 BMI 20-25 and 1 BMI>30. Therefore, we discovered that the incidence of rethrombosis in our patients is not higher in the obese group. The one obese patient was diagnosed of an adenocarcinoma in stage IV, also pneumonia (already per se with high thrombotic risk) and mutation in heterozygosis of prothrombin gene. As side effects, there was no anemia/thrombopenia secondary to treatment with tinzaparin.

We could not analyze what happened in "thin population "since we did not have any patients with BMI<20.

Discussion

Before considering the treatment of choice for obese patient, we would have to consider another risk factors (metastatic disease, recent tumor diagnosis), because in our patients ETV risk is not higher in this subpopulation.

Obesity per se is not a risk factor. In Rodger's study, risk factors for re-thrombosis were analyzed, with 52% of patients having 0 or 1 of the following: hyperpigmentation, edema, D dimer> 250 µg/L, BMI> 30 kg/m^2, Age> 65 years. Taking 0-1 factors the risk of annual rethrombosis was 1.6%, while those who had ≥ 2 points, amounted up to 14.1%. Therefore, even if they have 0 or 1 factors such as obesity, it is even safe to discontinue treatment. However, recurrence does increase when they present post-thrombotic signs [3].

We have other studies such as RIETE and ESSENCE (dalteparin and enoxaparin), which subdivided patients according to weight in >100 kg, 50-100 kg and <50 kg, showing no difference in complications in the extreme groups [4,5].

Regarding to safety, CATCH study demonstrates no more complications of tinzaparin (LMWH) compared to warfarin in oncologic patients [6].

Conclusion

Rate of rebleeding after treatment with tinzaparin is not higher in obese patients, occurring in our population when presenting also several cardiovascular risk factors.

-Rethrombosis is not higher in patients with BMI >30 than in other subgroups, being in this case in a patient with other factors of rethrombosis such as mutation of the prothrombin gene and a metastatic neoplastic disease with high risk of rethrombosis itself.

If it is true that we do not have many patients to conclude, but we offer a significant trend towards that presenting a single risk factor such as obesity does not predispose to have more thromboembolic complications.

Despite advances in the knowledge of the optimal management of anticoagulation, several areas of controversy persist. New studies like ours are needed to reflect the daily clinical practice and complications of patients outside clinical trials.

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