

Pathophysiology of itch

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Presentation

Education & Training

Hepatobiliary

Neurogastroenterology & Motility

Primary Care

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The speaker presented evidence that cholestatic itch is driven by bile salt accumulation within hepatocytes rather than in circulation, with autotaxin-produced lysophosphatidic acid as the probable main driver alongside synergistic factors including nerve growth factor.

KEY POINTS

- Two genetic experiments of nature demonstrate that bile salt accumulation within hepatocytes, not in circulation, causes itch: BSEP deficiency causes hepatocyte bile salt accumulation and severe itch, while NTCP deficiency causes higher circulating bile salts but no hepatocyte accumulation and no itch
- In a cohort of 55 cholestatic patients, autotaxin levels showed positive correlation with itch severity on visual analogue scale, and the speaker stated that LPA 24:4 (the autotaxin product containing arachidonic acid) correlated even better with itch intensity
- The speaker reported that intrahepatic bile salts trigger calcium release, activating the NFAT transcription factor which drives expression of autotaxin, IL-8, TNF-alpha, and IL-6, with IL-6 significantly differing between itchy and non-itchy patients
- A subgroup of itchy patients had normal LPA levels, indicating that LPA is not the sole factor; nerve growth factor was significantly elevated in itchy patients and synergizes with LPA signaling via receptor complex formation
- The speaker stated that cholestatic itch is multifactorial, involving autotaxin-LPA as the probable main driver plus synergistic contributions from nerve growth factor, serotonergic signaling, and the opioid-like ligand nociceptin

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