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Extended Abstract
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Pharma Conference 2018- How can we assess haemodynamic profile non-invasively? Evaluation of alterations in the cardiovascular system using examination with CNAP device in patients with cirrhosis- Aleksandra Bodys-Pełka- Medical University of Warsaw, Poland

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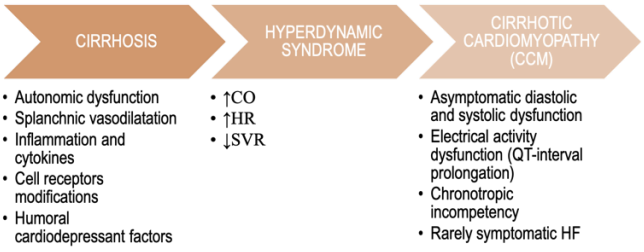
Abstract:

Cirrhotic cardiomyopathy (CCM) is a condition concerning heart muscle dysfunction in patients with cirrhosis. Cirrhosis leads to the development of a hyperdynamic syndrome, manifested by high cardiac output, increased heart rate and effective arterial blood volume, accompanied by reduced total systemic vascular resistance. Continuous Noninvasive Arterial Pressure(CNAP) device assess patient's haemodynamic profile in a non-invasive way. The results acquired from CNAP are highly accurate and precise compared to the invasive methods.
To screen patients with cirrhosis, which may lead to earlier diagnosing CCM and hyperdynamic syndrome.
The study included 70 patients over 18 years old, with cirrhosis, caused by alcohol ([ALD], 22), autoimmune (26), viral(9) other reasons(13), qualified for liver transplantation. We disqualified patients with a history of cardiovascular diseases. Each patient had a 6-minute walking test(6MWT) done and hemodynamic monitoring using CNAP device. Results Patients differ between etiologies of liver diseases. Median NTproBNP level was highest in ALD group (253pg/ml) and viral group (177,5 pg/ul) compared to autoimmune group(51 pg/ul) and other(114 pg/ml). Median QTc interval was more prolonged in patients with viral aetiology(456ms) and ALD aetiology(441ms) than autoimmune etiology(422ms) and other etiology(431ms). Highest median CO was observed in viral group(6L/min) and ALD group(5,7L/min). Median SVRI was lowest in viral group(1700 dyn- s/cm–5/m2) and ALD group(1888 dyn- s/cm–5/m2) and higher in autoimmune group(2067 dyn- s/cm–5/m2) and other group(2432 dyn- s/cm–5/m2). Haemodynamic parameters (CO, SV, SVRI) were not correlated with MELD score and Child Pugh score(p=NS). DBP was positively correlated with MELD score(r=-0,25; p=0,009) and Child-Pugh score(r=-0,31;p=0,003). Preliminary results show statistically significant correlations between distance in 6MWT and eGFR(r=0,78;p=0,0082), SVR (r=0,197;p=0,0011), DBP (r=0,45;p=0,014) and NT-proBNP (r=0,28;p=0,0008). Preliminary results show that we can detect subclinical alterations in patients' circulatory system by non-invasive methods. Patients with viral and ALD etiology presented more advanced liver cirrhosis stages and more pronounced manifestations of hyperdynamic syndrome which may progress to CCM. Positive correlation of liver cirrhosis stage and NTproBNP, QTc and 6MWT distance may suggest heart function impairment in course of liver disease.

Image



The incidence of cardiovascular diseases has increased significantly across the globe, in 2016 nearly 17.9 million died from cardiovascular diseases based on the estimates given by the World Health Organization. Hypertension, hyperlipidaemia, diabetes, or already established diseases are considered risk factors resulting in to cardiovascular diseases or increasing the chances of suffering from it. People facing these disorders require early detection, and they need to manage through counselling and medicines as per their condition. Attributing to all these factors, the demand

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for cardiovascular drugs is skyrocketed and the global market for cardiovascular drugs is witnessing high growth.

Regional concentration of cardiovascular diseases is high in North America. According to American Heart Association states, that between 2013 and 2016 nearly 121.5 million adults in America had some form of cardiovascular disease. Smoking, healthy diet, physical activity, body weight, blood pressure, control of cholesterol, and blood sugar are the major factor on which cardiovascular diseases are analysed. Smoking is one of the major cause leading to cardiovascular diseases and it is the leading preventable cause as well. Smoking is ranked fourth in instigating disability-adjusted life years (DALYs) as of 2016, and it took approximately 7.2 million lives in 2015. Thus with increasing number of smokers, chances of cardiovascular diseases is higher, which in turn increase the demand for cardiovascular drugs.

The scope of this report is broad and includes therapeutics used in the treatment of neurological disorders. The market analysis of neurology represents the largest and untapped market in medicine sector. This estimated market analysis is based on probability of approval and sales of products in late stage development, demographic trends and marketing of product. Emerging markets once again helps to boost revenues. CNS therapeutics covers approximately 15% of total pharmaceutical sales, almost $30 billion worldwide. The global market for neurology should grow from $33.3 billion in 2019 to $39.4 billion by 2024 at a compound annual growth rate (CAGR) of 3.5% for the period of 2019-2024. International neurology market consists of various therapeutics used for the treatment of different neurological disorders, the novel pipeline, patent expiry of blockbuster drug and new drug approval have affected the neurology market and it is estimated to grow during the forecast period. The biopharmaceutical companies are financing significantly in the development of innovative therapeutics for the treatment of neurological disorders. Government organizations are funding research & development related to neurology research. These factors are influencing the neurology market positively coupled with the growing prevalence of neurological disorders. The improved government funding in neurology research and an ever-growing demand for research centred on drug discovery for enhancement of novel therapies in neurological disorders are driving the growth of neurology market. The global market for psychotic disease is predicted to grow at a slow rate during the forecast period.

The slow progress is attributed primarily to the loss of patent exclusivity of branded drugs and the emergence of generic drugs. Manufacturers of branded drugs are expected to experience a decline in sales revenue due to the penetration of low-cost generic drugs in the market, which is likely to influence the growth of the market for antipsychotic drugs. New approaches for the treatment of neurology related indications were pursued by pharmaceutical companies. This new drug with a novel method of action or improved delivery system will present a powerful new option to currently prescribed neurology medicines. The global neurology market is growing due to a rise in the aging population, increased awareness regarding mental & neurological illness, increasing health insurance reforms and constant research & development in neurology by pharmaceutical companies. These factors along with technological advances such as 3D printed drugs, biomarkers, wearable technologies and mobile applications used to monitor and treat patients diagnosed with neurological disorders are expected to drive the neurology drugs industry. For market estimates, data is provided for 2018 as the base year, with forecasts for 2019 through 2024. Estimated values are based on drug manufacturers' total revenues. Projected and forecasted revenue values are in constant US dollars, unadjusted for inflation. European neurological disorders have been depicted in the below graph.

Ischemic stroke is caused by a dysfunction in the supply of blood to the brain due to emboli, thrombus or atherosclerosis occurring in cerebral arteries. According to a World Health Organization (WHO) estimate, around 17 million people die every year due to cardiovascular diseases. Heart attacks and strokes respectively account for the highest number of deaths

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due to cardiovascular diseases, globally. The statistics of the Centres for Disease Control and Prevention suggest that about 87% of all strokes are ischemic strokes. Stroke is one of the leading cause of long term disability, occurring at a higher rate in the old age population. Moreover, stroke leads to 1 out of every 20 deaths, costing around $35 billion to U.S. annually and higher rates of mortality associated with strokes highlight an impending need for innovative drugs and diagnostic devices.

Recent Publications (minimum 5)

1. Rimbas, R.C., et al., New Definition Criteria of Myocardial Dysfunction in Patients with Liver Cirrhosis: A Speckle Tracking and Tissue Doppler Imaging Study. Ultrasound Med Biol, 2018. 44(3): p. 562-574.
2. Naqvi, I.H., et al., The heart matters when the liver shatters! Cirrhotic cardiomyopathy: frequency, comparison, and correlation with severity of disease. Prz Gastroenterol, 2016. 11(4): p. 247-256.
3. Ruiz-del-Arbol, L. and R. Serradilla, Cirrhotic cardiomyopathy. World J Gastroenterol, 2015. 21(41): p. 11502-21.
4. Zardi, E.M., et al., Cirrhotic cardiomyopathy in the pre- and post-liver transplantation phase. J Cardiol, 2016. 67(2): p. 125-30.
5. Sharma, S., et al., Acute heart failure after Orthotopic liver transplantation: a case series from one center. BMC Anesthesiol, 2018. 18(1): p. 102.

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