Maximising effects and minimising complications of selective internal radiation therapy

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1. Introduction

All procedures in medicine require a rigorous evidence base to inform clinical decisions and thereby maximise effectiveness and minimise complications. Even when every precaution has been taken to reduce complications, due diligence is required to recognise unexpected events as early as possible. At the same time, a thorough understanding of the mechanism of action of a procedure will help to maximise the therapeutic benefits. In the following paragraphs, some of the most important technical aspects of selective internal radiation therapy (SIRT) are discussed.

2. Selectivity

Selectivity in the treatment of the tumour(s) is determined by the microcatheter positioning in the artery/arteries. This can be complicated by the heterogeneous pattern of vessels and occasionally a substantial part of a tumour cannot be accessed because the afferent vessel has not been detected. In these cases, tumour progression after an endovascular treatment should not be considered “recurrence” but rather “treatment failure”. The aim of the procedure is to provoke the necrosis of the tumour. Riaz and colleagues (2009) observed that it may take up to 6 months to achieve a complete response (100% necrosis in 68% of cases at 6 months) and that complete responses are more common in small tumours (100% necrosis in tumours <3 cm in 89% of cases). Another publication from the same group has recently presented results on a novel approach, namely radiation segmentectomy, which was associated with an improvement in both the safety and efficacy of SIRT in hepatocellular carcinoma. During this procedure, SIRT was applied as selectively as possible to relatively small tumours (median tumoral volume 110 cc) resulting in a response in 81% of 84 cases according to European Association for the Study of the Liver (EASL) necrosis criteria. Median time to progression in this case series was 13.6 months (95% confidence interval, 9.3–18.7 months) and median survival was 26.9 months (95% confidence interval, 20.5–30.2 months).
3. Histologic response

As mentioned previously, the intra-tumoral effect of SIRT evolves over time. SIRT provokes areas of confluent necrosis and hemorrhage leading to fibrosis and regenerative activity at tumour peripheries. The significant tumour necrosis associated with SIRT may not be accompanied initially by a corresponding decrease in size. This is most probably the reason why the EASL necrosis criteria can detect tumoral responses at an earlier time and in more cases than other methods based on volumetric measurements. Some preliminary reports have shown that there is no vascular endothelial damage to the major vessel walls.

Depending on the size of the microspheres and the caliber of the arteries at the portal space, most microspheres are confined within the portal space and very seldom enter the sinusoids. Previous experimental studies have demonstrated, however, that the microspheres (not loaded with yttrium-90 [90Y]) may enter the sinusoids and even may be very close to the central veins of the lobule. This area, and the surrounding sinusoids, can be very sensitive to radiation, and when irradiated, is associated with intimal vein fibrosis, thrombosis and sinusoidal congestion (a kind of veno-occlusive disease), which generates a specific syndrome (4 to 8 weeks after radiation) manifested as jaundice and ascites. This syndrome, described by Sangro et al., is called RadioEmbolization Induced Liver Disease (REILD) and occurs in 4–10% of cases.

Since most of the microspheres remain lodged within the portal space, radiation may provoke a kind of portal triaditis to the healthy, non-tumoral liver. With the passage of time, this portion of the liver becomes fibrotic and decreases in volume. With whole-liver treatment, liver fibrosis is associated with portal hypertension as evidenced by the presence of splenomegaly.

A very interesting finding, initially described by Sangro et al. (2009), has been carefully evaluated by Gaba et al. (2009). In their report, they demonstrate that the ipsilateral treated liver may decrease in size by as much as 52% and that the contralateral untreated liver may increase in size in as much as 40%. This volumetric change is similar to that obtained with direct portal vein embolisation.

4. Conclusions

In conclusion, SIRT has opened the door to new treatment options as part of the global therapeutic strategy for patients with liver tumours. SIRT should be tailored to the individual needs of the patient depending on their tumour burden, liver function and possible future treatment (including surgery), with consideration given to both the activity administered and also the volume of liver treated (both tumoral and non-tumoral).

Conflict of interest statement

The author has received honoraria from Sirtex Medical for giving lectures.

References


