検査成績、ウイルス学的効果に加え、治療後の肝発癌、肝線維化マーカーなどを検討した。

経口2剤による新規治療は、従来のIFN併用治療が困難な例（不適格、不耐容例）を多く含むため、高齢者や線維化進展例の割合が多い。国内臨床試験に登録し治療効果が判明している①群の年齢が中央値64歳（42-75歳）と、PEG-IFN/RBVの2剤併用やPIとの3剤併用例に比べて高齢であるが、製造販売後に導入した②群では中央値71歳（32-82歳）とさらに高齢者が対象となった。また、肝硬変症例の割合は、①群で14.6%であったが、②群では126例中54例（42.9%）とさらに上昇し、IFN難治と同時に肝発癌リスクの高い症例が対象とされている。

ASV/DCV併用療法におけるHCV RNA量の減少は治療早期から良好で、開始後24時間で2.84 log、1週間で4.25 logの減少を示した。治療効果判定が確定している①群におけるSVR率も89.6%と高い有効性を示した。

血液生化学的検査においても、治療開始後1週/終了時/1年後の経過において、ASV/DCV例のALT値は、開始時より41%/64%/69%の低下を示した。アルブミン濃度は、治療終了時/1年後/3年後に3%/7%/8%の上昇を、血小板数は1%/9%/8%の上昇をそれぞれ認めた。IFN併用群においてもSVR例においては同様の効果を示しているが、進行例の多いASV/DCV投与例において、同等以上の有効性が示された。

本研究では、肝線維化の評価をFIB-4 indexを指標として行った。治療開始時には高齢、肝硬変例が多い①群のFIB-4 indexが他群よりも高値であるが、治療終了時、1年後の変化率は他群より高い改善度を認めた。AFPも同様の傾向を示し、①群の治療開始時AFP値は他群よりも高めであるが、治療終了時、1年後の変化率は他群より高い低下を認めた。

抗HCV治療後の肝発癌に関しては、対象症例数や観察期間が異なり、各治療群の対等な比較は困難であるものの、ASV/DCV併用の①群において、2.3年（1.2-4.1年）の治療後経過観察の範囲内では肝癌発生例は認めていない。製造販売後の現在、さらに高齢、線維化進展例を含む症例数が増加するため、今後、DAA治療例からの肝発癌症例も増加することが予想されるが、現時点では、IFNベースの従来の治療例に比して治療後肝発癌症例が高率となる結果は認められない。

これまでにIFN治療によるSVR例では肝発癌が抑制されることが明らかにされてきたが、IFN自体の肝発癌に対する直接的抑制効果に関する臨床的検証は十分ではない。今回、IFNフリーの新規治療が導入され、SVR後の肝発癌率について興味が持たれるところであるが、少なくとも現時点まで、IFN使用例に比して肝癌発生が高率である成績は示されていない。ただし、今後、発癌高リスク例に対するIFNフリーDAA治療例が増加することが見込まれ、SVR後の肝発癌に関する十分な経過観察が重要である。

E. 結論

ASV/DCVのIFNフリーDAA経口2剤による新規治療は、従来からのIFNベース治療と比較して、高齢、線維化進展例の比率が高い症例が対象となっているが、ウイルス学的、生化学的には良好な反応を示し、線維化指標の低下も認めた。さらに、治療後の肝癌発生も現在までは低率であり、長期的にも有用な効果を認めた。

F. 健康危険情報

なし

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H. 知的財産権の出願・登録状況
(※予定を含む)
1. 特許取得
なし

2. 実用新案登録
なし

3. その他

Ⅳ．研究成果の刊行に関する一覧表

Ⅳ. 研究成果の刊行に関する一覧表

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