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EFFECT OF OXYGEN SUPPLEMENTATION ON LOW LANDERS ON ASCENDING TO HIGH ALTITUDE WITH PRECORDIAL ECG CHANGES WITHOUT HIGH ALTITUDE ILLNESS

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ABSTRACT High altitude syndromes are illnesses attributed directly to hypobaric hypoxia. Hypobaric Hypoxic pressure changes in the right side of the heart with ECG changes in right precordial leads are seen in cases like High Altitude Pulmonary Edema (HAPE), Pulmonary Thormboembolism (PTE) and thrombotic cause in acute coronary syndrome (ACS). Cases of these mimics with T wave inversion in precordial chest leads are seen in low landers on ascending to into high altitude without any high altitude illness, ACS or PTE. These findings may reflect asymptomatic pressure changes in the heart and pulmonary vasculature due to hypobaric hypoxia of high altitude to the point where they are not manifested. High altitude environment is itself being a procoagulant state compounded with hypobaric hypoxia, if these changes are not addressed in time and not treated with oxygen supplementation, these individuals may present at a later stage with HAPE or SAMS. We hypothesized that oxygen supplementation can reverse these changes. Intervention study with oxygen supplementation @ 6L/min intermittently over 12 hr/day was given in all those individuals who have T wave inversion in precordial ECG meeting inclusion criteria over a week. The study was conducted at peripheral hospital 11000ft in Himalayan ranges over a period of 06 months. 100 % of cases had shown normalization of T waves in response to oxygen supplementation. However 02 individuals had recurrence of ECG changes and they were send back to plains. None of them developed high altitude illness over next 06 months of followup.

KEYWORDS : High altitude illness, oxygen supplementation, precordial T wave inversions

INTRODUCTION:

High Altitude (HA) is defined as elevations above sea level between 1500 m to 3500m, very high altitude as 3500-5000m and extreme high altitude over 5000m. Altitude acclimatization allows low landers to achieve maximum physical work performance possible for an altitude to which they are acclimatized [1]. Once acquired, acclimatization is maintained as long as the low -lander remains at high altitude, but is lost upon return to lower elevations. Partial pressure of oxygen decreases with increasing altitude. Acute Mountain Sickness (AMS) is milder form which subsides within 2-3 days. High altitude syndromes are illnesses attributed directly to hypobaric hypoxia. Despite advances in high altitude medicine, significant morbidity and mortality persists. Electrocardiogram (ECG) changes in diseases like High Altitude Pulmonary Edema (HAPE) and Sub Acute Mountain Sickness (SAMS) are evident mainly by T inversion in right precordial leads [2].

Electrocardiogram has come in a long way in the identification of acute coronary syndrome. In high altitude findings of acute myocardial infarction and acute pulmonary thromboembolism on ECG are no different from plains. These illnesses and ECG pathological changes are seen in some young individuals with no coronary risk factors in first few days of induction into high altitude [T inversion with anterior precordial leads]

ECG changes in low landers mimicking these ischaemic changes were seen in recently inducted individuals to high altitude area with no cardiac disease or any other evidence of HAPO,HACO, SAMS, acute coronary syndrome or pulmonary thromboembolism (PTE) at a peripheral hospital in himalayan high altitude ranges. Induction(ascend) into high altitude area is largely by AIR and they undergo scheduled acclimatization of 06 days which includes complete bed rest in the first two days and are monitored for vitals or any high altitude symptoms occurrence.

We hypothesised that precordial ECG changes may represent the pressure changes on the heart in hypobaric high altitude environment as these similar ECG changes are seen in a case of HAPE/SAMS individuals. They respond to hyperbaric oxygen chamber therapy or de-induction(descend) to lower attitude with continuous oxygen supplementation.

The aim of this study is to see the effect of oxygen supplementation in low landers with precordial electrocardiogram T wave changes without HAPO,SAMS,ACS,PTE on induction into high altitude area and to find out the time taken for reversal of T wave changes, monitoring of any development of high altitude illness during therapy.

CLINICAL MATERIAL AND METHODS:

Siting: The study is carried at a peripheral hospital located at 11000 ft in the Himalayan ranges.

Study Design: Prospective Interventional study.
Study Population: All individuals who were found to have T wave changes on electrocardiogram(ECG) on induction into high altitude during acclimatization and after completion of acclimatization period over 06 months period

INCLUSION CRITERIA:

(i) All low landers who have T wave abnormalities on electrocardiogram referred from acclimatization camp to our hospital during and/or on completion of acclimatization without any signs and symptoms of High Altitude Pulmonary Edema (HAPE), Pulmonary Thromboembolism (PTE), Coronary Syndrome and High Altitude Cerebral Edema (HACE)
(ii) Patients with Acute Mountain Sickness (AMS) and T wave abnormalities

EXCLUSION CRITERIA:

(i) Patients with primary diagnosis of acute coronary syndrome, acute pulmonary thromboembolism, high altitude cerebral edema, sub acute mountain sickness, high altitude pulmonary edema, primary cardiac condition, chronic obstructive pulmonary disease,

Intervention:

Oxygen supplementation by face mask @ 6l/min over 12 hr/day for 07 days or till reversion (normalisation)of T wave changes which ever is earlier

METHODOLOGY:

All individuals meeting inclusion criteria clinico-dermographic details were taken and admitted to the hospital. Those who complained of any symptom were included in Symptomatic group and rest as Asymptomatic group for analysis. All of them were administered oxygen supplementation by face mask @6 L/min over 12 hours in a day intermittently [Rate of Oxygen supplementation by face mask was pre-standardized before the study where initially @3 L/min were given and gradually increased to 6L/min depending on the rate of response of depth of T wave inversion to normalization in few cases of these ECG abnormalities without high altitude illness]. They were given complete

bed rest for the first 48 hours and allowed to mobilize within the ward from 3rd day of admission depending on the clinical condition They were monitored with daily ECG for reversal of T wave changes and clinically for any development of high altitude illness. Patients with Acute Mountain Sickness (AMS) if any were included in the study, as in the literature there were no reports of ECG changes in AMS. Investigations done like, complete haemogram, renal/liver function tests, electrolytes, Chest x-ray, CK-MB, D-Dimer, Troponin T. Serial. When available 2D ECHO was done. After complete reversal of ECG changes, oxygen supplementation was stopped for 72 hours and monitored for any recurrence/sustenance of ECG changes or development of high altitude illness. Protocols were reviewed by institutional review committee and informed consent obtained.

RESULTS:

A total of 30 cases were studied. Out of them 26 were male and 04 were female. The most common age group among both groups is 3rd decade Most of the individuals are first time inductees (28/30) into high altitude of 11000 ft, all by AIR route and another two who developed dyspnoea on exertion on 4 the day of induction by road into an altitude of altitude at 14000 ft [Table 1].In this study only 08 (66% of asymptomatic group) could complete scheduled acclimatisation at the acclimatization camp [8/30] [Table 2]

100% of them had reported to have diuresis within 24 hours of induction, which is a normal acclimatization mechanism for high altitude region.There is no difference in oxygen saturation measured by pulse oximetry between symptomatic and asymptomatic group, with Sp02 in the range of 90-95% in 100 % of cases at ambient air [Table 2].

In our study [Table 2&3] 22 patients were referred during acclimatization period, out of them, 81.8% were symptomatic and remaining were referred for findings of raised blood pressure without any symptoms [18.2%;4/22]. Majority of symptomatic patients [55.5%; 10/18] reported on last two days i.e. 5th/6th day of acclimatization. The most common symptom was dyspnoea on exertion (77.8%; 14/18). Acute Mountain Sickness is seen in only two female patients and remaining had fatigue as the only symptom [Table 3].

Among asymptomatic group, four of them (4/8) were referred for hypertension. 86.67%(26 /30) individuals in the study group had normal blood pressure and remained normotensive throughout the hospital stay. Pulse rate was above 90/min regular among all individuals [Table 2] and those who had tachycardia (12/30) there pulse rate came below 100/min with treatment. [not shown in table].

Table 1 Demographic Profile Of Patients With ECG Abnormality In High Altitude

Demographic profile	Symptomatic patients(n=18)	Asymptomatic patients(n=12)
Age group 20-30yr 31-40 yr 41-50 yr >51 yr	 02(11.1%) 12(66..6%) 02(11.1%) 02(11.1%)	 04(33.3%) 06(50%) 02(16.6%) 02(16.6%)
Altitude at which reported/detected ECG abnormality At 11000 ft At 14000 ft	 16(88.9%) 02(11.1%)	 12(100%) 0
First Induction into High altitude	18(100%)	10 (83.3%)
Re-induction into High altitude after initial asymptomatic induction	0	02*(16.6%) *There is recurrence of T wave abnormality after 03 days of stopping oxygen after initial normalization with oxygen therapy for a week
Sex Male Female	 14 (77.8%) 04(22.2%)	 12(100%) 0
Mode of induction when ECG abnormality detected By Air By Road	 16(88.9%) 02(11.1%)	 02(11.1%) 12(100%) 0

Table 2 Clinical Parameters Of Patients In The Study With ECG Abnormality

S.No	Clinical Parameters	Asymptomatic (n=12) No. of patients (%)	Symptomatic (n=18) No. of patients((%)
1.	Pulse >100/min <100/min	 04 (33.3%) 08 (66.6%)	 18 (100%) 0
2	Blood Pressure >140/90 mm of Hg <140/90 mm of Hg	 04 (33.3%) 08 (66.6%)	 0 18 (100%)
3	Respiratory rate >18/min <18/min	 0 12 (100%)	 0 18 (100%)
4	Initial diuresis(within 24 hours of induction)	12 (100%)	18 (100%)
5	Spo2 >96% 90-95%	 04 (33.3%) 12 (100%)	 0 18 (100%)
6	Acclimatization Completed Not completed	 08(66.6%) 04 (33.3%)	 0 18 (100%)

Table 3: Symptoms At Presentation Of ECG Abnormality

Symptoms	No. of cases during acclimatization period			No. of cases after acclimatization period	Total
	< 2days of ascent	3rd-5th of ascent	5th-6th of ascent	7th day of ascent	
Dyspnoea on exertion	4	0	10	0	14 (77.8%)
Acute Mountain Sickness	0	2	0	0	02 (11.1%)
Fatigue	0	0	02	0	02 (11.1%)
Total	4	2	12	0	18

As shown in Table 4, 46.6 % of cases were found to have symmetrical to asymmetrical T wave inversions in only V1-V3 (14/30), in all precordial leads 33.3% (10/30) (illustrative fig 2,2a,2b) and T wave inversion to flattening in the lateral precordial leads only (V5-V6) in 20% (6/30). There were more number of males inducted into a high altitude area on occupational purpose, however, it is seen that in females these abnormal T wave changes are also seen in whom very rare HAPE cases were reported.

Table4: ECG Abnormalities Seen In Precordial Leads

T inversion in leads	Male	Female
V1-V3	12	02
V1-V5	10	0
V5-V6	04	02

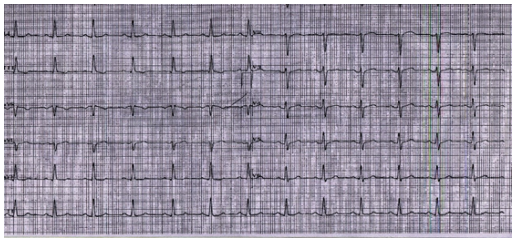

Fig :2

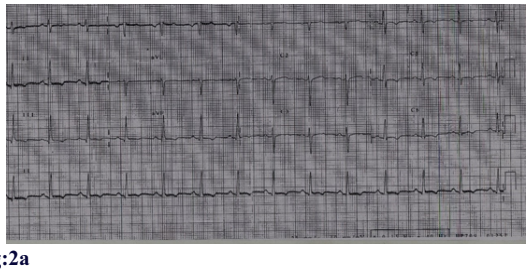

Fig:2a

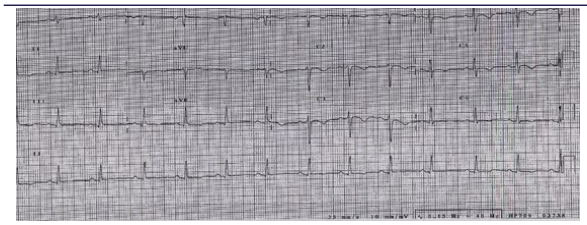

Fig 2b

Fig 2, 2a.2b., A case of 43 yr old, grossly obese individuals with detected hypertension during medical examination while on acclimatization on induction into the HAA, 11000 feet for the first time.. Symptomatic with dyspnoea. in high altitude. His CK-MB, troponin T were negative. He was started on a single drug antihypertensive along with oxygen supplementation. The ECG has done at 11000 ft had shown T inversion in V4 -V6. He was sent down to plains by air for cardiac evaluation where 2DECHO, TMT was normal. ECG abnormality normalised and blood pressure normalised on reaching plains, without anti hypertensives. He came back after a week stay at plains. On arrival at 11,000ft asymptomatic, normotensive and ECG showed recurrence of T wave abnormalities now in V1-V6. Clinically and biochemically, no evidence of high altitude illness. As he was asymptomatic and recent cardiac evaluation was normal, these changes were attributed to incipient changes of right heart strain on re-induction into high altitude, which may herald to high altitude illness, as the pathophysiology of right ventricular strain is attributed to HAPO, PTE and coronary event and high altitude is itself a procoagulant state, he was treated with oxygen supplementation over a period of a week with reversal of ECG changes (Fig not shown) and remained asymptomatic during his stay in high altitude.

All of them, 100% (30/30) responded to oxygen supplementation with reversal of T wave inversion in precordial leads with no progression to any high altitude illness in a week (illustrative fig 1,1a) with sustenance in 83 % of asymptomatic and 100% of symptomatic cases.In 02 asymptomatic individuals there was recurrence after 03 days of stopping oxygen supplementation with no development of high altitude illness and they were de-inducted to plains as it is the definitive management in this case. Days taken to complete reversal were 07 days of admission [Table 5]. Only in four pulmonary artery pressures were done by 2D ECHO and all four were found to have elevated pulmonary artery pressures and in one person with dilated right ventricle. All four had normalized pulmonary artery pressures after treatment with oxygen therapy[not shown in table]

Table 5: Effect Of Oxygen Supplementation On T Wave ECG Changes

S.No	Intervention with oxygen supplementation	Asymptomatic No. Responded	Symptomatic No. Responded
1	Time taken for normalization of ECG abnormality with oxygen therapy (a) A week therapy (b)More than week therapy	10(83.3%) 02* (*but before normalization descended to plains)	18 (100%) 0
2.	Response to oxygen therapy with normalisation of T wave inversion	10 (83.3%)	18 (100%)
3.	Development of High altitude illness during therapy and follow up for 06 months	0 (0%)	0 (0%)

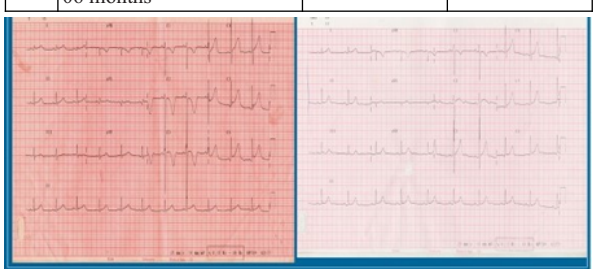

Fig 1(Fig 1 : T inversions in V1-V3 at presentation),1a(Fig 1a : Reversal of T inversions V1-V3 after oxygen supplementation of a week) :A case of 32 yr old male reported with complaints of dyspnea during the 4th day of induction (last day of 2nd stage of acclimatization) into high altitude at 14000 ft He was evacuated by air to 11000 ft where medical facilities are available. Clinically has no evidence of HAPO, HACO, PTE or acute coronary syndrome. His cardiac enzymes, troponin T, FDP were negative. ECHO s/o Pap 56 mm of Hg and RV dilatation. He was managed with complete bed rest continuous oxygen inhalation with a face mask to keep Sp02 95% with normalization of T waves, normal 2DECHO findings.

DISCUSSION

Compare the pathological ECG changes of myocardial ischaemia and pulmonary thromboembolism with that of non pathological ECG changes as in illustrative cases, Fig1 and Fig 2. Are these changes [as shown in illustrative cases] representing an incipient High Altitude Illness? We discuss can these ECG changes be a surrogate marker in a susceptible individuals to develop high altitude illness? and measures taken to revert these changes with an aim to prevent possible progression to high altitude illness.?

Life threatening high altitude illness includes high altitude pulmonary edema (HAPE) and high altitude cerebral edema (HACE). Over a period of months they can present as subacute mountain sickness (SAMS) Or over years as chronic mountain sickness (CMS). RV strain (T inversion in V1-V3) on ECG represent the effects of pressure overload on the right side of the heart due to changes in the pulmonary system. The basic cause is of hypobaric hypoxia, the cascade of events that follow the initial insult in a low lander ascending to high altitude, which are generally > 9000 ft results in metabolic and physiologic adaptation to new high altitude environment. The non-acclimatization of the individual leads to pathological state of high altitude illnesses [3].

In a case of HAPE the Echocardiography demonstrates high pulmonary artery pressures, tricuspid regurgitation, normal left ventricular function, and variable right-sided heart findings of increased atrial and ventricular size [4]. The electrocardiogram shows sinus tachycardia, and changes such as right axis deviation, right bundle branch block, voltage for right ventricular hypertrophy, and P wave abnormalities [2, 5, 6, 7,]. Also often T wave inversions in right sided precordial leads. Other findings which may be seen are qR pattern aVR, S waves in V5, V6 and P pulmonale. [8, 9]

Increase in pulmonary vascular resistance is the key factor in the progression of HAPE The pathological findings found on autopsy of persons who died of HAPE, had shown protein -rich, permeability-type edema, with thrombi or emboli [5, 8, 9]

Another condition where pathological ECG changes are seen is in Sub Acute Mountain Sickness, (SAMS) that was first described in Indian soldiers above 18,000 ft. SAMS occurs 8-12 weeks of stay in high altitude and presents with right heart failure. The ECG described in this condition includes right axis deviation, right ventricular hypertrophy and symmetrical 'T' wave inversions in right precordial leads. X-ray shows cardiomegaly with a prominent main pulmonary artery [10, 11]. The mainstay of treatment in all these high altitude illnesses includes oxygen supplementation by face mask around @ 8L/min for12-24 hrs and move to lower altitude with supportive and definitive treatment as deemed by the case.

The similar right precordial changes that were reported in HAPE and Adult Sub Acute Mountain Sickness with symptoms requiring immediate emergency management were seen in our study without these illnesses. And it is also known as these HA illnesses can present in an individual after a long stay at high altitude and especially when an occupational requirement demands frequent movements in different stages of high altitude

In our study all of them were either undergoing acclimatization or completed acclimatization as schedule protocol of our institution whoever comes to high altitude by air or road. Precordial T wave change were seen across all age groups in adults. Intermittent Oxygen supplementation @6L/min for 12 hr/day over a period of 7 days depending on the response of ECG T inversion reversal changes, was given in all cases and repeat ECG done after 72 hours of abstinence of oxygen supplementation had shown sustained reversal (normalization) of T wave inversion in precordial chest leads in all of them.

The number of males in the study are more, as they came to high altitude on occupational purpose. Two cases or re-ascend to high altitude, 11000 ft after 05 and 03 months of stay in high altitude area

respectively. They stayed at low land for 02 weeks and 06 weeks respectively. As shown in illustrative Fig 2, there were two cases where ECG precordial T wave abnormalities normalised on reaching plains and when re-ascended after a week stay at plains, ECG done again at high altitude showed recurrence of T wave inversions (They were included as 1st time inductee for analysis) They were then kept in hospital and treated with oxygen supplementation with good recovery. These individuals might be susceptible to high altitude illness if were the pulmonary artery pressures represented by T inversion in precordial leads are not addressed, which is evident by reversal of T inversion to upright T waves on treatment with oxygen supplementation and bed rest.

Are we impeding the acclimatization by giving oxygen supplementation during the acclimatization period? Is that development of right strain pattern seen on ECG is a reflection of increasing pulmonary artery pressure where in these individuals culminate in development of HAPE, Pulmonary Artery Hypertension or SAMS. Pulmonary hypertension is known to occur in individuals with HAPE, though the magnitude of pressures was different in different individuals. In our study due to limitation of 2D ECHO equipment only in four individuals 2DECHO was done and in both cases the pulmonary artery pressures were raised and in one showing right ventricular dilatation. All four of them had complaints of dyspnea at presentation, one young male developed at 14000 ft while undergoing acclimatization on induction by road. Due to non availability of 2DECHO machine and expertise, pulmonary artery pressure studies could not be done in others.

Pulmonary pressures can increase in hypobaric hypoxia leading to strain on right side of the heart

It can be fairly be deduced that the T inversion in right precordial leads represent raised pulmonary artery pressures, the pathophysiology of it in high altitude can be multifactorial ranging from sluggish coronary artery circulation due to raised haematocrit concentration to thrombogenic potential and back pressure changes in the lung leading to pulmonary edema.

Only two patients had Acute Mountain Sickness. In literature, there is no mention of T wave changes in AMS, however remaining individuals who were symptomatic with mild dyspnea on exertion with no cardiac or pulmonary abnormality cannot be termed to have acute mountain sickness as this symptom is commonly seen in individuals who couldn't adapt to high altitude in the initial days.. None of them had dyspnoea, angina pain, cough, headache, abdominal discomfort, fever or sleep disturbances. Initial diuresis was reported by all of them within 24 hrs of coming to high altitude, which occurred as a result of the body acclimatization response to hypobaric hypoxia in high altitude [12]. The consistent findings in these cases were that of symmetrical to non symmetrical T wave inversion in the precordial leads. In both groups haemtological,D-dimer , Chest x-ray and biochemical parameters were normal.

None of them devloped any high altitude illness and they were able to carry out their routine day to day activities. All but 04 individuals after treatment with oxygen therapy were deinducted to plains due to administrative reasons and remaining continued to stay in high altitude and followed up for 06 months with no development of high altitude illness.

Though the answer to whether are we impeding acclimatization by supplementing oxygen remains debatable till -case control study is done. We consider to be unethical not to treat when these pathophysiological mimic changes of ECGs are seen in the high altitude illness, pulmonary thromboembolism, coronary syndrome and high altitude is itself being a thrombogenic state which can be fatal. Case control study was not done and response to oxygen therapy has led us to believe that oxygen supplementation during acclimatization will not impede the acclimatization process. These patients are generally advised to undergo an extended acclimatization period after the hospital stay and were found to be asymptomatic throughout their stay in high altitude.

These findings reflect asymptomatic pressure changes in the heart and pulmonary vasculature due to hypobaric hypoxia of HA. If these changes are not addressed in time and not treated with oxygen supplementation, these individuals may present at a later stage with HAPE or Adult Sub Acute Mountain Sickness (SAMS).

They were timely addressed from us and reverted these ECG changes which herald impending high altitude illness, These incipient ECG changes in a healthy individual occurring in HA can be considered as a tool to recognize impending high altitude illness. We term this condition as Incipient high altitude illness (Incipient HAPE).

CONCLUSION

High and dry mountain regions of the himalayan ranges, pose a great challenge for people reaching high altitude on the profession. Hypobaric hypoxia is the corner stone in the pathogenesis of high altitude illness like AMS, HAPE and SAMS later. Rise in pulmonary pressures, sluggish blood circulation and the cascade of events that follow lead to life threatening high altitude disease. In these cases the electrocardiogram findings of T inversions in precordial chest leads were well explained in the literature, when a low lander is affected with high altitude illness over a variable period of stay at high altitude. In an asymptomatic new comer and re-entrants the similar changes seen may indicate their non acclimatization to hypobaric hypoxia pressure changes in the heart to the present acclimatization schedule of 06 days and can represent an incipient change heralding dangerous high altitude illness. These changes seen early in all these individuals, whether during acclimatization or after scheduled acclimatization and timely institution of treatment with oxygen will reverse these changes and can impede high altitude life threatening illness.

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